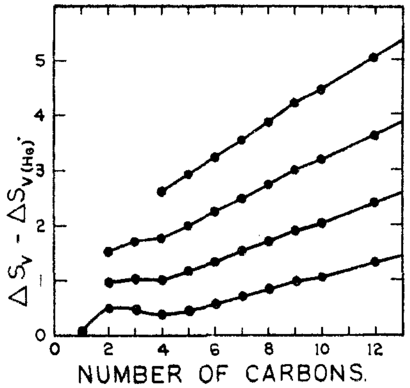

Fig. 3.

entropies are a linear function of the number of carbon atoms from 4 to 12 carbon atoms.

The increase in excess entropy of vaporization with increasing molal volume of vapor (which corresponds to decreasing temperature) is evidence for the freezing in of degrees of freedom in the liquid state as the molecules are crowded more closely together in the contracting liquid. Halford[7] suggested that hindered rotation could be the cause of such departures, but investigated this only for the case of log $(P/T) = 0.1$.

TABLE III

$(\Delta S_v - \Delta S_{v(Hg)})$ for normal hydrocarbons (Cal. Mole^{-1} Deg.$^{-1}$)

	$\log_{10}(P_{mm}/T)$			
	0.1	−0.4	−0.9	−1.4
Methane	0.06			
Ethane	.49	0.95	1.51	
Propane	.46	1.02	1.69	
Butane	.36	1.00	1.76	2.60
Pentane	.43 (0.6)	1.15	1.99	2.92
Hexane	.54 (1.4)	1.32	2.23	3.24
Heptane	.67 (1.4)	1.51	2.48	3.55
Octane	.81 (1.1)	1.69	2.73	3.87
Nonane	.95	1.90	3.00	4.22
Decane	1.04	2.03	3.18	4.45
Dodecane	1.31	2.40	3.66	5.04
$\Delta S_{v(Hg)}$	22.46	25.11	27.70	30.28

SYRACUSE, N. Y.

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[7] R. S. Halford, *J. Chem. Phys.*, **8**, 496 (1940).

NOTES

Preparation of Glycerol Evenly Labeled with C^{14} [1]

BY S. ABRAHAM

RECEIVED JUNE 20, 1952

Various methods for the preparation of glycerol singly labeled with C^{14} have already been reported.[2-4] Although certain of these procedures could be adapted to the preparation of this compound with all of its carbons uniformly labeled with C^{14}, I should like to report here an alternate method utilizing uniformly labeled glucose[5] as starting material.[6]

Evenly labeled glucose with a specific activity of 3×10^5 c.p.m. per mg.[7] was prepared photosynthetically.[5] It was converted in 84% yield to the methyl glucopyranoside with methanol and hydrochloric acid.[8] No attempt was made to isolate the isomers of methylglucopyranoside.

The methyl glucoside was treated with sodium periodate at 2° for 24 hours. The reaction was quantitative as determined by titration of the resulting formic acid. The solution was treated with barium chloride, and the resulting precipitate was filtered and washed. The filtrate was concentrated[9] under reduced pressure at a temperature below 60°.

The dialdehyde remaining in solution was then hydrogenated with Raney nickel at 2,700 p.s.i. and 140° for 18 hours. The dialdehyde in the filtered solution was hydrolyzed with H_2SO_4. Addition of 2,4-dinitrophenylhydrazine solution precipitated the glycolaldehyde as its hydrazone. Excess 2,4-dinitrophenolhydrazine was removed by the addition of formaldehyde.

The solution containing the radioactive glycerol was neutralized with solid $BaCO_3$. The filtrate was clarified with charcoal and concentrated *in vacuo*, at 40°, to a thick, viscous mass. Extraction with boiling, anhydrous acetone (C.P.) and final evaporation of the acetone at room temperature yielded the C^{14}-glycerol. The over-all yield based on glucose was 64%.[10] The refractive index of this glycerol was 1.4398 at 25°. This represents 77.6% glycerol in water.[11] The specific activity of the resulting glycerol was 3×10^5 c.p.m. per mg. $BaCO_3$.

Two-dimensional paper chromatography using phenol: water and butanol:acetic acid:water[12] revealed only one radioactive spot, and this spot was identical with the color spot obtained with inactive glycerol, using a solution of lead tetraacetate in benzene as the color spray.

Two similar experiments with inactive glucose yielded glycerol (65%) which was identified in the following manner: (a) by its refractive index, as given above, (b) by the preparation of the crystalline glycerol tribenzoate, and (c) two-dimensional paper chromatography.

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[1] Aided by a grant from the American Cancer Society as recommended by the Committee on Growth of the National Research Council.

[2] A. P. Doerschuk, THIS JOURNAL, **73**, 821 (1951).

[3] H. Schlenk and B. W. DeHaas, *ibid.*, **73**, 2921 (1951).

[4] M. L. Karnovsky and L. I. Gidez, *Federation Proc.*, **10**, 205 (1951).

[5] E. W. Putman, W. Z. Hassid, G. Krotkov and H. A. Barker, *J. Biol. Chem.*, **173**, 785 (1948).

[6] For complete details order Document 3658 from American Documentation Institute, 1719 N Street, N.W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

[7] All compounds were oxidized, and assayed as $BaCO_3$, with an end-window counter.

[8] E. Fischer, *Ber.*, **28**, 1145 (1895).

[9] The formic acid distilled assayed at 3×10^5 c.p.m. per mg.

[10] Corrected for 78% glycerol in water as judged by refractive index.

[11] "International Critical Tables," Vol. 7, McGraw-Hill Book Co., Inc., New York, N. Y., 1930, p. 68.

[12] S. M. Partridge, "Partition Chromatography," Vol. 3, Biochemical Society Symposia, Cambridge, 1950, p. 52.

Glycerol tribenzoate was prepared and recrystallized from ethanol, m.p. 74–75° (lit. 75°). A mixed melting point with the tribenzoate prepared from C.P. glycerol was not depressed.

A small aliquot of the C^{14}-glycerol was dissolved in absolute ethanol, and inactive glycerol was added. The ethyl alcohol was removed *in vacuo* at room temperature, and the resulting diluted C^{14}-glycerol was degraded according to the procedure outlined elsewhere.[13] The C^{14} content of each of its carbons was determined; this confirmed that the synthesized glycerol was evenly labeled with C^{14}. The results are recorded in Table I.

TABLE I

C^{14}-GLYCEROL PREPARED FROM 24-HOUR PHOTOSYNTHETIC C^{14}-GLUCOSE

Compound	Reaction	Glycerol carbons converted to CO_2	Specific activity expressed as $BaCO_3$, c.p.m. per mg.
Glycerol	Periodate oxidation[a]	C-1 + 3	18.6
Glycerol	Lead tetraacetate oxidation	C-2	18.4
Glycerol	Combustion	C-1 + 2 + 3	18.5

[a] The HCHO formed was oxidized to CO_2 with $KMnO_4$.

Acknowledgment.—The author wishes to thank Dr. I. L. Chaikoff of the Division of Physiology of the School of Medicine, and Dr. W. G. Dauben of the Department of Chemistry, University of California, for their many helpful suggestions in this work.

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(13) D. Kritchevsky and S. Abraham, *Arch. Biochem. Biophys.*, **39**, 305 (1952).

DIVISION OF PHYSIOLOGY
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Occurrence of Cinnamic Acid in Sugar Pine (*Pinus lambertiana* Dougl.)

BY ARTHUR B. ANDERSON

RECEIVED JULY 14, 1952

Cinnamic acid (*trans*-isomer) is a common constituent of many plants and is the chief component of the oil of *Storax*.[1] In addition to being in the free form, it is likewise found as esters in various plant oils and resins.

While investigating the distribution and amount of pinitol present in sugar pine heartwood, on occasions a sublimate in the form of small white crystalline flakes would appear on the walls of the evaporating dish, as the aqueous extract was being concentrated to a sirup.[2] This substance melted at 131–133°, was insoluble in cold water, dissolved readily in dilute sodium bicarbonate solution, took up bromine, decolorized potassium permanganate, and has been identified as *trans*-cinnamic acid. While this acid was found in various heartwood sections from the bole of the tree, the largest quantity was obtained from the stumpwood area (*i.e.*, 3.20 g. from 400 g. of heartwood). This is believed to be the first report of the isolation of cinnamic acid from pine wood.

Experimental[3]

Four hundred grams of air-dried sugar pine heartwood sawdust was extracted four times with hot water in a 4-liter glass percolator. The aqueous extracts were combined, neutralized with sodium bicarbonate, and the solution concentrated to about 400 ml. This was cooled and centrifuged to remove insoluble material. The decanted solution was then extracted several times with ethyl ether. The extracted, slightly alkaline, solution was poured slowly, with stirring, into an excess of dilute hydrochloric acid, resulting in the precipitation of a light-tan crystalline material. This precipitate was filtered, washed with water and recrystallized several times from hot dilute ethanol (charcoal) to constant melting point 134–135°; yield 3.2 g. (0.8%).

Anal. Calcd. for $C_9H_8O_2$: C, 72.95; H, 5.44; neut. equiv., 148.15. Found: C, 72.70; H, 5.54; neut. equiv., 147.5.

The *p*-nitrobenzyl- and phenacyl esters of the acid melted at 116–117° and 142–143°, respectively, mixed melting point with corresponding authentic derivatives of cinnamic acid were unchanged.

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(1) G. Klein, "Handbuch der Pflanzenanalyse," Vol. 2, Springer, Wien, 1932, pp. 537–538.

(2) Arthur B. Anderson, *Tappi*, **35**, No. 5, 198 (1952).

(3) All melting points uncorrected taken on Fisher melting-point block; microanalysis by Microchemical Laboratory, University of California.

FOREST PRODUCTS LABORATORY
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Solvent Effects in the α-Chymotrypsin–Hydrocinnamic Ester System[1]

BY M. LUCETTA BARNARD AND KEITH J. LAIDLER

RECEIVED MAY 16, 1952

Consideration of the entropies of activation associated with the formation and breakdown of enzyme–substrate complexes has suggested the possibility that specific solvent or structural effects occur during these processes.[2,3] The available data indicate that complex formation is associated with a negative entropy of activation when the substrate is uncharged, and with a positive one when the substrate is charged. This can be explained if charge separation occurs in the former case, with binding of water molecules, and charge neutralization in the latter case, with release of water molecules.

In the present note we describe an approach which is designed as a check on the plausibility of this type of hypothesis. The entropy terms associated with the electrostriction of solvent molecules have been evaluated by measuring rates in mixed solvents, the work being done on the α-chymotrypsin–hydrocinnamic ester system, in which the substrate is uncharged. It is emphasized that in view of the complications of enzyme systems a rigorous application of the theoretical treatment is not possible; consequently a detailed experimental study of solvent effects has not been thought worth while, although a rough application of the general method to other systems may well be useful and is being carried out in this Laboratory.

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(1) Abstracted from a dissertation submitted by Sister M. Lucetta Barnard, C.S.C., to the Graduate School of the Catholic University of America in partial fulfillment of the requirements for the degree of Master of Science. The work was carried out in part under Contract N8onr-05300 with the Office of Naval Research, Biochemistry Branch.

(2) K. J. Laidler, "Symposium on Biochemical Kinetics," Diamond Jubilee Meeting of the American Chemical Society, September 6, 1951.

(3) E. J. Casey and K. J. Laidler, THIS JOURNAL, **72**, 2159 (1950).

It is known from simple electrostatic theory[4] that the rate constant k of a reaction in which charges of valence z_A and z_B are produced in the activated state at a distance r apart is given by

$$\ln k = \ln k_0 - \frac{\epsilon^2 z_A z_B}{\mathbf{k}Tr}\left(1 - \frac{1}{D}\right) \qquad (1)$$

Here D is the dielectric constant, k_0 is the rate at unit D, ϵ is the electronic charge, **k** is Boltzmann's constant and T the absolute temperature. This equation may be written in the general form

$$\ln k = \ln k_0 - \frac{A}{T}\left(1 - \frac{1}{D}\right) \qquad (2)$$

and A may be determined experimentally by measuring k at different values of D.

The magnitude of the entropy changes associated with electrostatic effects may then be determined as follows. The free energy is equal to $\ln(\mathbf{k}T/h) - RT\ln k$, and that part of it, $(\Delta F^*)_{\text{e.s.}}$, that is associated with electrostatic interactions is thus

$$(\Delta F^*)_{\text{e.s.}} = RA\left(1 - \frac{1}{D}\right) \qquad (3)$$

The electrostatic entropy of activation is given by

$$(\Delta S^*)_{\text{e.s.}} = -\left(\frac{\partial(\Delta F^*)_{\text{e.s.}}}{\partial T}\right)_P \qquad (4)$$

and differentiation of eq. (3) with respect to T, allowing for the temperature dependence of D, gives

$$(\Delta S^*)_{\text{e.s.}} = -\frac{RA}{D^2}\left(\frac{\partial D}{\partial T}\right)_P \qquad (5)$$

In an aqueous solution D is about 80 and $\partial \ln D/\partial T$ is about -0.0046; it thus follows that

$$(\Delta S^*)_{\text{e.s.}} \simeq 1.13 \times 10^{-4} A \qquad (6)$$

We are applying this treatment to a number of enzyme reactions by measuring rates at different substrate concentrations and in mixed methanol–water solvents. Methanol is one of the few solvents suitable for this purpose, since it has no specific effect on proteins; however, only dilute solutions may be used, as enzymes are deactivated at higher concentrations. The present work was carried out in mixtures up to 25% in methanol.

The procedure is to determine, by the usual extrapolation procedures,[5] the values of k_2K and k_2 at various dielectric constants. The logarithms of these constants are then plotted against $1/D$, and the value of A determined. The electrostatic entropies calculated using eq. (6) are denoted as $(\Delta S^*)_{\text{e.s.}}$ and $(\Delta S_2^*)_{\text{e.s.}}$, respectively, and refer to the formation of the enzyme–substrate complex and to its breakdown. If the over-all entropies of activation are also known, the corresponding non-electrostatic terms $(\Delta S^*)_{\text{n.e.s.}}$ and $(\Delta S_2^*)_{\text{n.e.s.}}$ are obtained by subtraction.

The results for the α-chymotrypsin–hydrocinnamic ester system are as follows, the over-all entropies, which we have confirmed, being those of Snoke and Neurath.[6]

Complex formation:

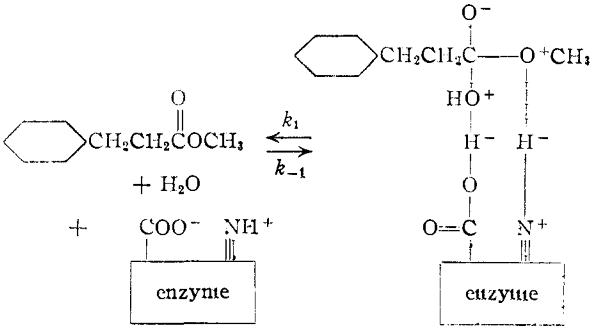
$$\Delta S^* = 23 \qquad (\Delta S^*)_{\text{e.s.}} = -38 \qquad (\Delta S^*)_{\text{n.e.s.}} = 15$$

Breakdown of complex:

$$\Delta S_2^* = -12 \quad (\Delta S_2^*)_{\text{e.s.}} = -20 \quad (\Delta S_2^*)_{\text{n.e.s.}} = 8$$

The value of -38 e.u. for $(\Delta S^*)_{\text{e.s.}}$ is of special interest in suggesting that there is considerable charge separation during the formation of the complex, and the value of -20 for $(\Delta S_2^*)_{\text{e.s.}}$ indicates further charge separation during the subsequent reaction. The value $(\Delta S_2^*)_{\text{n.e.s.}}$ is a normal one for a unimolecular reaction, but the value of 15 e.u. for $(\Delta S^*)_{\text{n.e.s.}}$ implies some structural change (perhaps unfolding) during complex formation, as discussed previously[7] for other reactions on the basis of the pressure data.

The charge separations occurring during reaction are capable of explanation in terms of a model which also explains other features of the reaction. The position of the pH optimum (7.8) and the shape of the rate-pH curve for the reaction are consistent with the hypothesis that the active site on the enzyme consists of a $-COO^-$ group and an $\equiv NH^+$ group, the latter belonging to the imidazole ring in a histidine residue. Formation of the complex can thus be represented as which clearly involves considerable charge separation. Such a formulation of the complex satisfactorily explains the catalytic action (which is of the ordinary acid–base type) and explains the stability of the complex.



Data are also available in the literature for making a similar, but less complete, analysis of the α-chymotrypsin-catalyzed hydrolysis of benzoyl-L-tyrosine ethyl ester, a substrate that is also uncharged. The data are given by Kaufman, Neurath and Schwert[8] in the form of k_2K at three different methanol concentrations. The results obtained are

$$\Delta S^* = -38 \qquad (\Delta S^*)_{\text{e.s.}} = -27 \qquad (\Delta S^*)_{\text{n.e.s.}} = -11$$

The value of -11 is reasonable for bimolecular interaction, and it is not necessary to suggest structural change. The negative electrostatic term again implies charge separation.

The hydrolysis of acetyl-L-tyrosinamide has also been studied at different methanol concentrations,[9] and analysis of the results gives -30 e.u. for $(\Delta S^*)_{\text{e.s.}}$ and 0 e.u. for $(\Delta S_2^*)_{\text{e.s.}}$. For the closely analogous substrate benzoyl-L-tyrosinamide the

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(4) *Cf.* K. J. Laidler, "Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1950, p. 133.

(5) *E.g.*, G. S. Eadie, *J. Biol. Chem.*, **146**, 85 (1942).

(6) J. E. Snoke and H. Neurath, *Arch. Biochem.*, **21**, 351 (1949); *J. Biol. Chem.*, **182**, 577 (1950).

(7) K. J. Laidler, *Arch. Biochem.*, **30**, 226 (1951).

(8) S. Kaufman, H. Neurath and G. W. Schwert, *J. Biol. Chem.*, **177**, 793 (1949).

(9) S. Kaufman and H. Neurath, *ibid.*, **180**, 181 (1949).

entropy values[8] are $\Delta S^* = -43.0$ and $\Delta S_2^* = -13.0$. If these values can be accepted tentatively for the acetyl compound the non-electrostatic contributions are found to be $(\Delta S^*)_{\text{n.e.s.}} = 13$ and $(\Delta S_2^*)_{\text{n.e.s.}} = -13$. The value of -30 for $(\Delta S^*)_{\text{e.s.}}$ suggest that, as with hydrocinnamic ester, there is considerable charge separation during complex formation: this is rather to be expected for an uncharged substrate. There appears to be little further separation during the reaction of the complex. The non-electrostatic entropy values indicate some structural change in this system, the enzyme unfolding during complex formation and folding during the subsequent process.

Experimental

The enzyme, salt-free α-chymotrypsin, was used in solution at a concentration of 8.41×10^{-6} *M*, calculated on the basis of a molecular weight of 27,000.[10] The solvents used were methanol-water mixtures of various concentrations. All water used was triply distilled in an all-glass apparatus. The kinetic procedure was very similar to that employed by Snoke and Neurath,[6] the main difference being that the buffer concentration used was very much lower in the present experiments, a 0.0045 *M* $NaOH-NaH_2PO_4$ buffer being used. The *p*H optimum was found to be 7.8, and all work was done at this *p*H.

Rates were measured in 15, 20 and 25% methanol-water, and at the two extreme substrate concentrations, 0.00075 *M* and 0.01 *M*. The values of k_2 and k_2K obtained from the intercepts on the two axes are given in Table I. The values of *A* calculated from the plots of log k_2 and log k_2K *vs.* $1/D$, and the corresponding entropies, are also shown in Table I. The dielectric constants were taken from the work of Davies and Jones.[11]

TABLE I

VALUES OF k_2 AND k_2K

% Methanol (by weight)	D	$k_2 \times 10^2$	k_2K
15	72.48	1.84	17.1
20	70.25	1.38	12.5
25	68.01	1.07	6.2
		$A - -1.77 \times 10^5$	-3.38×10^5
		$(\Delta S_2^*)_{\text{e.s.}} = -20$ e.u.	$(\Delta S^*)_{\text{e.s.}} = -38$ e.u.

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[10] E. Jansen, M.D. Fellows-Nutting, R. Jang and A. K. Balls, *J. Biol. Chem.*, **179**, 189 (1949); E. Jansen, M.D. Fellows-Nutting and A. K. Balls, *ibid.*, **179**, 201 (1949).

[11] R. Davies and T. Jones, *Phil. Mag.*, **28**, 307 (1939).

DEPARTMENT OF CHEMISTRY
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Solubility of Cerium(IV) Pyrophosphate

BY J. C. BRANTLEY[1a] AND J. R. HUIZENGA[1b]

RECEIVED JULY 14, 1952

The solubility of cerium(IV) pyrophosphate was measured in water and in four sulfuric acid solutions ranging from 0.114 to 0.684 *N*. Phosphorus-32[2] was used to trace the cerium(IV) pyrophosphate. The results are given in Table I.

The solubility increases linearly with sulfuric acid concentration in the region 0.114 to 0.342 *N* acid. Cerium(IV) pyrophosphate has a greater solubility in sulfuric acid than the analogous thorium pyrophosphate[3] has in hydrochloric acid solutions of similar normalities. An examination of our data plus data of Moeller and Schweitzer[3] also indicates that cerium(IV) pyrophosphate is more soluble in hydrochloric acid solutions than in the same normality sulfuric acid solutions by about a factor of two.

TABLE I

Acid concn., *N*	Average c./min.	CeP_2O_7, g./liter	CeP_2O_7, moles/l. $\times 10^4$	ThP_2O_7,[3] moles/l. $\times 10^4$
H_2O	4.5	0.00007 ± 0.00005	0.002	...
0.114	1,740	.026 ± .005	0.8	0.2
.228	3,090	.046 ± .005	1.5	.4
.342	4,950	.073 ± .005	2.3	.6
.684	14,000	.207 ± .010	6.6	...
Standard	9,610			

Experimental

Labeled cerium(IV) pyrophosphate was prepared by reaction of a solution of cerium(IV) ammonium sulfate with an excess of labeled sodium pyrophosphate solution, allowing the precipitate to digest overnight and washing the filtered precipitate thoroughly with warm water and hot ethyl alcohol. The resulting precipitate was a light yellow powder of very fine grain. The labeled sodium pyrophosphate was prepared by heating 4 g. of disodium phosphate with a trace of phosphoric acid containing 400 microcuries of phosphorus-32 in a furnace at 450° for two hours.

The labeled sodium pyrophosphate solution was standardized[3] by treating an excess with a standard solution of thorium nitrate. Thorium pyrophosphate is quantitatively precipitated[3,4] and the activity of the supernatant liquid was measured; 2.521 milligrams of Th^{+4} in 50 ml. precipitated 48.1% of the original pyrophosphate activity. From the decrease in the activity of the sodium pyrophosphate solution and the known amount of thorium nitrate added, the pyrophosphate concentration of the standard solution is calculated to be 3.927 mg. of $P_2O_7^{-4}$ per 50 ml.

The labeled cerium(IV) pyrophosphate was divided among five 50-ml. volumetric flasks containing various amounts of sulfuric acid (Table I). The flasks were shaken regularly for 72 hours in a bath maintained at 25.0°. The supernatant liquids were filtered and the radioactivity of each determined in a glass-jacketed Geiger counter tube with a conventional amplifying and scaling circuit. The standard pyrophosphate solution was counted in a similar manner.

Calculation

$$CeP_2O_7 \text{ (g./liter)} = \text{concn. of std. } (78.54 \times 10^{-3} \text{ g. of } P_2O_7^{-4}\text{/liter})(1.81)\left(\frac{\text{c./min. of unknown}}{\text{c./min. of std.}}\right)$$

1.81 = factor converting pyrophosphate into CeP_2O_7

Acknowledgment.—The experimental work was done as part of a laboratory course in radiochemistry taught by Prof. R. B. Duffield.

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[1] (a) Linde Air Products Company, Tonawanda, New York; (b) Argonne National Laboratory, Chicago, Illinois.

[2] Tracer supplied by Oak Ridge National Laboratory.

[3] From data of Moeller and Schweitzer, *Anal. Chem.*, **20**, 1201 (1948); their solubility data were determined in HCl.

[4] R. J. Carney and E. D. Campbell, THIS JOURNAL, **36**, 1134 (1914).

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On the Production of Electronically Excited Molecules in the Oxidation Products of Graphite

BY R. H. BUSSO

RECEIVED JULY 14, 1952

The determination of hydrocarbon and carbon monoxide flame temperatures has revealed the existence of a latent energy in the combustion products. These products are also the center of an after-burning.

Light emission spectral studies (visible or near ultraviolet) have, for a number of years led investigators to consider that a large part of this light emission is due not to thermal causes but to chemiluminescent reaction products.[1a]

For a number of years systematic investigations of the emission of large quanta of energy by chemical reactions have been carried out in the laboratory of Professor Audubert.[1b] These studies have revealed the role played by high activation energies. It has therefore seemed useful to give an idea of some of the results obtained for carbon combustion since they have sometimes escaped the notice of American publications. These results have been obtained using copper iodide photon counters which are very sensitive in the 1,900 to 2,800 Å. wave length region.[2] It has been shown that the gases leaving the zone of strong reaction surrounding the pure graphite filament (burning at 1773°K. in a rapid stream of low pressure oxygen or air one to 25 cm.) contain carbon dioxide and carbon monoxide electronically excited metastable molecules.[3]

If θ is the apparent mean lifetime ($1/\theta = (1/\tau) + kp$ where τ is the real mean lifetime, p the pressure, k the kinetic constant of deactivation by collision with non-activated molecules), then the form of the curve of variation of $1/\theta$ as a function of pressure shows that these two molecular species can exist in different pressure ranges. At air pressure lower than 2 cm. there are only metastable excited CO molecules whereas at pressure greater than 3 cm. metastable activated CO_2 molecules are present under certain conditions. This identification was made by means of rapid condensation (in liquid air) or through the influence of CO combustion inhibitors (CCl_4 in a proportion of 2%).[4]

A recent preliminary spectral investigation between 1,900 and 2,800 Å. has shown that in the reaction zone (where solid–gas reactions and homogeneous gas reactions occur) surrounding the filament there is emission of bands due to highly activated OH radicals (2,600–2,680 Å.) and of a series of other bands extending almost to 1,900 Å. some of which are due to O_2 and others to CO. It has not yet been possible, however to specify which bands should be attributed to the transitions O_2 ($^3\Sigma u^- \rightarrow {}^3\Sigma g^-$), CO($A\,^1\Sigma \rightarrow X\,^1\Sigma$), CO($a\,^3\Pi \rightarrow X\,^1\Sigma$). The Cameron bands are probably present, but with very low intensity because they correspond to partially forbidden transition. All these bands are superposed on a continuous background which seems to extend to 1,900 Å. and can be attributed to the recombination processes $O^1D + O^3P$ and CO $a\,^3\Pi + O^3P$.

As for the metastable molecules whose lifetime we have determined it is thought that at low pressures where deactivation is less important, CO $a\,^3\Pi$ molecules are observed which either emit the partially forbidden bands or go over to the CO $A\,^1\Pi$ level through collision with another molecule, subsequently falling to the ground state with emission of light. In the same way activated CO_2 in the $^3\Pi$ state[5] falls to the ground state with emission of forbidden band or else transfers its activation energy to O_2 $^3\Sigma g^-$ (emission in the infrared) by formation of a CO_2–O_2 transition complex.[6]

The very small concentrations (10^{-13}) have prevented even qualitative spectral determinations of the above mentioned metastable molecules from being carried out.

One particular point should be made. In the 1,900–2,000 Å. region there is particularly intense emission. It should be noted that the excited levels CO and O_2 are energetically very close to each other and so transfer of energy by resonance is consequently facilitated.

The experimental demonstration of the existence of very high quanta in relatively large amounts in the combustion processes gives them an importance which has been denied to chemiluminescent processes. The investigations of Gaydon, *et al.*,[7] our investigations and those of Laidler seem to imply that highly excited molecules play an important role in the energy chain which occurs in chain reactions or in their initiation. However, as we have attempted, an explanation remains to be found for the origin of these molecular excitation energies some of which exceed 150 kcal. in the case of carbon combustion.

In conclusion it can be said that the results which we have obtained for carbon oxidation (together with those of Whittingham in another wave length)[8] demonstrate that there is a close analogy with the phenomena accompanying flame combustions: identity of active free radicals, presence of large quanta of energy, etc. The following schemes summarize our results.

$$\left.\begin{matrix}\text{C* (active centers)}\\ \text{C}\end{matrix}\right\} + \left\{\begin{matrix}O_2\,^3\Sigma g^-\\ O_2\,^3\Sigma u^-\end{matrix}\right\} \longrightarrow \left\{\begin{matrix}\text{CO}\\ \text{CO*}\\ \text{CO* metastable}\end{matrix}\right.$$

$$\text{CO*} \longrightarrow \text{CO} + h\nu' \text{ (4th positive)}$$

$$\text{CO*met}' \longrightarrow \text{CO} + h\nu'$$

$$\text{CO}^* \xrightarrow{*} O_2\,^3\Sigma g^- \longrightarrow O_2\,^3\Sigma u^-$$

$$O^1D + O^3P \longrightarrow O_2\,^3\Sigma u^- \text{ (continuum)}$$

$$\text{CO} + \left.\begin{matrix}O^1D\\ O^3P\end{matrix}\right\} \longrightarrow \left\{\begin{matrix}CO_2 \text{ (continuum)}\\ CO_2^*\\ CO_2^* \text{ metastable}\end{matrix}\right.$$

$$CO_2^* \longrightarrow CO_2 + h\nu'' \text{ (bands of Gaydon)}$$

$$CO_2^*\text{met} \longrightarrow CO_2 + h\nu'''$$

$$CO_2^* + O_2\,^3\Sigma g^- \longrightarrow CO_2 + O_2\,^3\Sigma u^-$$

$$O_2\,^3\Sigma u^- \longrightarrow O_2\,^3\Sigma g^- + h\nu'''' \text{ (Schumann–Runge)}$$

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[1] (a) For example: V. Kondratjew, *Z. Physik*, **63**, 322 (1930); Fowler and Gaydon, *Proc. Roy. Soc. (London)*, **A142**, 362 (1933); David and all. etc. (b) R. Audubert and Van Doormal, *Compt. rend.* **196**, 1883 (1933) (first research); *Trans. Faraday Soc.*, **35**, 197 (1939). review by R. Audubert in "Contribution à l'étude de la structure moléculaire," Desoer, Lièges, 1948.

[2] R. Audubert, *Compt. rend.*, **200**, 918 (1935).

[3] R. Audubert and C. Racz, *ibid.*, **218**, 752 (1944); **219**, 244 (1944); R. H. Busso and R. Audubert, *ibid.*, **227**, 1961 (1948).

[4] R. H. Busso, *ibid.*, **228**, 683 (1949); R. Audubert and R. H. Busso, *J. chim. phys.*, **47**, 331 (1950).

[5] V. Griffing and K. J. Laidler in "Third Symposium on Combustion and Flame and Explosion Phenomena," Williams and Wilkins Co., Baltimore, Md., 1949, p. 432; K. J. Laidler, *ibid.*, p. 441.

[6] G. A. Hornbeck, *ibid.*, p. 501; G. A. Hornbeck and H. S. Hopfield, *J. Chem. Phys.*, **17**, 982 (1949).

[7] A. G. Gaydon, *et al.*, in "Spectroscopy and Combustion Theory," Second edition, Chapman and Hall, Ltd., London, 1948.

[8] Whittingham, *Fuel*, **24**, 244 (1950).

Concerning the Behavior of Aqueous Thenoyltrifluoroacetone

By Edward H. Cook and Robert W. Taft, Jr.

Received June 16, 1952

King and Reas have reported a stable crystalline monohydrate (TTA·H_2O) of thenoyltrifluoroacetone (TTA).[1] Zebroski has found the chemistry of TTA and TTA·H_2O to be markedly different. The addition of solid TTA·H_2O to dilute aqueous sodium hydroxide results in a rapid and nearly complete cleavage to acetylthiophene and the salt of trifluoroacetic acid. On the other hand, the same treatment of solid anhydrous TTA produces essentially complete conversion to the enolate ion.[2]

We have found that the addition of an aqueous solution of TTA to an appreciable excess of base gives very nearly the same results as the addition of solid TTA·H_2O or its aqueous solution. This result supports the conclusion of the previous investigators,[1,2] based upon spectral and bromination data, that the principal species in an aqueous solution of TTA is TTA·H_2O (keto hydrate). We have been able to interpret several apparently anomalous results on this basis.

The potentiometric titration of an acidified aqueous solution of TTA with sodium hydroxide solution requires in the low *p*H region (<3) of the titration curve, an appreciable excess of base over the added mineral acid. An aqueous solution of TTA, however, gives a titration curve resembling that of a typical weak acid. These results suggested that an acid-catalyzed cleavage to trifluoroacetic acid and acetylthiophene occurred in the former case. We have eliminated this possibility, however, by obtaining a nearly quantitative recovery of TTA (as TTA·H_2O) from a one molar aqueous HCl solution of TTA which stood for 24 hours at 50°. The formation of the strong acid in the titration of an acidified aqueous TTA solution must therefore be the result of the cleavage of the TTA·H_2O present obtained by momentary local concentrations of high *p*H during the addition of base.

Further, the titration of an aqueous TTA solution with strong base, although deceitful from the appearance of the titration curve, is not a simple neutralization of a weak acid by strong base. The titration curve cannot be reproduced by back-titration with strong acid. Instead a typical back-titration shows that about half of the diketone is converted to a strong acid.[3] Spectral data indicate cleavage occurs during the addition of base since there is only partial conversion to enolate ion.

Either TTA or TTA·H_2O can, however, be converted to enolate ion in a buffer of *p*H 8. Essentially complete enolization results from addition of either (1) aqueous TTA solutions; (2) dry ethanol solution of anhydrous TTA; (3) solid TTA·H_2O; or (4) solid anhydrous TTA to a buffer of *p*H 8.

Preliminary work has indicated the rate of enolization of aqueous TTA solutions takes place appreciably more rapidly at *p*H 8 than in solutions of *p*H below 4.[4] The latter rates have been determined by rates of bromination,[5] the former by the rates of appearance of the absorption band due to enolate ion. At *p*H 8 the rate is first order with respect to β-diketone, but also dependent upon the salt component of the buffer and its concentration. Results indicating that TTA·H_2O enolizes at a slower rate than TTA have also been obtained. Quantitative rate studies are in progress.

If aqueous TTA solutions are allowed, even momentarily, to become more basic than *p*H 9, cleavage of the TTA·H_2O (the principal species present) results, *i.e.*, above *p*H 9 the rate of cleavage of TTA·H_2O becomes the same order or exceeds its rate of enolization. By conducting experiments in such a manner as to reduce the hydration of TTA, cleavage in strongly basic solution can however be reduced and enolization increased. When a dry ethanol solution of anhydrous TTA is added to an equivalent amount of aqueous sodium hydroxide about 85% of the TTA is converted to enolate ion and 15% is cleaved. Similar treatment of aqueous TTA results in better than 95% cleavage, thus indicating that in the previous experiment an appreciable amount of enolate ion is formed before the TTA from the alcohol solution hydrates.

The only way we have found to obtain complete conversion to enolate ion in strongly basic aqueous solution is by the addition of solid anhydrous TTA. When added to either an equivalent or an excess of aqueous sodium hydroxide, this substance gives 100% enolate ion.[6] In this case protons must be removed at the surface of the solid phase before the TTA has hydrated, with the result that TTA goes into solution as enolate ion. Back-titration of enolate ion gives a value of 4.2 × 10^{-7} for the apparent ionization constant for aqueous TTA.

The data presented indicate not only that TTA·H_2O is much more susceptible to cleavage than TTA, but also that the conversion to enolate ion protects the diketone from cleavage in basic solution.[7] Further, the cleavage of TTA·H_2O at high *p*H's rather than enolization represents an important case in which the rupture of a C–C bond proceeds at a markedly faster rate than the breaking of a C–H bond. The great rapidity with which the cleavage must occur is remindful of the strong activating influence of the CF_3 group in base-catalyzed ester hydrolysis.

Experimental

Materials.—The TTA used (m.p. 44–45°) was obtained from the Dow Chemical Company and the TTA·H_2O was prepared from it by the method of King and Reas.[1]

Spectral Data.—The ultraviolet spectra of a slightly acidified aqueous solution of TTA (or TTA·H_2O) is closely equivalent to that of acetylthiophene with maxima in the regions 260–270 mμ and 285–295 mμ.[2] Similar results have been obtained by us in 50% (vol.) aqueous dioxane. The spectral data (in agreement with other information) there-

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[1] E. L. King and W. H. Reas, This Journal, **73**, 1806 (1951).

[2] E. Zebroski, Atomic Energy Commission Report BC-63 (1947); Ph.D. Thesis, University of California.

[3] Titration results are not generally reproducible but depend upon the rate of addition of base and of stirring. See also ref. 2.

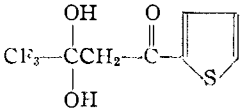
[4] Compare ref. 2.

[5] (a) J. C. Reid and M. Calvin, This Journal, **72**, 2948 (1950); (b) unpublished work of the present authors.

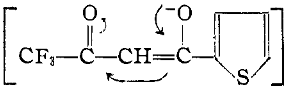
[6] The quite slow disappearance of enolate ion from these solutions (see ref. 2) seems best accounted for on the basis of a slow hydrolysis of enolate ion to TTA·H_2O followed by cleavage, rather than a direct cleavage of enolate ion.

[7] See, for similar results, R. G. Pearson and E. A. Mayerle, This Journal, **73**, 926 (1951).

fore indicate that TTA·H_2O is the principal species in an aqueous TTA solution and that its structure is[1,2]



The optical density at 340 mμ of aqueous solutions of TTA obtained by addition of TTA in the forms indicated below to aqueous buffer solutions (phthalate, phosphate and borate buffers have been used) increases exponentially with *p*H reaching a maximum at approximately *p*H 8. Very nearly equivalent results were obtained by adding the ketone as TTA(s), TTA·H_2O(s), TTA(aq.) or TTA(s) dissolved in a small volume of dry ethanol. Typical optical densities[8] at 340 mμ for 1.00 × 10^{-4} *M* solutions are (cell length 1 cm.): *p*H 4.0, 0.04; *p*H 5.0, 0.11; *p*H 6.0, 0.58; *p*H 8.0, 1.95. The addition of TTA(s) to an excess of aqueous sodium hydroxide gives an optical density of 2.00 at otherwise equivalent conditions.[8] The absorption at 340 mμ must be due to the formation of enolate ion and the relatively high maximum and extinction (ε molar 20,000) require that the enolate ion be the unhydrated species[2,9]



The buffer solution results indicate that TTA·H_2O or TTA can be essentially completely converted to enolate ion at *p*H 8. However, when aqueous solutions of TTA are added to buffer solutions of *p*H 9 or greater the optical densities at 340 mμ fall markedly below that expected for complete enolization. Addition of an aqueous TTA solution to a 0.066 *N* sodium hydroxide solution gave an absorption of only 0.059 at 340 mμ for a 1.00 × 10^{-4} *M* solution.[8] Nearly equivalent results are obtained with TTA·H_2O(s) or TTA·H_2O(aq.). Since sodium trifluoroacetate and acetylthiophene do not absorb appreciably at 340 mμ, the 97–98% of TTA which should have, but was not, converted to enolate ion must have cleaved to these products. This is confirmed by titration data given below and by the work of Zebroski.[2] In the latter work it was found that TTA·H_2O (solid or in aqueous solution) was 96% hydrolyzed by sodium hydroxide to the above cleavage products and the remaining 4% was converted to enolate ion. Spectral data also indicate that in the titration of aqueous TTA solutions with sodium hydroxide, even though the equilibrium *p*H is held below 8, appreciable hydrolysis occurs. Samples withdrawn during a titration did not give results similar to those above for buffer solutions, but instead gave optical densities much smaller than that corresponding to the equilibrium *p*H of the solution.

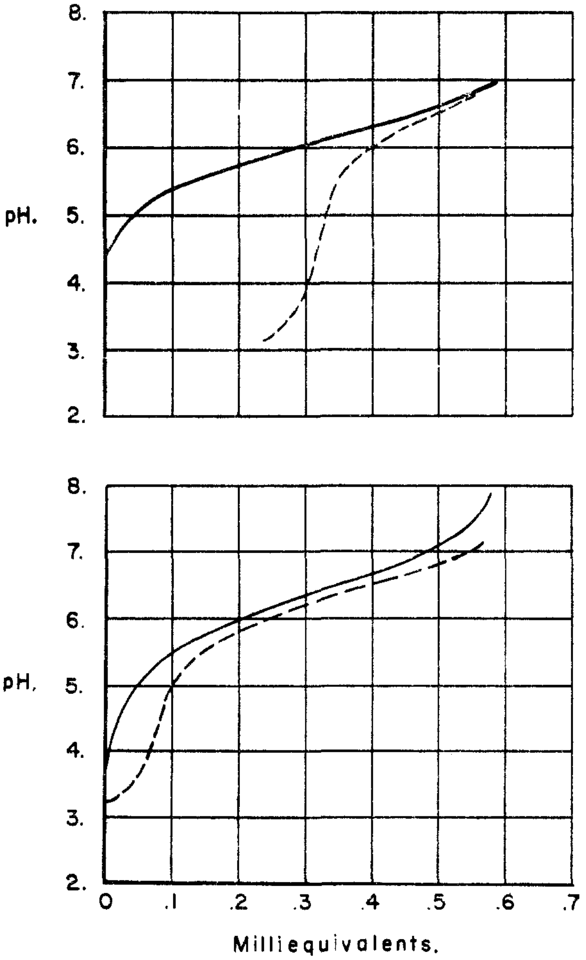


Fig. 1.

When 1 ml. of a solution of TTA in dry ethanol was added to 99 ml. of 0.066 *N* sodium hydroxide, the optical density of a 1.00 × 10^{-4} *M* at 340 mμ was 1.85.[9]

Titration Data.—Titrations were made with a Beckman "G" *p*H meter using type "E" glass and calomel electrodes. In the upper half of Fig. 1 is shown by the full line a typical curve for the titration of an aqueous TTA solution with sodium hydroxide. In the present case the titration was carried only to an equilibrium *p*H of 6.95 and then back-titrated, as shown by the dashed line, with HCl solution. Since data given above demonstrate that TTA·H_2O (the principal species in aqueous TTA solutions) can be converted to enolate ion without interfering hydrolysis if the *p*H is not made to exceed 8, the fact that the back-titration follows a completely different course than the original (in the present case indicating about 50% of the ketone is converted to the strong trifluoroacetic acid) confirms the spectral evidence showing that cleavage occurs during the addition of base. Back-titration of a solution obtained by adding aqueous TTA to an excess of base shows no more than 5% of the TTA remained unhydrolyzed, as acid equivalent to only 5% of the diketone titrated in the *p*H region above 3.

In the lower half of Fig. 1 is given by the dashed line the back-titration curve for a solution prepared by addition of 1 ml. of a dry ethanol solution of TTA to 99 ml. of an aqueous solution containing sodium hydroxide slightly less than that required for complete neutralization of the TTA. The results indicate that about 15% of the diketone is converted to the trifluoroacetic acid, the remainder being converted from enolate ion to diketone. The full line in the lower half of Fig. 1 gives the back-titration curve (HCl) for a solution prepared by dissolving 0.567 milliequiv. wt. of TTA(s) in a solution containing 0.572 millieq. wt. NaOH. The results indicate no hydrolysis occurs when TTA(s) is dissolved in the base since the theoretical amount of enolate ion was titrated in the high *p*H region. Making a small correction for ionic strength an apparent pK_a of 6.38 is obtained from this curve from the *p*H corresponding to one-half neutralization of the enolate ion. This value is in good agreement with the *p*H corresponding to one-half maximum optical density at 340 mμ obtained from a plot of the buffer solution data referred to above. Other investigators[5a,10] have reported lower *pK*'s based upon the *p*H obtained when one-half of the diketone present is titrated directly with base, but this method is not accurate since it ignores the hydrolysis which accompanies the titration.

Acknowledgment.—The authors express their thanks to Dr. W. C. Fernelius for suggesting this investigation. We are also indebted to the Atomic Energy Commission for the support for one of us, E. H. C., which made this work possible.

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[8] The optical densities given here are maximum values (obtained in every case within a few minutes after reaction was initiated) and were constant for a period of several hours. With long standing the optical densities of the solutions decrease—see ref. 6.

[9] (a) R. N. Jones, *Chem. Revs.*, **32**, 1 (1943); (b) J. R. Platt and H. B. Klevens, *Rev. Modern Phys.*, **16**, 182 (1944).

[10] L. Van Uitert, Master's Thesis, The Pennsylvania State College, 1951.

On the Dielectric Constant of Trifluoroacetic Acid[1]

By Walter Dannhauser and Robert H. Cole

Received August 1, 1952

Simons and Lorentzen[1a] have reported dielectric constants for trifluoroacetic acid, measured at 1000 c./sec., which increase with temperature from 26.2 at −11° to 43.4 at 27.7°. These values are much larger than those of 6.07 at 10° to 6.60 at 70° reported by Smyth and Rogers[2] for acetic acid, which one might expect to have more similar properties, and the temperature dependence is the opposite of that normally found for liquids of high dielectric constant.

The observed values might be explained as the result of a monomer–dimer equilibrium quite different from that in either acetic or formic acid, but it also seemed to us quite possible that they resulted from electrode polarization effects at low frequencies because of appreciable specific conductance of the liquid, as found in formic acid, for example.[3]

Measurements were therefore undertaken on both acetic and trifluoroacetic acids over a frequency range 20 c./sec. to 5 mc./sec. and at temperatures from the respective melting points to about 50°. The bridge used has been described elsewhere.[4]

A stainless steel cell with coaxial cylindrical electrodes[5] was employed. Interchangeable inner cylinders giving electrode separations of either 3.2 or 1.6 mm. were used to distinguish surface and intrinsic properties of the sample measured. Acetic acid was prepared by essentially the method of Eichelberger and LaMer[6] and finally distilled directly into the test cell from the all-glass apparatus using ungreased joints. The starting material for preparation of trifluoroacetic acid was a sample of better than 99% stated purity,[7] which was dried by refluxing over P_2O_5 and then redistilled directly into the cell. Melting points agreed with the literature values to 0.1°; specific conductances at 25° were of the order 5–10 $\times$ 10^{-8} mho/cm. for acetic acid, 3-5 $\times$ 10^{-7} mho/cm. for trifluoroacetic acid. The latter slowly attacked the cell, but this caused only slight rises in observed conductance.

The dielectric constant results for acetic acid were found to confirm those of Smyth and Rogers and extensive study was therefore unnecessary. The values for trifluoroacetic acid increased markedly for frequencies below 1 kc./sec., as shown by the data of Fig. 1 which were taken with the 1.6-mm. electrode separation. Measurements with 3.2 mm. separation gave the same values within experimental error above 5 kc./sec., and similar but considerably smaller increases at lower frequencies.

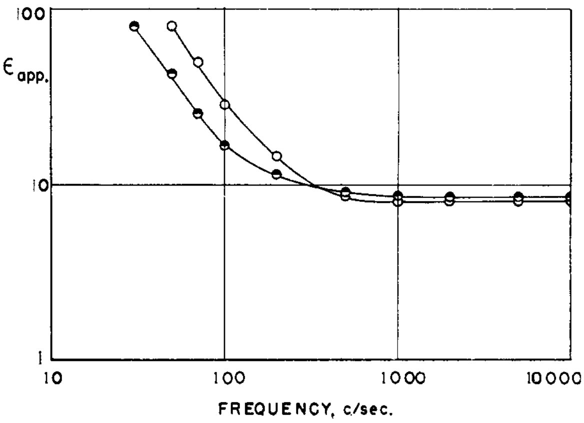

Fig. 1.—Dependence of apparent dielectric constant on frequency for trifluoroacetic acid: ◒, 19.7°; ○, 46.9°.

An analysis of electrode impedance errors[3] predicts that for identical electrodes at varying separations the increase in apparent capacitance should vary as the square of the specific conductance of the sample and in inverse ratio to the electrode spacing. This was found to be approximately true for these measurements, exact agreement not being expected because a different inner electrode was used to change the separation. The dependence of the increase in apparent dielectric constant on frequency was approximately as $f^{-1.8}$. This indicates that the electrode polarization effect was equivalent to a complex impedance, rather than a pure capacitance which would give a dependence as f^{-2}, and is similar to observations of Shaw[8] and Wolf.[9]

We conclude that the frequency independent values observed above a few kilocycles are characteristic of the liquid, and such values interpolated at several temperatures are listed in Table I, together with values for acetic acid. These show that the fluorine derivative has a somewhat higher dielectric constant, with a normal negative temperature coefficient, rather than the slight positive one observed for acetic acid. Attempts to account for the differences on the basis of associative equilibria or electronic polarization have been inconclusive.

Table I

Dielectric Constants of Acetic and Trifluoroacetic Acids

Temp., °C.	Dielectric constant Acetic acid Smyth and Rogers	 This work	 Trifluoroacetic acid Simons and Lorentzen	 This work
−10	..	..	..	9.16
0	..	..	29.5	8.90
+10	6.07	..	34.5	8.65
20	6.13	6.18	39.0	8.42
30	6.20	6.27	44.5[a]	8.22
40	6.27	6.36	...	8.02
50	6.36	6.45	...	7.83
60	6.47	6.54[a]	...	..

[a] Extrapolated value.

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(1) Supported in part by O. N. R.

(1a) J. H. Simons and K. E. Lorentzen, This Journal, **72**, 1426 (1950).

(2) C. P. Smyth and H. E. Rogers, *ibid.*, **52**, 1824 (1930).

(3) J. F. Johnson and R. H. Cole, *ibid.*, **73**, 4536 (1951).

(4) R. H. Cole and P. M. Gross, Jr., *Rev. Sci. Instruments*, **20**, 252 (1949).

(5) P. M. Gross, Jr., and R. C. Taylor, This Journal, **72**, 2075 (1950).

(6) W. C. Eichelberger and V. K. LaMer, *ibid.*, **55**, 3633 (1933).

(7) Supplied through courtesy of Minnesota Mining and Mfg. Co.

(8) T. M. Shaw, *J. Chem. Phys.*, **10**, 609 (1942).

(9) I. Wolf, *Phys. Rev.*, **27**, 755 (1926).

An Attempted Preparation of a Simple Tetrahydroporphine[1]

By G. D. Dorough and J. R. Miller

Received April 18, 1952

We have for some time been interested in the properties of two simple porphyrins, $\alpha,\beta,\gamma,\delta$-tetraphenylporphine and $\alpha,\beta,\gamma,\delta$-tetraphenylchlorin.[2] In an effort to extend our studies to include a representative of the third type of porphyrin ring (see Fig. 1), we have attempted to convert tetraphenylchlorin to tetraphenyl-tetrahydroporphine by catalytic hydrogenation.[3] The preparation and properties of two compounds (designated alpha and beta) which may be isolated from such a hydrogenation are reported here.

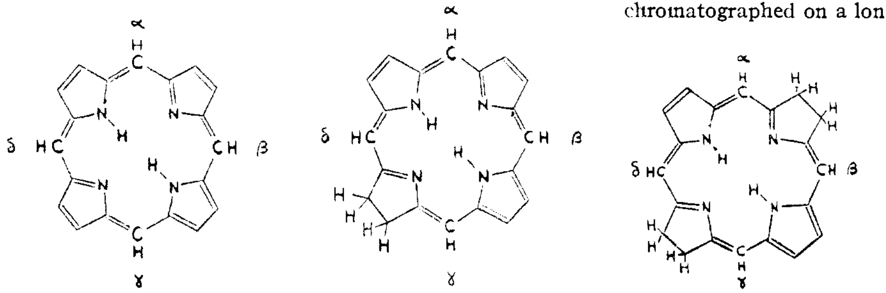

Fig. 1.—Porphyrin rings: a, porphine; b, chlorin (dihydroporphine); c, tetrahydroporphine.

Experimental

Preparation of the Compound Alpha.—One hundred cc. of a 2×10^{-4} M ether solution of $\alpha,\beta,\gamma,\delta$-tetraphenylchlorin is stirred gently under hydrogen at a pressure of 1 atmosphere with 0.1 cc. of gravity packed Raney nickel prepared according to Pavlic and Adkins.[4] The time of stirring varies with the activity of the catalyst, and may range from one-half hour for freshly made catalyst to 4 hours for 3 month old catalyst. Catalyst in amounts appreciably larger than that given above causes the chlorin to be reduced to leuco compounds quite rapidly; stirring for periods in excess of those given results in a decreased yield. Evidence of reaction is the appearance of a very intense peak in the near infrared at 7425 Å. When this peak, which is due to alpha, appears to be at an optimum, the alpha is separated from the reaction mixture by filtering off the Raney nickel, and extracting the ether filtrate with 8 to 10 100-cc. aliquots of 5 N hydrochloric acid. This removes the chlorin from the ether solution, but leaves alpha. The extraction is best done in a minimum of light. The ether solution is washed with water, with 6 N ammonium hydroxide, and with water again. It is then dried over anhydrous sodium sulfate, and finally evaporated to dryness under vacuum. The solid residue is taken up in a minimum of trichloroethylene, and chromatographed on a column tightly packed with talc (an aspirator vacuum is applied to the bottom of the column). After 5 to 10 minutes development with trichloroethylene, the column shows three distinct color separations as follows (from the bottom of the column upwards): a tan band which contains alpha, a green band which contains mostly unreacted chlorin, and a thin blue-gray band which contains some beta and some chlorin. A long chromatographic development of the mixture results in considerable conversion of alpha to chlorin; a very short column (2.5 cm. long by 1.0 cm. in diameter) is therefore used in order that the alpha will have progressed sufficiently in 5 to 10 minutes to begin eluting from the column. Alpha also deteriorates upon standing in trichloroethylene, but pyridine added to the solution inhibits this decomposition. The yield on the basis of the amount of chlorin used in the experiment is about 2%; on the basis of chlorin actually reacted (subtracting out the chlorin recovered), 4%.

Alpha may be converted readily to a magnesium derivative by the action of ethylmagnesium iodide in ether solution.

Preparation of the Compound Beta.—Although beta is formed in the above reduction, greater yields are obtainable if the hydrogenation is conducted in a purified dioxane solution. Twenty ml. of a dioxane solution of tetraphenylchlorin (about 10^{-3} M) is reduced in a manner similar to that described above. The amount of catalyst employed is 0.2 cc. of gravity packed Raney nickel. The reaction time again depends on the activity of the catalyst, and varies from one-half hour for freshly prepared material to 4 hours for 3 month old catalyst (much longer reaction periods result only in loss of chlorin). The Raney nickel is filtered, and the dioxane evaporated to dryness under vacuum. The residue is taken up in a minimum of trichloroethylene, and chromatographed on a long talc column (1 cm. × 10 cm.), developing for several hours with the same solvent. Even though the compound decomposes slowly under the conditions of the chromatographic separation, a long development is necessary if a fairly pure sample of beta is to be obtained. A typical column after a three-hour development consists essentially of only two bands, a green chlorin band toward the bottom of the column, and above and next to the chlorin band, a blue band which contains beta. The beta band is cut out from the extruded column, repacked in a small sintered-glass filter, and eluted with pyridine. The beta thus obtained contains from 5 to 10% chlorin, and is obtained in a yield of only about 2%.

Discussion

Alpha has been identified tentatively as a tetrahydroporphine. The identification is based on the following reasoning: (1) It has long been recognized[5] that porphyrin ring compounds exhibit very characteristic absorption spectra. Thus compounds containing either a porphine or a chlorin ring absorb in two regions of the visible in such a characteristic and uniform way as to permit their easy differentiation by spectral means from other organic structures, and even to permit their separate identification. Tetrahydroporphines absorb in the same two regions of the visible as porphines and chlorins and, in addition, absorb strongly in the near infrared, a region where neither porphines nor chlorins absorb. In Fig. 2 are shown the spectrum of the magnesium derivative of alpha and the spectrum of the naturally occurring magnesium tetrahydroporphine, bacteriochlorophyll. The close resemblance of these two spectra, the fact that alpha is prepared by the reduction of a chlorin, and the knowledge that of all organic structures there are few with electronic transitions in the infrared, together constitute strong presumptive evidence that alpha is a tetrahydroporphine.

(2) It has been observed[6] that simple chlorins may be quantitatively converted to the corresponding porphine by photochemically effecting the

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[1] Sixth in a series on fundamental properties of porphyrin ring systems. Article five: This Journal, **74**, 3977 (1952).

[2] For the system of nomenclature employed, see *ibid.*, **73**, 4315 (1951), footnote 2; **74**, 3974 (1952), footnote 2.

[3] W. Schlesinger, A. H. Corwin and L. Sargent, *ibid.*, **72**, 2867 (1950), have reported the preparation of a simple tetrahydroporphine by the reduction of etiohemin II with sodium and alcohol.

[4] A. A. Pavlic and H. Adkins, *ibid.*, **68**, 1471 (1946).

[5] F. Haurowitz, *Ber.*, **68**, 1795 (1935); E. Rabinowitch, *Rev. Modern Phys.*, **16**, 226 (1944); H. C. Longuet-Higgins, C. W. Rector and J. R. Platt, *J. Chem. Phys.*, **18**, 1174 (1950).

[6] M. Calvin, *et al.*, This Journal, **70**, 699 (1948); **71**, 4025 (1949).

transfer of two hydrogens to a suitable quinone. When alpha and 1,2-naphthoquinone are illuminated in a deoxygenated solvent with light of wave length longer than 6900 Å., the alpha band at about 7500 Å. completely disappears, and a new colored product is formed which agrees spectrally point for point from 8000 to 4000 Å. with a known sample of tetraphenylchlorin (see Fig. 3). Illumination with wave lengths higher than 6900 Å. presumably prevents any photochemical oxidation of the chlorin which is formed, since the chlorin does not absorb at these wave lengths. The fact that 1,2-naphthoquinone, which is known to be capable of removing two hydrogen atoms from adjacent saturated β-pyrrole carbons in a porphyrin, brings about the conversion of alpha to a chlorin is evidence in agreement with a tetrahydroporphine structure for alpha.

(3) Alpha is most reluctant to form acid salts or metal derivatives as reported for other tetrahydroporphines, a result which is in agreement with simple resonance theory.[7]

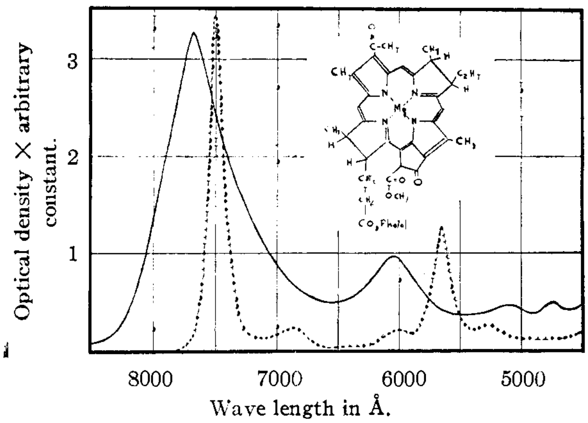


Fig. 2.—Absorption spectra: dotted line, magnesium derivative of alpha in benzene; solid line, bacteriochlorophyll in ethyl alcohol (after French, ref. 4). The currently accepted structure of bacteriochlorophyll is shown in the inset.

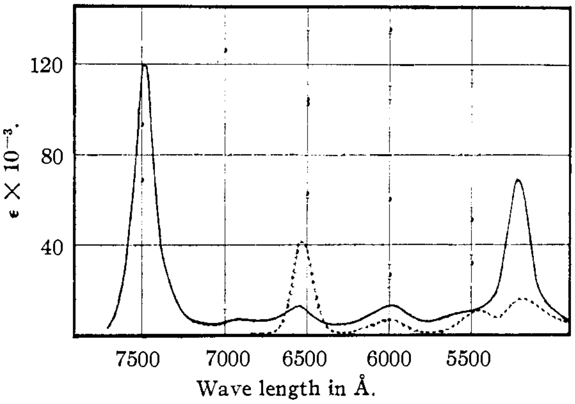
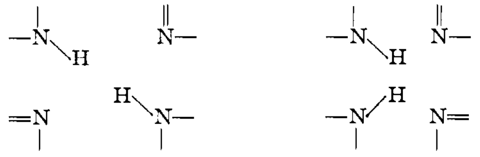


Fig. 3.—Absorption spectra in benzene: dotted line, tetraphenylchlorin free base; solid line, alpha free base. The extinction coefficient of the alpha is calculated on the assumption that one mole of chlorin is formed for each mole of alpha used up in the conversion of alpha to chlorin by 1,2-naphthoquinone (see discussion).

(4) The spectra of porphine and chlorin free bases show very marked changes with changes in temperature. The spectra of alpha, however, is unaffected by temperature changes (other than the usual band sharpening at low temperatures (see Fig. 4)). The spectral shifts observed with porphine and chlorin free bases have been interpreted on the basis of changes in the equilibrium concentrations of very similar N–H tautomers of the type[8]



In the case of a tetrahydroporphine, such isomers are not of nearly identical energy as they are for porphines and chlorins but are of much different energy due to the fact that a hydrogen cannot be bonded to a reduced pyrrole ring without requiring either a disruption in the conjugated single–double system or a separation of charge in the molecule. A tetrahydroporphine should therefore exist essentially as a single species over a wide range of

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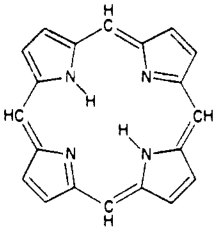
[7] For example, consider the equilibrium, $PH_2 + 2H^+ \rightleftarrows PH_4^{++}$. In the case of the porphine, two resonance forms of type I and eight of type II may be written for the free base, and 12 resonance forms of type III may be written for the acid salt. In the free base, the contribution of type II forms to the resonance hybrid results in a negative charge on the two center nitrogens which will accept the protons, facilitating their acceptance. In the acid salt, the two positive charges on the nitrogens are distributed among all four nitrogens, thus decreasing the tendency of any one nitrogen to lose its proton. Both of these effects operate in the direction of increasing the base strength. In the case of tetrahydroporphine, low energy forms of type II may not be written, and only two low energy resonance forms for the acid salt may be written, both of which carry single positive charges on the two nitrogens which are in the reduced pyrrole rings. Relative to the porphine, then, the tetrahydroporphine has less of a tendency to pick up a proton, and the acid salt more of a tendency to lose a proton. (This argument may be made on the basis of resonance energies rather than on the basis of the charge displacements resulting from resonance; the two treatments are in reality the same.) The base strength of the chlorin is predicted to lie between the two extremes of the porphine and the tetrahydroporphine.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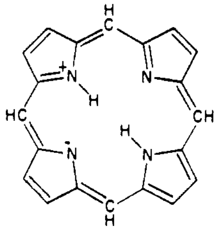
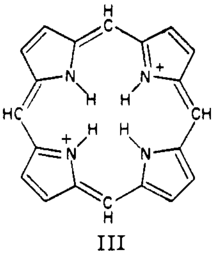

II


III

A similar resonance treatment predicts the equilibrium $PH_2 \rightleftarrows P^{--} + 2H^+$ to lie further to the left in the case of the tetrahydroporphine as compared to the porphine, with the chlorin again occupying an intermediate position.

[8] G. D. Dorough and K. T. Shen, THIS JOURNAL, 72, 3939 (1950).

temperature. The spectral behavior of alpha with changing temperature is therefore indicative of a tetrahydroporphine structure.

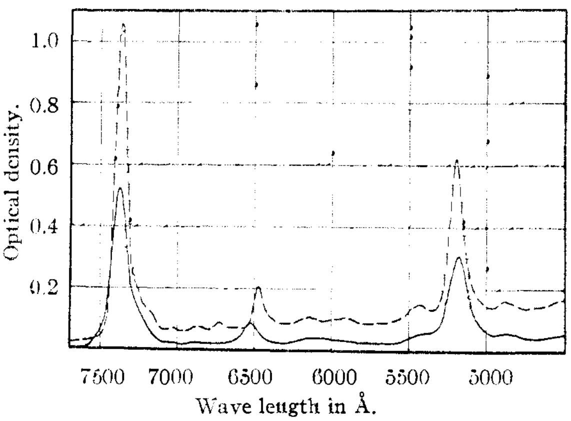


Fig. 4.—Spectra of alpha free base at different temperatures: solid line, room temperature; dotted line, liquid nitrogen temperature. (Uncorrected for contraction of solvent. The factor is 0.76. Notice that the peak at 6500 Å., which is due to a small amount of chlorin impurity, shifts with temperature. The solvent for this experiment was an ether, isopentane, alcohol mixture in the ratio of 5:5:2.)

To summarize, alpha has a spectrum like that of a known tetrahydroporphin, is at a reduction level more reduced than a chlorin, can be oxidized to the chlorin by a reagent which attacks saturated pyrrole rings in reduced porphyrins, and possesses chemical and physical properties either recorded for or to be expected of tetrahydroporphines. Alpha therefore appears to be a tetraphenyltetrahydroporphine.

A complete identification of alpha would require some type of quantitative analysis which would show that it possessed two more hydrogens than tetraphenylchlorin, and some sort of information which would permit one to place the extra hydrogens on either adjacent or opposite pyrroles. We have no information which could be considered to meet the latter requirement, other than the somewhat tenuous evidence that bacteriochlorophyll is reduced on opposite pyrroles, and that alpha is spectrally similar to bacteriochlorophyll. (The spectral characteristics of a tetrahydroporphine with adjacently reduced pyrroles are unknown.) The former requirement might be met by the usual analysis for the percentage of the elements, although the C and H values of tetraphenyltetrahydroporphin do not differ very much from those of the corresponding chlorin. (For tetraphenylchlorin: C, 85.68; H, 5.24. For tetraphenyltetrahydroporphin: C, 85.41; H, 5.54.) However, since alpha is obtainable in only very low yields from a starting product which itself is not too readily available, we were not able to procure enough alpha for a conventional microanalysis. Several attempts were made to follow the reaction of 1,2-naphthoquinone and alpha quantitatively on a 15–30 microgram scale, the assumption being that if a 1:1 ratio of alpha reacted to naphthoquinone used could be demonstrated, this would be strong evidence that alpha was a tetrahydroporphine. The experiments were not successful due to difficulties involved with oxygen removal and quinone volatility.

The identification of beta has proven to be very elusive. Like alpha, beta may be photoöxidized to tetraphenylchlorin with 1,2-naphthoquinone, which would suggest that beta might also be a tetrahydroporphine (*e.g.*, a tetrahydroporphine with adjacent pyrroles reduced is a possibility). However, the other properties of beta such as its spectrum, its ability to form readily acid salts and metallo-derivatives, and the behavior of its spectrum when the temperature is changed are similar to the properties of a chlorin. One possibility is that the catalytic hydrogenation has effected a reduction of a benzene ring to a cyclohexadiene ring to give a compound which would have the properties of a chlorin and yet be more reduced than a chlorin. The absorption spectra of the free base and the zinc derivative of beta are given in Fig. 5. The molar extinction coefficient of the free base was calculated from a quinone oxidation experiment on the assumption that one mole of chlorin is formed for each mole of beta oxidized. The value was 29,000 at 5910 Å. in benzene solution at room temperature.

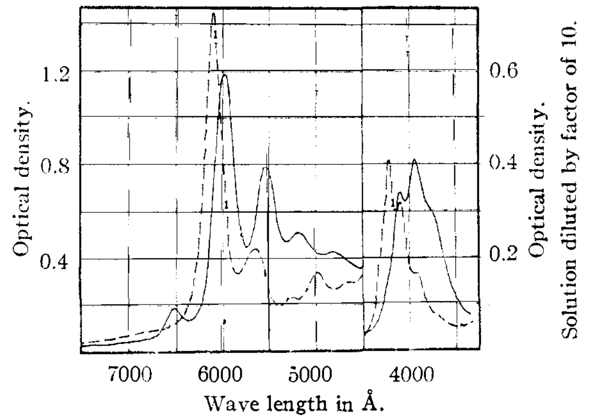


Fig. 5.—Absorption spectra in benzene: dotted line, zinc-derivative of beta; solid line, beta free base. The small peak at about 6500 Å. is due to chlorin impurity.

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The Diffusion Coefficient of Cupric Glycinate

BY ROBERT B. DEAN[1] AND HENN SOONPÄÄ[2]

RECEIVED AUGUST 5, 1952

Cupric glycinate is one of the few non-ionic water-soluble colored molecules. Since it showed promise as a colorimetric standard for calibrating diffusion cells we have determined the diffusion coefficient, D, in sintered glass diffusion cells[3] using KCl as a standard.[4] The membrane surfaces were stirred by magnetic stirrers encased in polythene. The denser solution was on top to facilitate stirring of the more remote parts of the cells.

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(1) Borden Co., Chemical Division, Bainbridge, N. Y.

(2) Based on material in the thesis of Henn Soonpää filed in the University of Oregon Library; M.S., 1953.

(3) J. W. McBain and C. R. Dawson, *Proc. Roy. Soc.* (*London*), **A118**, 32 (1935).

(4) A. R. Gordon, *Ann. N. Y. Acad. Sci.*, **46**, 301 (1945).

Cupric (di) glycinate was prepared from glycine and a small excess of freshly precipitated and washed basic cupric carbonate. It was purified by repeated crystallization from water and obtained as the monohydrate. The solutions were analyzed on a Beckman spectrophotometer. The composition of the crystals was determined by iodometric titration for copper. At 25° the solubility was 0.0364 M and the molar extinction coefficient at 6300 Å. was 46. The molar conductivity was 2.8×10^{-6} mho cm.$^{-1}$ indicating very slight dissociation into ions.

Values of D obtained at 0.00917 M and 0.0274 M were not significantly different and the pooled results gave a normal cumulative probability distribution. The mean value of D at 25.0 was $0.723 \pm 0.004 \times 10^{-5}$ cm.^{2} sec.$^{-1}$. The indicated error is the 95% confidence range for the mean.[5] The molar volume was found from density measurements to be 100.4 cm.^{3} and independent of concentration. D calculated from the Einstein–Sutherland equation assuming a sphere is 0.717×10^{-5}. If approximate corrections for departures from a spherical shape are applied D is calculated to be 0.67×10^{-7}.[6]

[5] R. B. Dean and W. J. Dixon, *Anal. Chem.*, **23**, 636 (1951).

[6] F. Perrin, *J. phys. radium.* [7] **7**, 1 (1936).

DEPARTMENT OF CHEMISTRY
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EUGENE, OREGON

The Distribution of the Subgroup VII Elements between Pyridine and 4 N NaOH[1]

BY W. GOISHI[2] AND W. F. LIBBY

RECEIVED JULY 28, 1952

In the course of studies directed toward the development of a new method for isolating technetium activities from meson irradiated silver samples, extraction from basic media with pyridine was attempted. It appeared reasonable to try this in view of the fact that permanganate has been found to be extractable under these conditions.[3] A preliminary experiment with carrier-free $NH_4Tc^{99}O_4$ indeed showed that pyridine extracted pertechnetate almost quantitatively from 4 N NaOH. The following is a report of the results of the distribution measurements which were made. The distribution of +7 rhenium and of +7 manganese between the same liquids was also studied.

Experimental

Perrhenate.—Measured volumes of 4 N NaOH containing known amounts of NH_4ReO_4 were equilibrated with measured volumes of pyridine saturated with 4 N NaOH. The layers were analyzed by acidifying to about 4 N with HCl, heating almost to boiling, precipitating Re_2S_7 by passing in hydrogen sulfide,[4] dissolving the collected precipitate in a 1:1 mixture of 6 N NaOH and 30% H_2O_2, and gravimetrically determining the amount of rhenium by conversion to the tetraphenylarsonium derivative.[5] In each case the sulfide precipitation was repeated on the filtrate from the first sulfide precipitation after first diluting with 4 N HCl, until no more sulfide was precipitated.

Technetium.—Carrier-free $NH_4Tc^{99}O_4$ solutions were extracted with pyridine exactly as in the perrhenate extractions. Measured volumes of standardized NH_4ReO_4 solution were added to the separated layers and the sulfide precipitated[6] and determined as the tetraphenylarsonium derivative as before. The tetraphenylarsonium perrhenate precipitates carrying the pertechnetate[7] were measured with a Geiger counter for their Tc^{99} content.

Manganese.—A small measured volume of a freshly prepared dilute solution of $KMnO_4$ was poured into a centrifuge bottle containing some pyridine. After shaking for a few seconds 4 N NaOH was poured into the bottle, the mixture again shaken for a few seconds and then immediately centrifuged to hasten the separation of the layers. Speed was essential to minimize the decomposition of the permanganate to form the green manganate. The alkaline layer was siphoned off and a measured portion of it was reextracted with a measured volume of pyridine. A measured volume of the first pyridine extract was diluted with pyridine until a color match was obtained visually between the diluted solution and the second pyridine solution with the two solutions in long test-tubes filled to the same depth.

The results obtained are summarized in Table I.

TABLE I

DISTRIBUTION BETWEEN PYRIDINE AND 4 N NaOH

Element, M	Distribution coefficient, $\frac{[M]_{Py}}{[M]_{aq}}$	$[M]_{Py}$, (mg. of M/ml.)
Re	255	3.8
	195	7.4
	130	12.8
	30	13.5
Tc	778	3.8×10^{-5}
Mn	8000	5

It is clear from Table I that all the subgroup VII elements in their heptavalent states are extractable into pyridine from strongly alkaline aqueous solution.

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[1] This research was supported in part by the Office of Scientific Research of the Air Research and Development Command of the U. S. Air Force.

[2] A.E.C. Predoctoral Fellow.

[3] H. C. Hornig, G. L. Zimmerman and W. F. Libby, THIS JOURNAL, **72**, 3808 (1950).

[4] W. Geilman and F. Weibke, *Z. anorg. Chem.*, **195**, 289 (1931).

[5] H. H. Willard and G. M. Smith, *Ind. Eng. Chem., Anal. Ed.*, **11**, 305 (1939).

[6] C. Perrier and E. Segrè, *J. Chem. Phys.*, **5**, 712 (1937).

[7] C. D. Coryell and N. Sugarman, "Radiochemical Studies: The Fission Products," Book 3, Part VI, Paper 259 by L. E. Glendenin, National Nuclear Energy Series, McGraw-Hill Book Co., Inc., New York, N. Y., 1951.

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Polarographic Behavior of Organic Compounds. XIII. Chloroacetic Acids and their Ethyl Esters. *p*H-Independence of Carbon–Halogen Bond Fission. Wave Splitting Due to Buffer Interaction

BY PHILIP J. ELVING* AND CHING-SIANG TANG

RECEIVED NOVEMBER 20, 1951

In view of the S-shaped relation between pH and $E_{1/2}$ for the polarographic reduction of acids of various types[1,2] including those involving carbon–halogen bond fission, the related system of acid–

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* University of Michigan, Ann Arbor, Mich.

[1] P. J. Elving, I. Rosenthal and M. K. Kramer, THIS JOURNAL, **73**, 1717 (1951). This paper includes a bibliography on the polarographic reduction of carbon–halogen bonds, to which the following studies in unbuffered solution should be added: (a) L. Riccoboni, *Gazz. chim. ital.*, **72**, 47 (1942); (b) G. K. Simpson and D. Traill, *Biochem. J.*, **40**, 116 (1946); (c) A. C. Stromberg and L. M. Resinus, *J. Gen. Chem.* (*U.S.S.R.*), **16**, 1431 (1946); in buffered solution, P. J. Elving and C. L. Hilton, THIS JOURNAL, **74**, 3368 (1952).

[2] P. J. Elving, J. C. Komyathy, R. E. Van Atta, C. S. Tang and I. Rosenthal, *Anal. Chem.*, **23**, 1218 (1951).

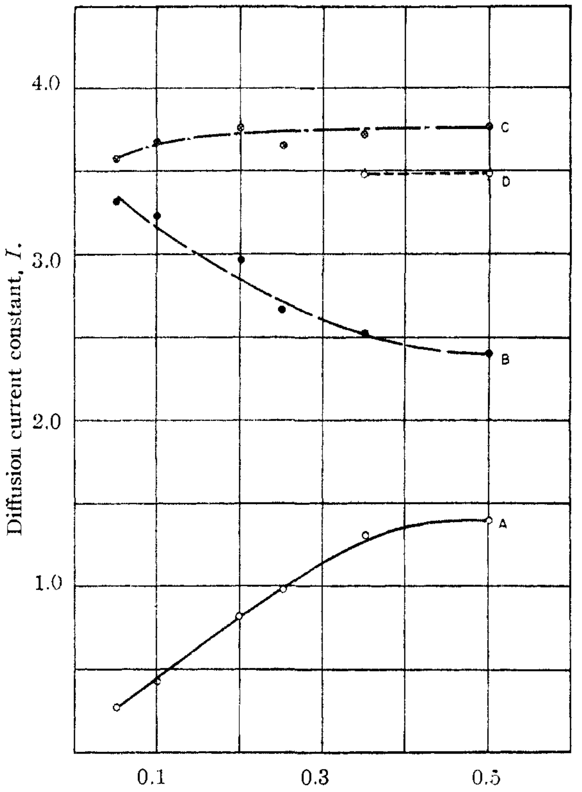

Fig. 1.—Variation of diffusion current constant, I, of trichloroacetic acid with concentration of buffer component: (A) Cl-3 wave (interaction with buffer component); (B) Cl-3 wave (non-interaction with buffer component); (C) total Cl-3 wave; (D) Cl-2 wave.

anion–ester was investigated in order to (1) elucidate further the connection between the S-shaped curve and the nature of the electroactive species and (2) determine the relative effect of the functional entities of carboxyl, carboxylate anion and carboxylate ester on carbon–halogen bond fission. The three chloroacetic acids were studied over *p*H range 0.7 to 11 at an ionic strength of 0.5 *M;* for comparison, runs were made at other ionic strength levels. In order to decrease the extent of hydrolysis observed at 25°, their ethyl esters were also studied at 0°. In addition, various substituted acetic acids were examined.

Chloroacetic Acids in Buffered Solution.—The data[3] were extended to cover the *p*H range at different ionic strength levels (Figs. 1 and 2). The waves, as indicated by the temperature coefficient of i_d, were diffusion-controlled; n, based on the Ilkovic equation, was 2 for all normal waves.

Within the potential range available, no wave was observed for chloroacetic acid. Dichloroacetic acid gave one wave (Cl-2 wave[1]) between *p*H 6.85 and 11.3, whose $E_{1/2}$ was *p*H-independent. Due to hydrogen ion discharge, no wave was obtained below *p*H 6.85.

Up to *p*H 3.1, trichloroacetic acid gave one wave, whose $E_{1/2}$ varied slightly from *p*H 0.7 to 2.2 and rapidly from *p*H 2.2 to 3.1. The diffusion current constant, I, and α values diminished with increasing *p*H. From *p*H 7.7 to 11.3 two waves were obtained; the characteristics of the second wave are those of the Cl-2 wave. $E_{1/2}$ of the first wave (Cl-3 wave) was also *p*H-independent; I values of both waves were equal. Two waves of *p*H-independent $E_{1/2}$ were obtained in the intermediate *p*H region of 4.4 to 5.9; the sum of their I values was equal to I of the Cl-3 wave. Three waves were obtained at *p*H 6.9, 7.1 and 8.8; the third wave is a Cl-2 wave. Since the sum of the I values of these first two waves is equal to I for the Cl-3 wave, the result of the processes giving rise to the first two waves at *p*H 4.4 to 8.8 is equivalent to the Cl-3 wave.

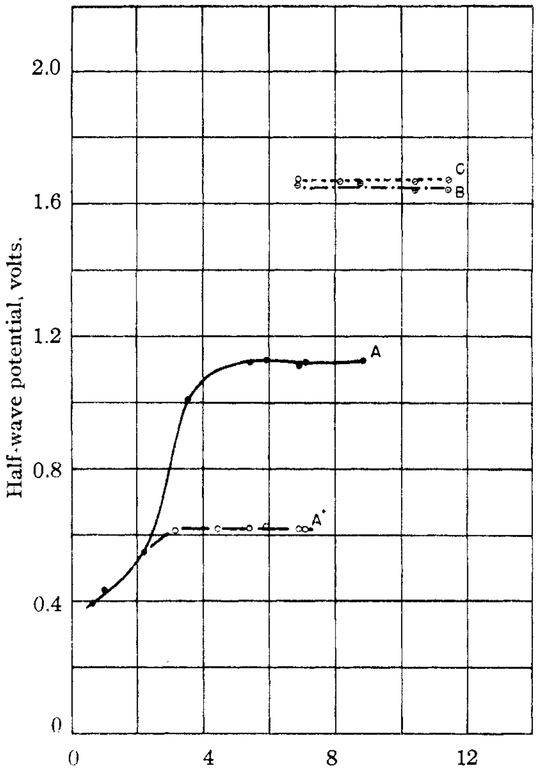

Fig. 2.—Variation of half-wave potential, $E_{1/2}$, with *p*H: (A) first wave of Cl-3; (A′) second wave of Cl-3; (B) Cl-2 wave of trichloroacetic acid; (C) Cl-2 wave of dichloroacetic acid.

The Split Anion Wave.—The characteristics of these first two waves are as follows for varying experimental conditions. (1) *p*H: From *p*H 4.4 to 7.1 $E_{1/2}$ and I values are independent of the *p*H at constant buffer component concentration and ionic strength.

(2) Buffer component concentration: At *p*H 8.8, I for the first wave increased as the buffer component concentration was increased while that of the second wave decreased. The sum of the I values was the same at each concentration. I of the first wave is lower in buffer 4 than in buffer 3 at the same concentration of buffer component. The I total of the two waves is identical in both buffers.

(3) Ionic strength: Ionic strength was increased by either increasing the buffer component concentration or adding potassium chloride. Two well-

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(3) P. J. Elving and C. S. Tang, This Journal, **72**, 3244 (1950).

defined waves were obtained at low ionic strength; these merged gradually at higher ionic strength. As the latter was increased from 0.05 to 0.5 at pH 5.4, $E_{1/2}$ for the first wave became 0.4 v. more negative, while $E_{1/2}$ for the second wave became 0.15 v. more positive. Within experimental error, both of these changes of $E_{1/2}$ with ionic strength appear to be linear. When the concentration of the buffer component was increased at constant ionic strength, $E_{1/2}$ values were not changed; I of the first wave increased and that of the second wave decreased. Increasing KCl concentration at constant ionic strength did not affect I of either wave.

(4) Temperature coefficients of i_d indicate diffusion-controlled processes.

Since the amount of acid present above pH 4.4 is practically nil and the amount formed by the anion recombination during the reduction process is apparently negligible, the reduction processes involved are due to the anion of trichloroacetic acid. The effects observed can be explained on the basis that the anion exists in two reducible forms, one of which is due to interaction with the buffer component. Since I values for the first wave increase with increasing buffer component concentrations, that wave is due to the anion–buffer component complex. Since both waves are diffusion-controlled, the equilibria involving anion and buffer component are slow in rate as compared to the rate of reduction of the more readily reduced species.

$E_{1/2}$ of the complexed wave shifts to a more negative value as the ionic strength is increased, as found for the undissociated form of an acid,[2] while $E_{1/2}$ of the uncomplexed wave shifts to a more positive value in conformity with the expected behavior for an anionic form.[2] Accordingly, the interaction is between the trichloroacetate and $H_2PO_4^-$, $HPO_4^{=}$ or HOAc to form a more acidic species than the anion itself, since the fission of a carbon–halogen bond is more easily accomplished in the acidic form than in the corresponding anion form.[1,2] In view of the lack of interaction in the more alkaline region, it would seem that $H_2PO_4^-$ is the interacting species in phosphate solution.

Since only one Cl-3 wave was obtained in buffers 5 and 6, it is presumed that they did not interact in the same manner with trichloroacetate.

The $E_{1/2}$-pH relation for trichloroacetate tends toward the S-shape (Fig. 2). No limiting portion is obtained in the acidic region because trichloroacetic acid is a strong acid, and pH 0.7 is not sufficiently acidic for the pH-independent portion of the relation to be revealed.

Acids in Unbuffered Solution.—It is probable that many of the waves reported in the literature for organic acids in unbuffered solution are actually due to hydrogen ion discharge. Acetic, chloroacetic, 2-chloropropionic and phenylacetic acids gave no polarographic wave, other than base solution decomposition, in buffered solution over pH range 0.7 to 11; each gave one well-defined wave in unbuffered 0.5 M KCl solution. The latter wave is due to hydrogen ion discharge; its $E_{1/2}$ varies with the dissociation constant and concentration of the acid, *i.e.*, with the pH of the solution. The hydrogen discharge waves of dichloro- and trichloroacetic acids in unbuffered solution were poorly defined because they combined with the Cl-2 wave; i_d of the hydrogen wave can be estimated by deducting i_d of the Cl-2 wave from the observed i_d. The Cl-3 wave of trichloroacetic acid was clear; its $E_{1/2}$ and i_d are identical to those of the wave in the alkaline region. Therefore, trichloroacetic acid behaves in 0.5 M KCl solution (pH 3.5) as a mixture of hydrogen ion and trichloroacetate anion; the first wave is the Cl-3 anion wave and the second wave is composed of the Cl-2 and hydrogen waves. The hydrogen discharge wave for the chloroacetic acids has been reported by Korshunov, *et al.*,[4] who did not observe any wave due to carbon–halogen bond fission and therefore did not differentiate the discharge and fission waves.

Esters.—Ethyl chloroacetate gave one pH-independent wave in buffered and unbuffered solution ($E_{1/2} = -1.43$ at 25°). Below pH 6.8, hydrogen ion discharged before or with the reduction of the ester. Above pH 9.0, the ester was hydrolyzed. At 0°, $E_{1/2} = -1.50$ from pH 6.8 to 10.4 where the ester wave was obtainable. In buffered and unbuffered solution where hydrogen ion discharge or hydrolysis did not interfere, ethyl dichloroacetate gave two waves of $E_{1/2}$ -0.70 and -1.43 at 25°, and -0.86 and 1.50 at 0°. Under similar conditions, ethyl trichloroacetate gave three waves only at 0° of $E_{1/2}$ -0.22, -0.86 and -1.51.

The I values for the different waves, *e.g.*, Cl-1 wave, was smallest for ethyl trichloroacetate, intermediate for dichloroacetate and largest for chloroacetate in conformity with the size and expected diffusion coefficients of the esters. Each wave is diffusion-controlled and irreversible; α varied from 0.3 to 0.4 for the Cl-1 and Cl-2 waves, and from 0.7 to 0.8 for the Cl-3 wave; n was two for each wave.

Relative Effect of the Functional Group.—Reduction of the polychloroacetic acids and their esters involves the successive removal of halogen atoms, *i.e.*, trichloroacetate to dichloroacetate to chloroacetate to acetate.[1,3] $E_{1/2}$ values of the esters are pH-independent. $E_{1/2}$ values of the acids are independent of pH in the region where the acid exists practically entirely as either the undissociated acid or the anion; in the intermediate pH region, $E_{1/2}$ becomes more negative as pH increases.

The effect of the polychloromethyl group on the fission of a carbon–chlorine bond in that group may be considered to be the same for all species derived from the same acid. The principal factor in the $E_{1/2}$ values obtained, therefore, must be the presence of the undissociated carboxyl group, the dissociated carboxyl group or the carboalkoxyl group. In determining the mechanism of carbon–halogen bond fission at an electrode, it would be helpful to know the effect of these groups on the chemical bond fission; this information is not available.

The electrochemical reduction of the carbon–halogen bond is accomplished most easily in the

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[4] I. A. Korshunov, Z. B. Kuznetsova and M. K. Shchennikova, *Zhur. Fiz. Khim.*, **23**, 1292 (1949); *C. A.*, **44**, 2873 (1950).

ester, followed in turn by the acid and then the anion. Comparison of the behavior of acid, anion and ester must be made in light of the equilibrium effects[1,2] involved in the reduction of the anion. Study of the effect of the alkoxyl group in halo esters[5] indicates that as the electron-releasing power of the ester group increases, the ease of fission increases. Similar evidence is found for the effect of chain length on the ease of carbon–halogen bond fission in the 2-bromo-*n*-alkanoic acids.[6]

Role of *p*H.—The behavior of the esters, in conjunction with the nature of the S-shaped curve for the *p*H-dependence of reduction in the acids, definitely establishes the fission of the carbon–halogen bond at the mercury electrode as a *p*H-independent process.

Experimental.—The general technique used has been described.[1,2,6] The buffers used and their *p*H range were: (1) KCl + HCl, 0.7 to 2.2; (2) NaOAc + HOAc, 4.5 to 5.5; (3) Na_2HPO_4 + citric acid, 3.1 to 7.3; (4) Na_2HPO_4, 8.6 to 8.9; (5) $NH_4Cl + NH_3$, 7.7 to 8.8; (6) Na_2HPO_4 + NaOH, 10.4 to 11.3.

Acknowledgment.—The authors wish to thank the Atomic Energy Commission and the Research Corporation for grants-in-aid.

[5] I. Rosenthal, C. S. Tang and P. J. Elving, THIS JOURNAL, **74**, 6112 (1952).

[6] I. Rosenthal, C. H. Albright and P. J. Elving, *J. Electrochem. Soc.*, **99**, 227 (1952).

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Polarographic Behavior of Organic Compounds. XIV. Carbon–Halogen Bond Fission in System Acid–Anion–Ester; Estimation of Acid Half-wave Potentials

BY ISADORE ROSENTHAL, CHING-SIANG TANG AND PHILIP J. ELVING*

RECEIVED MAY 8, 1952

A plot of half-wave potential, $E_{1/2}$ *vs.* *p*H for the α-halogenated acids yields an S-shaped curve,[1] of which only the low *p*H branch appears to be free of the influence of kinetic factors involving dissociation of the acid.[2] It is in this region, therefore, that comparison of $E_{1/2}$ values should have the clearest relation to the strength of the bonds cleaved at the dropping mercury electrode. Often, $E_{1/2}$ values for acids cannot be obtained in this low *p*H region due to prior appearance of a hydrogen discharge wave.[1b] The present study shows how these values may be obtained with reasonable accuracy from the $E_{1/2}$ values of the corresponding esters and sets forth the possibility that the relationship between acid and ester forms found with the halogenated acids may be used to good advantage in studying other difficultly reducible acids.

Study of the effect of *n*-alkyl substituents on $E_{1/2}$ of bromoacetic acid[2b] indicated that the ease of reduction increased with the size of the alkyl group. The present paper contains a similar study on the size of the alkoxyl group in chloroacetic ester; shifts in ease of reduction are interpreted in terms of structure.

Experimental

The experimental procedure has been described.[1b] The buffer solutions used (ionic strength of 0.5) and their *p*H were: (1) 0.5 *M* KCl with added HCl, 0.81, 1.20, 1.80; (2) 0.5 *M* NaOAc with added HOAc, 4.51, 5.51; (3) 0.5 *M* NH_4Cl (unbuffered), 4.9; (4) 0.5 *M* KCl (unbuffered), 5.5; (5) 0.5 *M* NH_4Cl with added NH_3, 8.20, 8.80.

Fresh stock solutions of the esters were prepared in aqueous 40% purified 1,4-dioxane as needed; the final test solution had a dioxane concentration of 2% which did not measurably affect the *p*H or polarographic behavior.

Results and Conclusions

Diffusion-controlled, irreversible waves[3] were obtained, whose *n* values (Ilkovic equation) indicated each wave to be due to a two-electron process as found for other carbon–halogen bond fission processes.[1,2]

Ethyl bromoacetate and the three chloroesters each give one well-defined wave of *p*H-independent $E_{1/2}$ in both unbuffered and buffered solution; this wave represents conversion to ethyl acetate (Br-1 and Cl-1 waves[1b,c]). Ethyl dibromoacetate and tribromoacetate each give two waves. The more negative wave is, in each case, identical in behavior with that of ethyl bromoacetate. The more positive wave is due to the conversion of dibromoacetate ester to bromoacetate ester; the expected Br-3 wave representing the reduction of the ethyl tribromoacetate to dibromoacetate cannot be observed due to mercury oxidation.

The diffusion current constants, *I*, for the bromoacetate wave of each bromo ester are constant over the *p*H range, but are different among the three esters with ethyl bromoacetate having the largest *I* (2.7), followed in decreasing order by the dibromoacetate (2.2) and the tribromoacetate (1.6). This decrease in *I* is connected with the nature of the step-wise reduction process. With ethyl tribromoacetate, *e.g.*, the only monobromoacetate present is that formed by the reduction of the tribromoacetate and so the rate of supply of the monobromoacetate to the electrode is controlled by the rate of diffusion of the tribromoacetate. This explains why *I* values vary inversely with the size of the parent molecule even though the carbon–halogen bond fission in each case occurs in the same molecule.

Similarly, the slightly different *I* values (Me 2.2, Et 1.8, Bu 1.7) among the chloroesters are expected since the methyl ester being the smallest molecule of the three esters would be expected to have the largest diffusion coefficient and hence the largest i_d.

At 25° and *p*H 8.8, ethyl bromoacetate gave two well-defined waves ($E_{1/2}$ −0.43 and −1.24). The more positive wave was due to ester reduction, while the other wave was that of bromoacetic acid, indicating partial hydrolysis of the ester. Accord-

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[1] (a) P. J. Elving and C. S. Tang, THIS JOURNAL, **72**, 3244 (1950); (b) *ibid.*, **74**, 6109 (1952); (c) P. J. Elving, I. Rosenthal and M. K. Kramer, *ibid.*, **73**, 1717 (1951).

[2] (a) P. J. Elving, A. J. Martin, C. S. Tang and I. Rosenthal, *Anal. Chem.*, accepted for publication; (b) I. Rosenthal, C. H. Albright and P. J. Elving, *J. Electrochem. Soc.*, **99**, 227 (1952).

[3] $E_{1/2}$ values in volts at 0°. Ethyl esters: bromoacetate −0.47 (−0.43 at 25°); dibromoacetate −0.08 and −0.48; tribromoacetate −0.08 and −0.48. Chloroacetate esters: methyl −1.54, ethyl −1.50, *n*-butyl −1.41.

ingly, the kinetics of hydrolysis of the ester could be studied polarographically.

In order to compare the reduction of undissociated acid and ester, a check run was made with dibromoacetic acid under the same experimental conditions used with the esters. $E_{1/2}$ for the two waves at pH 1.0 and 0° are −0.16 and −0.62.

Discussion

Waves for carbon–chlorine bond fission in chloro- and dichloroacetic acids cannot be obtained in the pH region where these acids are undissociated, due to hydrogen wave interference. This is not the case with bromo- and dibromoacetic acids or with the most positive wave of trichloroacetic acid. The esters of the latter acids are uniformly more easily reduced than the corresponding acid, the differences ranging from 0.08 to 0.23 v.

On the basis of this behavior, it is possible to predict from a knowledge of $E_{1/2}$ for the esters of chloro- and dichloroacetic acids the $E_{1/2}$ values for the corresponding waves in the undissociated acids (Table I). The average $\Delta E_{1/2}$ (0.15 v.) between the ester and undissociated acid forms for the species for which data are available has been added to the experimental value of $E_{1/2}$ for the ester to obtain a probable $E_{1/2}$ value for the acid. The error given for the latter value is the average deviation of the $\Delta E_{1/2}$ values. Although the error may seem large compared to the $\Delta E_{1/2}$ value, the magnitude of the latter plus the error is small compared to the range of potential in which the acid $E_{1/2}$ may fall.

TABLE I

COMPARISON OF $E_{1/2}$ VALUES FOR ESTER, UNDISSOCIATED ACID AND ANION FORMS OF THE BROMO- AND CHLOROACETIC ACIDS[a]

	Ethyl ester	Acid[b]	Anion[b]
Bromoacetic	−0.48	−0.62	−1.22
Dibromoacetic	−0.08	−0.16	−1.41
Tribromoacetic	Merges with Hg oxidation	At pH 3.7, E is −0.08 v.	−0.32
Chloroacetic	−1.49[c]	1.64 ± 0.07[e]	
Dichloroacetic	−0.86[c]	1.01 ± 0.07[e]	−1.60[c]
Trichloroacetic	−0.22[c]	−0.45[d]	−1.00[c]

[a] All data at 0° except for the anion values of the bromoacetic acids which are at 25° (reference 1c). [b] The acid value is taken from the pH-independent branch of the $E_{1/2}$ *vs.* pH plot, that occurs in the low pH region. This region varies with the acid but occurs generally between pH 0.0 and 2.0. The anion values are taken similarly from the high pH branch of the $E_{1/2}$–pH plot that starts at about pH 6.0 to 8.0, *i.e.*, all anion values are taken with NH_4Cl–NH_3 buffers at pH 8.2 except that of tribromoacetic acid, which is taken with a MacIlvaine buffer at pH 7.7. [c] These values are from reference 1b. [d] This value is the result of an extrapolation of data in reference 1b to the pH-independent acid value. Due to the strongly acidic nature of trichloroacetic acid, the $E_{1/2}$–pH curve in the acid region is not truly pH-independent at the lowest pH values, *ca.* 1.0, for which measurements were taken. However, sufficient data exist to permit extrapolation to the pH-independent region which appears to start at about pH 0.0. [e] Postulated values; see text.

The importance of this type of relationship in $E_{1/2}$ for acid, anion and ester is exemplified when the polarographic behavior of chloroacetic acid is analyzed. The wave for the latter could not be obtained in buffered solution in the usual pH range although different buffers, ionic strengths and temperatures were used. In the acid region, its $E_{1/2}$ of −1.64 (calculated from the ester value) is beyond the hydrogen discharge wave; in the higher pH region, $E_{1/2}$ shifts so that it is beyond the discharge potentials of the common cations. For similar reasons, the wave for its ester cannot be obtained in the acid region. However, since $E_{1/2}$ for the ester wave is pH-independent, its value can be determined at any pH, *e.g.*, in the alkaline region where the available potential span before background electrolyte decomposition is much greater than in the acid region. In general, if the wave for a particular acid cannot be obtained in buffered solution, the possibility exists of studying its ester in buffered or unbuffered solution to obtain a value characteristic of the undissociated acid.

In studying the effect of alkyl substituents on $E_{1/2}$ of bromoacetic acid,[2b] it was found that replacement of a hydrogen by a methyl group, *i.e.*, insertion of a methylene group, caused a shift of about +0.20 v. Successive insertions of methylene groups, *i.e.*, 2-bromo-*n*-butyric acid to 2-bromo-*n*-octanoic acid, caused a smaller (+0.04 v.) but steady decrease in $E_{1/2}$. Since the inductive effect would vanish after at least the ethyl group, the cause for the continuing decrease was thought to be due to an increase in the free energy of adsorption as the alkyl fragment of the molecule increased. Support for this concept is found in the adsorption of alcohols from the vapor phase on mercury,[4] where the increase in the free energy of adsorption is constant in going from butyl to hexyl alcohol. The data for the esters of chloroacetic acid fall in line with the explanation given for the behavior of the α-bromo acids, since there is a similar steady shift of about +0.04 v. in $E_{1/2}$ per methylene group. (It was assumed that the shift from ethyl to propyl would be one-half of that from ethyl to butyl.) The inductive effects on the carbon–halogen bond of replacing the hydroxyl hydrogen of the carboxyl group by a methyl group should be less than the corresponding case where the methyl group replaced a hydrogen on the α-carbon, since in the former case the substituent is further removed from the bond being broken.

An attempt to evaluate the effect of the substitute on the basis of Shikata's rule,[5] would lead to the prediction of an opposite shift, since any influence that increasing the size of the alkoxy group might have, would be in the direction of increasing the electron density on the α-carbon. Such behavior, according to Shikata, should cause polarographic reduction to become more difficult. The contrary nature of the experimental data indicates the caution necessary in attempting to predict polarographic behavior from Shikata's rule.

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Flavonoids of Various Prunus Species. I. The Flavonoids in the Wood of *Prunus yedoensis*

BY MASAO HASEGAWA AND TERUO SHIRATO

RECEIVED MAY 5, 1952

Introduction

Prunus yedoensis is the most commonly cultivated species of cherry tree in Japan. From the bark of this tree, Asahina[1] isolated sakuranin and proved that it is the 5-glucoside of sakuranetin, 4′,5-dihydroxy-7-methoxyflavanone.[2] Using the procedure of Asahina, *et al.*,[2] sakuranin has been easily obtained in the present study from the sample bark, of *Prunus yedoensis.* No sakuranin or sakuranetin, however, have been found in the heartwood or sapwood of this tree. Instead, detailed investigation has revealed the presence of genkwanin, naringenin and *d*-catechin in the heartwood and *d*-catechin and a new glucoside of naringenin in the sapwood.

Genkwanin was isolated for the first time from a Chinese drug "Yuen Hua" (flower buds of *Daphne Genkwa*) and characterized as 4′,5-dihydroxy-7-methoxyflavone by Nakao and Tseng.[3] It has also previously been isolated from the bark of *Prunus puddum*[4] and from the bark of *P. serrulata* var. *spontanea*[5] as a glycoside called glucogenkwanin.[6] The well-known naringenin and *d*-catechin are 4′,5,7-trihydroxyflavanone and 3,3′,4′,5,7-pentahydroxyflavane, respectively.

Since the new glucoside of naringenin gives a brownish coloration when treated with ferric chloride, it is evident that the hydroxyl group in the position 5 of naringenin is free. When this glucoside was methylated by means of an insufficient quantity of diazomethane and then hydrolyzed, it gave a mixture of the unchanged and a methylated naringenin. This mixture was examined by paper chromatography, using benzene–ligroin (1:1) saturated with water, and added with a small quantity of methanol as the mobile phase.[7] By comparing with the spots given by the authentic specimens in the same chromatogram, we were able to detect with ease naringenin and isosakuranetin (naringenin 4′-methyl ether), but no trace of sakuranetin. Then it must be concluded that this glucoside is naringenin-7-glucoside and is therefore new to the literature. The name "prunin" is now proposed for it.

Prunin must be definitely different from salipurpin (naringenin-5-glucoside), which was isolated from *Salix purpurea* of Europe by Charaux and Rabaté[8] and determined in its constitution by Zemplén, *et al.*,[9] because the latter is said to give no coloration with ferric chloride.

A sample of floribundin, a naringenin glucoside from the flowers of *Acacia floribunda*,[10] which was sent by Prof. R. Paris, also gave a negative ferric chloride reaction. No direct comparison could be made with the naringenin glycoside isolated from the flowers of *Antirrhinum majus* by Seikel and Geissman.[11] These workers did not obtain this glycoside in crystalline form.

Experimental

Isolation of Naringenin, Genkwanin and *d*-Catechin from the Heartwood.—Three hundred grams of heartwood chips of *Prunus yedoensis* prepared from living stems (those from previously cut dead stems gave almost the same results) was twice extracted with 3-l. portions of methanol for 3 hours. The methanolic filtrates were concentrated to about 150 ml. on a water-bath and then filtered. Yellow crystals of crude genkwanin separated out gradually in the course of a week or two. On recrystallization from methanol, yellow needles, m.p. 267°, uncor., were obtained with a yield of 0.4 g. After 3 recrystallizations from methanol the m.p. was 282°.

The mother liquor was repeatedly extracted with ethyl acetate, and the combined extract was evaporated to dryness and the residue dissolved in hot water. The aqueous solution was extracted with ether until the extract gave no color with magnesium powder and concentrated hydrochloric acid. After the combined ethereal extract was evaporated, the residue was dissolved in methanol and allowed to stand. Naringenin gradually deposited in white needles of m.p. 236° (yield 5.1 g.). After 3 recrystallizations from methanol, m.p. was 248°.

The mother liquor treated with ether was evaporated to dryness, the residue was extracted with hot water, and the solution was filtered. From the filtrate, *d*-catechin was precipitated, yield 1.1 g. After 5 recrystallizations from water, colorless needles of *d*-catechin (m.p. 97°) were obtained. From the water-insoluble portion, a further small amount of naringenin was eventually obtained.

I. **Genkwanin.**—The crystals contained no water of crystallization.

Anal. Calcd. for $C_{15}H_9O_4(OCH_3)$: C, 67.13; H, 4.89; OCH_3, 10.91. Found: C, 66.59; H, 4.43; OCH_3, 10.41.

Absorption: λ_{max} 355 mμ, log ϵ 4.38; λ_{max} 256 mμ, log ϵ 4.28; λ_{min} 290 mμ, log ϵ 4.13.

The diacetate of genkwanin was obtained in white needles of m.p. 202°.

Anal. Calcd. for $C_{15}H_7O_4(OCH_3)(CH_3CO)_2$: OCH_3, 8.42. Found: OCH_3, 8.60.

4′-Monomethyl ether of genkwanin was prepared by gently boiling a mixture of genkwanin (0.2 g.), acetone (30 ml.), dimethyl sulfate (1 ml.) and potassium carbonate (3 g.) on a water-bath; yellow prisms of m.p. 171°. This melting point was not altered by admixing with authentic specimens of acacetin 7-methyl ether (5-hydroxy-7,4′-dimethoxyflavone) of m.p. 171°.

Anal. Calcd. for $C_{15}H_8O_3(OCH_3)_2$: OCH_3, 20.80. Found: OCH_3, 20.66.

The 5-acetate of this methyl ether was colorless needles of m.p. 195°.

II. **Naringenin.**—The crystals of naringenin contained no water of crystallization.

Anal. Calcd. for $C_{15}H_{10}O_5$: C, 66.17; H, 4.41. Found: C, 66.75; H, 4.66.

Absorption: λ_{max} 312 mμ (inflection); λ_{max} 288 mμ, log ϵ 4.23; λ_{min} 252 mμ, log ϵ 3.17.

Naringenin triacetate was obtained in colorless long needles of m.p. 126°, as described by Seikel and Geissman[11]; 3.45 mg. subst., 2.41 ml. 0.01 *N* NaOH; calcd. CH_3CO, 32.41; found CH_3CO, 32.34.

The 7,4′-dimethyl ether was prepared by heating an acetone solution of naringenin with dimethyl sulfate and potassium carbonate; colorless crystals of m.p. 120°; 4.870 mg. subst., 7.441 mg. AgI; calcd. OCH_3, 20.66; found: OCH_3, 21.06.

The acetate of this methyl ether was colorless needles of m.p. 161°.

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III. *d*-Catechin.—Water of crystallization: 12.64 mg. subst. (dried 1 hour over P_2O_5 in a vacuum) H_2O, 2.56 mg.

Anal. Calcd. for $C_{15}H_{14}O_6 \cdot 4H_2O$: H_2O, 20.25. Found: H_2O, 19.89.

The melting point of the anhydrous substance rose to 171–173°.

Anal. Calcd. for $C_{15}H_{14}O_6 \cdot 4H_2O$: C, 49.72; H, 6.07. Found: C, 49.39; H, 6.20.

Absorption: λ_{max} 280 mμ, log ϵ 3.60; λ_{min} 255 mμ, log ϵ 2.70.

d-Catechin acetate was colorless prisms of m.p. 131°.

Isolation of *d*-Catechin and Prunin from the Sapwood.—Five hundred grams of the sapwood chips were boiled for 3 hours with 3 l. of methanol. The methanolic extract was concentrated to 100 ml., and the solution was extracted with ether. The ethereal layers were evaporated and the residue was recrystallized from water. After 5 recrystallizations, *d*-catechin of m.p. 97° (yield 0.95 g.) was obtained.

The mother liquor was then extracted exhaustively with ethyl acetate. After evaporation of the solvent, the residue was dissolved in 100 ml. of water and 50 ml. of ethyl acetate was added. From the solution an oily mass was gradually separated after standing several days. From the filtered solution ethyl acetate was distilled off, and the residue was dissolved in methanol. The methanolic solution was, after evaporation to a sirup, allowed to stand at room temperature. After about 3 days standing, white crystals of prunin appeared in the solution. The white mass of prunin was collected and crystallized from a small amount of methanol, added with a few drops of water. Prunin was then obtained in colorless needles of m.p. 225°. The yield of the crude substance was 0.7 g.

IV. Prunin.—Prunin is soluble in alcohol, ethyl acetate and acetone, sparingly so in methanol and insoluble in ether benzene and chloroform. A methanolic solution gave a brown-violet coloration with ferric chloride. In alcoholic solution it gave a reddish purple coloration with magnesium powder and concd. hydrochloric acid; specific rotation: 0.311 g. subst., 25 ml. acetone, 1 dm. tube; $\alpha_D = -0.52°$, $[\alpha]_D = -41.8°$.

Absorption: λ_{max} 308 mμ (inflection), log ϵ 4.12, λ_{max} 283 mμ, log ϵ 3.44.

The sample was dried over P_2O_5 in a vacuum at 110–115°; 3.084 g. subst., 6.532 g. CO_2, 1.366 g. H_2O.

Anal. Calcd. for $C_{21}H_{22}O_{10}$: C, 58.0; H, 5.0. Found: C, 57.80; H, 4.96.

Hydrolysis of Prunin.—Three-tenths gram of prunin, suspended in 20 ml. of 10% sulfuric acid, was heated 30 minutes on a water-bath. The aglycone which gradually deposited was filtered (yield 0.15 g.), m.p. 246°. This substance was identified with naringenin through a mixed melting point determination. After extracting with ether, the mother liquor was carefully neutralized with barium carbonate, filtered and evaporated on a boiling water-bath to a small volume, and then filtered again. When the filtrate was heated with phenylhydrazine hydrochloride and sodium acetate, glucosazone was formed. After recrystallization from methanol, it melted at 207°, both alone and on admixture with the authentic specimen. By the paper chromatographic method any sugar except glucose could not be detected.

A suspension of 0.31 g. of prunin in 50 ml. of 1% sulfuric acid was boiled for 1 hour. After extraction with ether, the mother liquor was neutralized with 10% sodium hydroxide. In this solution 121.5, 118.5 mg. of glucose was found according to the method of Bertrand. When postulated as naringenin: glucose = 1:1, the theoretical yield of glucose would be 128.9 mg.

Position of the Sugar in Prunin.—Fifty mg. of prunin was methylated by heating in 30 ml. of acetone with 1 mg. of dimethyl sulfate and 5 g. of potassium carbonate for 30 minutes under reflux.

After filtering, the solution was evaporated, and the residue was recrystallized from dilute methanol. A small amount of crystals thus obtained was hydrolyzed by boiling with 1% hydrochloric acid for 30 minutes and the resultant solution was shaken several times with ether. The ethereal solution was evaporated to dryness, and the residue was examined by paper chromatography, using a mixture of benzene and ligroin (1:1), saturated with water, and added with a small quantity of methanol as the mobile phase.[7] When developed with 1% methanolic ferric chloride solution, two spots, with R_f values of 0.05 and 0.00, respectively, were obtained. Authentic specimens of naringenin gave an R_f value of 0.05 and that of isosakuranetin 0.00, whereas sakuranetin gave the R_f value 0.73 in the same chromatogram.

Prunin Dimethyl Ether.—Two-tenths gram of prunin was dissolved in 30 ml. of acetone and heated after addition of 5 g. of potassium carbonate and 2 ml. of dimethyl sulfate for 6 hours. At that time, it gave no color reaction with ferric chloride. After filtering, acetone was removed by distillation, and the residue crystallized from dilute methanol in white needles of m.p. 231°; yield poor; 3.21 mg. subst., 3.345 mg. AgI.

Anal. Calcd. for $C_{21}H_{20}O_8(OCH_3)_2$: OCH_3, 13.42. Found: OCH_3, 13.31.

Hydrolysis of Prunin Dimethyl Ether.—Hydrolysis of 50 mg. of prunin dimethyl ether was effected by heating in 20 ml. of 2% hydrochloric acid on a boiling water-bath for an hour. The turbid liquor was extracted 3 times with ether. After the ethereal extract was evaporated, the residue was recrystallized from dilute methanol. White needles of naringenin dimethyl ether (m.p. 187°) were obtained. As only a small quantity was available, no analysis could be made.

Acetate of Prunin. (1).—One-tenth gram of prunin was treated with acetic anhydride (1 ml.) and pyridine (1 ml.) in the cold for one hour. Cold water was then added and the solidified mass was filtered, washed and recrystallized from methanol. Colorless needles of m.p. 187–189° were obtained. The substance gave a purplish color reaction with ferric chloride. Owing to the scarcity of pure substance, no analysis was made.

(2).—One-tenth gram of prunin was mixed with acetic anhydride (1 ml.) and pyridine (3 drops) and the mixture was heated one hour on a water-bath. The reaction mixture was poured into water and the solidified mass was filtered, washed and recrystallized from carbon tetrachloride. Colorless needles of m.p. 138–139° were obtained. This substance was not analyzed because of the lack of a pure specimen.

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Hydrolysis and Halide Complexing of Indium(III)

BY L. G. HEPLER AND Z Z. HUGUS, JR.[1]

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In connection with other work in this Laboratory it became desirable to have a knowledge of the hydrolysis constant of In^{+3}. Hattox and DeVries,[2] from *p*H measurements in sulfate solutions at 23°, gave for the hydrolysis constant 2×10^{-4} in their most dilute (0.00631 *M*) solution. Sulfate complexing and bisulfate formation doubtless occurred in their solutions, and correction for these factors is difficult. Moeller[3] has measured the *p*H of aqueous solutions of $InCl_3$, $InBr_3$ and InI_3 over a range of concentrations at 25°. It is evident from

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(2) E. M. Hattox and T. DeVries, THIS JOURNAL, **58**, 2126 (1936).

(3) T. Moeller, *ibid.*, **63**, 1206 (1941); **64**, 953 (1942).

his calculated hydrolysis constants that complexing of In^{+3} by halide ions occurs in such solutions. We have systematically interpreted his data on the assumption of equilibria (1) and (2)

$$In^{+3} + H_2O = InOH^{+2} + H^+ \qquad (1)$$

$$In^{+3} + X^- = InX^{+2} \qquad (2)$$

X^- stands for Cl^-, Br^- or I^- in the appropriate cases. We may write the equilibrium constants for these reactions in terms of concentrations (moles/liter) of the various species $K_1 = (InOH^+)(H^+)/(In^{+3})$; $K_2 = (InX^{+2})/(In^{+3})(X^-)$.

If we denote the total concentration of indium (III) by m, it follows that

$$m = (In^{+3}) + (InOH^{+2}) + (InX^{+2}),\ (InX^{+2}) = 3m - (X^-), \text{ and } (InOH^{+2}) = (H^+)$$

Combining these relations we obtain equation (3)

$$\frac{m - (H^+)}{(H^+)^2} = \frac{3m\ K_2/K_1}{1 + (K_2(H^+)^2/K_1)} + \frac{1}{K_1} \qquad (3)$$

Assuming that $K_2(H^+)^2/K_1$ is small compared to unity equation (4) results.

$$\frac{m - (H^+)}{(H^+)^2} = 3m\frac{K_2}{K_1} + \frac{1}{K_1} \qquad (4)$$

From the experimental data,[3] the quantity $m - (H^+)/(H^+)^2$ was calculated for various values of m, in the range 5.10^{-4} M to 4.10^{-2} M, and plotted as a function of m. In accordance with equation (4) this plot was linear in dilute solutions. From the slope and intercept of this line values of K_1 and K_2 were calculated. An analytical treatment of the data using the interpolation formula of Lagrange[4] was also made. The values of K_1 and K_2 thus obtained agreed quite well with those found by the graphical method. Actually the graphical extrapolation is, to a certain extent, subjective and the agreement with the analytical procedure provides some justification for the graphical values. Although corrections involving the activity coefficients of the several species might be expected to affect the values of K_1 and K_2 by as much as 20%, we have not incorporated such corrections in our treatment since the graphical values (presumably pertaining to infinite dilution) and the analytical values (which are, in a sense, averages over a range of concentrations) are in accord.

Table I gives the values of K_1 and K_2 obtained by the analytical method. These values bear out the validity of the assumption that $K_2(H^+)^2/K_1$ is small compared to unity since (H^+) is of the order of 10^{-4} M in the solutions upon which the above calculations are based. K_1 is independent of the anion, and the halide complexing constants decrease with increasing anion radius as might be expected for electrostatically bonded complexes.

TABLE I

Solution	$K_1 \times 10^4$	K_2
$InCl_3$	1.36	225
$InBr_3$	1.38	159
InI_3	1.46	95.5

Equation (3) may be solved for (H^+) in terms of m, K_1 and K_2. Inserting the above values for these constants we have calculated (H^+) for various values of m. These calculated values of (H^+) together with the experimental values of Moeller are presented in Table II for several dilute solutions of each of the indium halides.

TABLE II

Solution	$m \times 10^3$	$(H^+) \times 10^4$ Calcd.	Exptl.
$InCl_3$	0.5	1.8	1.8
	5	4.1	4.0
	10	4.7	4.8
	20	5.0	5.7
$InBr_3$	2.5	3.8	3.8
	5	4.8	4.7
	20	6.0	6.6
	40	7.0	7.9
InI_3	2.5	4.3	4.3
	5	5.4	5.3
	10	6.5	6.6
	20	7.5	8.1

The agreement of the experimental and calculated values of (H^+) provides substantiation of the original assumption of equilibria (1) and (2) and also of the tabulated values of K_1 and K_2.

From the magnitude of the values given in Table I for K_1 and K_2 it may be seen that in concentrated solutions the hydrolysis reaction becomes

$$InX^{+2} + H_2O = InOH^{+2} + H^+ + X^- \quad (5)$$

since reaction (2) is virtually complete. Designating the equilibrium constant of reaction (5) as K_5 and using our previous notation

$$K_5 = \frac{(2m + (H^+))(H^+)^2}{m - (H^+)}$$

The values of K_5, calculated for solutions in which m is greater than 0.04 M, increase with m as would be qualitatively expected from the decrease in the activity coefficients of ionic species with increasing ionic strength. Quantitatively, however, the increase in K_5 is so great that the quotient of the activity coefficients must fall below the limiting Debye–Hückel values. While further halide complexing of InX^{+2} to form InX_2^+ doubtless occurs, the trend in K_5 can only be interpreted by assuming that the species $In(OH)X^+$ is also formed, and that it is more important than InX_2^+ in these solutions.

Since activity coefficient corrections are so important in these concentrated solutions (greater than 0.04 M) any quantitative calculation involving the complexes InX_2^+ and $In(OH)X^+$ is not possible with the present data.

We have selected an unweighted average of the values of K_1 given in Table I, $K_1 = 1.40 \times 10^{-4}$, as the "best" value for the hydrolysis constant of In^{+3}.

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Acetylation of Amylaceous Polysaccharides

BY ALLENE JEANES AND R. W. JONES

RECEIVED JULY 16, 1952

The frequent use of acetates of amylaceous substances in investigations on particle weight and

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[4] See for example, H. Margenau and G. M. Murphy, "The Mathematics of Physics and Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1943.

structure has motivated a long-continued search for practical methods for obtaining fully acetylated, undegraded products with favorable solubility characteristics. One of the most recently described procedures for acetylation is cumbersome and time-consuming, apparently because the polysaccharides were in an unfavorable physical state.[1] Recently, variable molecular weight data have been reported on materials acetylated by various, non-standardized procedures[2,3]; the poor solubility of the acetates has been a matter of much concern; and physical measurements have been reported on incompletely acetylated products.[4] These same inadequacies in application of methods have characterized the literature on starch acetates for many years. Most of them can be corrected easily, as is shown here.

The data reported here show that if the polysaccharide is in a suitable physical condition, complete acetylation can be accomplished directly, rapidly, and without degradation by any one of three different methods. These employed acetic anhydride catalyzed by either pyridine or by sodium acetate at 100°, or acetic anhydride catalyzed by pyridine in the presence of formamide at room temperature. As is shown later, the products from each of the methods had desirable solubility characteristics. Contrary to recently expressed opinion,[1] no evidence of degradation was obtained for the products acetylated at 100°. However, under certain conditions recommended by others, variable results were obtained by acetylation in formamide (Table I).

TABLE I

COMPARISON OF AMYLOSE TRIACETATES PREPARED BY DIFFERENT METHODS

Corn amylose sample[a]	Method of acetylation	Acetyl content ±0.2 %[b]	[η], trichloroethane, 25°
A	Pyridine, 100°	44.8	2.08
B	Pyridine, 100°	45.1	2.15
A	Sodium acetate, 100°	44.7	1.97
A (complex)[c]	Formamide	44.9	2.01
A	Formamide	44.6	2.00
A (treated)[d]	Formamide, two steps[e]	45.1	1.88
B (treated)	Formamide, two steps	44.8	2.02
A (treated)	Formamide, heated[f]	45.2	1.60
	Repeated	45.2	1.66
	Repeated	44.6	1.90[g]

[a] Amylose samples from two different corn starch preparations were used. [b] For method of analysis see Allene Jeanes and C. A. Wilhant, THIS JOURNAL, **74**, 5339 (1952). [c] The butanol complex was acetylated. [d] Pretreated as described in reference (1) except that treatment in potassium hydroxide was at 0° and some of the excess ether was removed *in vacuo*. [e] Acetylation carried out in two steps.[1] [f] The pretreated amylose was dissolved in formamide by heating to 85°.[3] [g] The variation in values for duplicate acetylations by other procedures did not exceed ±0.12. The measurement of intrinsic viscosity of samples was reproducible to ±0.04.

Acetylations by pyridine or sodium acetate catalysis at 100° were carried out on amylose isolated from the butanol complex[5] in an exceptionally reactive, dry state in which all particles reacted uniformly. Further treatment before acetylation was not necessary. Our acetylations in formamide were successful on the same amylose preparations without recourse to pretreatment,[1] two-step acetylation,[1,3,6] and filtration[1] deemed necessary by others. Still more direct was the acetylation in formamide of the amylose–butanol complex without isolation of the amylose in the dry state. Each of these procedures is applicable to large- or small-scale operations.

Equally successful acetylations catalyzed by pyridine at 100° or at room temperature in the presence of formamide have been obtained on suitably prepared waxy corn starch, corn starch and corn amylopectin, and could, without doubt, be obtained similarly on any amylaceous polysaccharide.

Heating our polysaccharide preparations in formamide to obtain solution, as recommended by some investigators[3,6] was unnecessary, it appeared to cause variable results (Table I), and seems questionable in view of the fact that formyl derivatives have been obtained under similar conditions.[7]

From our experimentation and results we conclude that the formamide method has two distinct advantages. Polysaccharides which are separated originally from aqueous solutions need not be isolated in the dry state before acetylation. Furthermore, the triacetates produced show the superior property of dissolving in certain solvents in which the products from other methods are insoluble.

Experimental

Materials and Methods.—The starches and starch fractions[5] used met high standards for homogeneity of composition and freedom from extraneous non-carbohydrate substances.

Formamide was a neutral fraction obtained from a commercial product by distillation *in vacuo*.

Viscosity measurements were made in Ostwald–Cannon–Fenske tubes No. 100 at concentrations of 0.2 to 0.4%.

Preparation of Dry, Reactive Polysaccharides for Acetylation.—Recrystallized corn amylose–butanol complex was collected in the bowl of a continuous supercentrifuge, and thence added to a large volume of absolute ethanol which was agitated in a Waring Blendor. The precipitated amylose was washed thrice by resuspension in absolute ethanol with care to protect it from atmospheric moisture. It was collected on a filter and freed from ethanol *in vacuo* at room temperature over anhydrous calcium chloride. It was then equilibrated with atmospheric moisture and sieved.

A concentrated aqueous solution of corn amylopectin (one volume) was added slowly to five volumes of absolute ethanol which was agitated in a Waring Blendor. The precipitate was washed and dried as described for amylose.

In order to obtain starches in a physical state in which all particles reacted readily and uniformly, they were gelatinized in water at 100° and dehydrated to fluffy, amorphous products. The swollen granules were either left intact or disintegrated by vigorous mechanical agitation for about 5 minutes, and the cooled paste then was treated as described for amylopectin.

Acetylation.—Acetylation in formamide was by an adaptation of the method of Carson and Maclay,[6] and for the purposes of comparison, the proportion of reagents reported by Potter and Hassid[1] was used. Five grams of air-dried, homogeneously reactive polysaccharide (60 mesh), or 5 g. of amylose in the form of its butanol complex, was mixed uniformly with 70 ml. of cold formamide, and then 125 ml. of

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(1) A. L. Potter and W. Z. Hassid, THIS JOURNAL, **70**, 3774 (1948).

(2) F. C. Cleveland and R. W. Kerr, *ibid.*, **71**, 16 (1949).

(3) R. W. Kerr and F. C. Cleveland, *ibid.*, **71**, 3455 (1949).

(4) B. A. Dombrow and C. O. Beckmann, *J. Phys. Colloid Chem.*, **51**, 107 (1947).

(5) T. J. Schoch, THIS JOURNAL, **64**, 2957 (1942).

(6) J. F. Carson and W. D. Maclay, *ibid.*, **68**, 1015 (1946).

(7) K. M. Gaver, E. P. Lasure and L. M. Thomas, U. S. Patent 2,538,903 (January 23, 1951).

pyridine and 100 ml. of acetic anhydride were added slowly, with stirring and slight cooling.

After several hours a clear solution, free of undissolved particles, resulted. After 20 hours at room temperature, the solution was added to a large volume of vigorously stirred ice and water and the dingy-looking precipitate was washed free of acid with water. A second acetylation treatment[1,8] resulted in no change in acetyl content or in intrinsic viscosity. To provide comparison with the results of others, several variations of this procedure are indicated in Table I.

For acetylation with pyridine as catalyst at 100°, 5 g. of oven-dried polysaccharide (60 mesh) was stirred for 3 hours with 20 ml. of pyridine and 17 ml. of acetic anhydride. The homogeneous solution was cooled, poured into vigorously agitated ethanol, and the colorless precipitate was washed free of acid and dried in the air.

For acetylation with fused sodium acetate as catalyst at 100°, 5 g. of air-dried corn amylose (60 mesh) was soaked in 75 ml. of acetic anhydride overnight, then 1.5 g. of fused sodium acetate was added and the mixture stirred at 100° for 6 hours. The homogeneous solution was cooled, poured into vigorously stirred ice-water, and the colorless product was washed free of acid with water.

Solubility of the Triacetates.—Corn amylose triacetates prepared by the formamide or sodium acetate methods were soluble in acetone; that prepared by the pyridine method at 100° was not. All corn amylose triacetate preparations, as well as the triacetates from corn starch, were soluble in chloroform and 1,1,2-trichloroethane. Preparations of waxy corn starch triacetate from both the pyridine method at 100° and the formamide method were soluble in acetone as well as in the chlorinated solvents. Corn amylopectin triacetate prepared by the pyridine method at 100° was insoluble in the chlorinated solvents, but that prepared by the formamide method was readily soluble.

Acknowledgment.—We wish to acknowedge our indebtedness to Dr. G. E. Hilbert for his interest in the early phases of this work, and to C. H. Van Etten and R. Tobin for the acetyl determinations.

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[8] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

Alkylation of 2-Naphthol by Esters of Aliphatic Acids

BY SAUL PATAI AND M. BENTOV

RECEIVED JULY 17, 1952

In the course of a study on the preparation of aromatic methacrylates[1] the transesterification of methyl methacrylate with 2-naphthol in the presence of sulfuric acid was investigated. Instead of the expected ester, 2-methoxynaphthalene was formed. In order to elucidate this reaction, the transesterification of other aliphatic esters with other phenolic compounds was tried, using sulfuric acid, orthophosphoric acid or metallic sodium as the catalyst. Phenol, 1-naphthol, 4-hydroxybiphenyl and 4-nitrophenol did not react with methyl methacrylate or ethyl acetate. 2-Naphthol, on the other hand, reacted readily in the presence of sulfuric acid, but not of phosphoric acid or sodium, with methyl methacrylate, methyl acetate, ethyl acetate and ethyl butyrate, yielding 2-methoxynaphthalene with the methyl esters and 2-ethoxynaphthalene with the ethyl esters, but failed to react with ethyl formate or dimethyl oxalate. With methyl benzoate the normal product of transesterification, 2-naphthyl benzoate, was obtained.[2]

2-Naphthol is known to be one of the very few phenols which can be alkylated by alcohols in the presence of acids.[3] This fact may be related to the tautomerizability of 2-naphthol.[4]

As, however, our experiments were carried out under strictly anhydrous conditions, no alcohol could be formed as an intermediate in the reaction. It must, therefore, be assumed, that the alkylation is caused in both cases by the hydrogen alkyl sulfate, formed in the conditions of our experiments from the ester and sulfuric acid. The dissociation constant of formic acid is about ten times, and that of oxalic acid about a thousand times greater than that of either acetic, butyric or methacrylic acid: the failure of the reaction with the esters of formic and oxalic acid could then be due to the strength of these acids, which prevents the formation of the alkylsulfuric acids by interaction of the esters with sulfuric acid.

Acknowledgment.—This investigation was carried out under the auspices of the Scientific Department, Israeli Ministry of Defence, and is published with its permission. The authors wish to thank Dr. E. D. Bergmann for helpful advice and discussions.

Experimental

A mixture of 0.04 mole of 2-naphthol, 0.1 ml. of concencentrated sulfuric acid and 0.08 mole of the ester was refluxed for four hours with the exclusion of moisture. (In the case of methyl methacrylate, some hydroquinone was added to the reaction mixture.) The product was poured into an excess of 5% aqueous sodium hydroxide solution and cooled for one hour in an ice-bath, and the resulting precipitate filtered and recrystallized from ethanol. 2-Methoxy- and 2-ethoxynaphthalene were identified by melting point (72 and 37°, respectively) and mixed melting point with authentic samples. Yield of 2-methoxynaphthalene from methyl acetate 20–25%; from methyl methacrylate 45–50%; of 2-ethoxynaphthalene from ethyl acetate 40–45%; from ethyl butyrate 20–25%.

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(1) S. Patai, M. Bentov and M. E. Reichmann, THIS JOURNAL, **74**, 845 (1952).

(2) C. A. Bischoff and A. Hedenstrom (*Ber.*, **35**, 3449 (1902)) obtained di-2-naphthyl oxalate from diphenyl oxalate and 2-naphthol, and report the failure of the reaction with diethyl oxalate.

(3) C. Liebermann and A. Hagen, *ibid.*, **15**, 1427 (1882); L. Gattermann, *Ann.*, **244**, 72 (1888); W. A. Davis, *J. Chem. Soc.*, **77**, 33 (1900); L. F. Fieser and W. C. Lothrop, THIS JOURNAL, **57**, 1459 (1935).

(4) N. N. Voroshcov, *Bull. Inst. Polyt. Ivanovo-Voznesensk*, **6**, 125 (1922); *C. A.*, **17**, 1637 (1923); J. C. Salfeld, *Ber.*, **73**, 376 (1940).

Cohumulone, a New Hop Constituent

BY F. L. RIGBY AND J. L. BETHUNE

RECEIVED JULY 16, 1952

In the course of an investigation to develop a quantitative method for the estimation of the isohumulone content of beer, petroleum ether extracts of several beers were distributed in a 100-tube all-glass countercurrent apparatus using a solvent system of 2,2,4-trimethylpentane and a phosphate-citrate buffer pH 4.9. The concentration in each tube was established by dissolving an aliquot of the upper phase in alkaline methanol and reading the optical density at 255 mμ. Figure 1 shows the distribution pattern for a typical extract after 100 transfers. Two major constituents and at least one minor constituent are present with partition ratios of 0.9, 1.9 and 3.2. In addition, the tubes at each extremity of the distribution train contain mixtures of unidentified substances. A sample of pure humulone (*o*-phenylenediamine complex, m.p. 117°), after conversion to isohumulone either by the method of Windisch, *et al.*,[1] or by boiling in aqueous phosphate buffer of *p*H 5.2, yields a product conforming to the properties of isohumulone and also having a partition ratio of 1.9 when distributed using this solvent system. A search for the origin of the substance showing maximum concentration in tube 47 and a partition ratio of 0.92 revealed that this substance did not arise from lupulone, soft resins, hard resins or humulinone but was produced, together with isohumulone, by boiling the lead salt salt fraction of a hop extract.

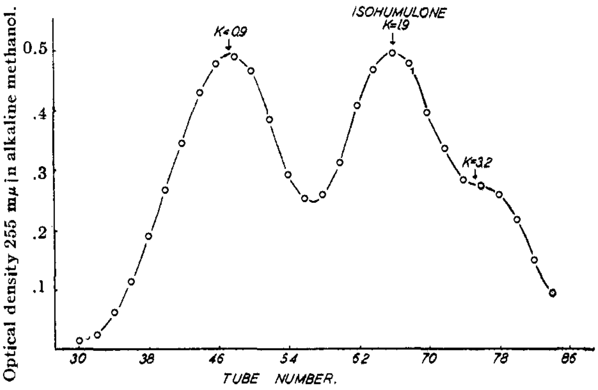

Fig. 1.—Distribution pattern for a beer extract: $n = 100$; solvent system, 2,2,4-trimethylpentane and phosphate-citrate buffer *p*H 4.9.

It was necessary therefore as a result of these observations to make a critical study of the lead salt fraction. Figure 2 shows the distribution pattern for the lead salt fraction of 1951 B. C. Bullion hops after 65 transfers using the system 2,2,4-trimethylpentane–phosphate buffer *p*H 8.5. The substance showing maximum concentration in tube 22 and a partition ratio of 0.53 is believed to be a new constituent of hops and has been assigned the name *cohumulone*. This substance was purified by repeated distributions using two solvent systems and high transfer numbers. The final product was a light-yellow oil at room temperature which formed a waxy solid on slight cooling. *Anal.* Calcd. for $C_{20}H_{32}O_5$: C, 69.23; H, 8.79; mol. wt., 364. Found: C, 69.1, 69.4, 69.4; H, 8.6, 8.8, 8.8; mol. wt. (by titration), 354. Cohumulone, like humulone, forms both a lead salt and an *o*-phenylenediamine complex but the solubility of the cohumulone product in each case is slightly greater than that of the humulone product. When boiled in phosphate buffer, *p*H 5.2, cohumulone is transformed to the new bitter substance of beer.

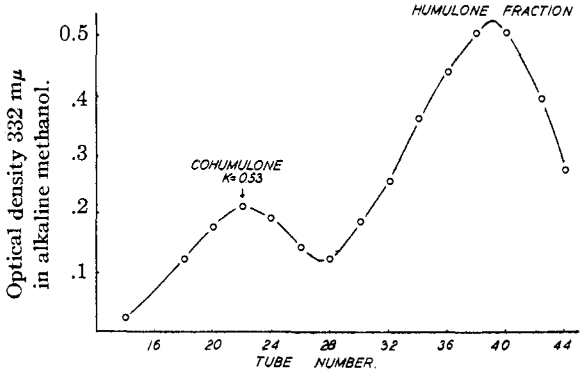

Fig. 2.—Distribution pattern for the lead salt fraction of a hop extract: $n = 65$; solvent system, 2,2,4-trimethylpentane and phosphate buffer *p*H 8.5; optical density units, mμ.

Cook and Harris[2] have reported the presence of humulinone in the lead salt fraction of Kent Golding and Worcester Fuggle hops. In the present investigation humulinone has been isolated from several varieties of Canadian and American hops. Purified humulinone from these sources distributes with a partition ratio of approximately 1 in a system of 2,2,4-trimethylpentane and 0.5 *M* monosodium phosphate adjusted to *p*H 3.2 with phosphoric acid. No humulinone, however, can be detected in these hops by distribution of either the lead salt fractions or the complete extracts. This evidence is supported by infrared and ultraviolet absorption spectra of humulinone, humulone and the lead salt fraction and permits us to conclude only that humulinone is not a natural constituent of hops but is an artifact in the method of isolation.

The second maximum in the distribution pattern, Fig. 2, is due predominantly to humulone but a theoretical curve for one substance cannot be fitted to this portion of the pattern. It is apparent, therefore, that a third component is present in the lead-salt fraction and it may be possible to accomplish its isolation by the use of a larger number of transfers or another solvent system.

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[1] W. Windisch, P. Kolbach and R. Schleicher, *Wochschr. Brau.*, **44**, 453, 473, 485, 497 (1927).

[2] A. H. Cook and G. Harris, *J. Chem. Soc.*, 1873 (1950).

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Derivatives of *o*-, *m*-, and *p*-Aminobenzotrifluoride. II. Azomethines Containing the Trifluoromethyl Group[1]

BY PAUL M. MAGINNITY AND JOHN L. EISENMANN

RECEIVED JUNE 30, 1952

A previous paper in this series[2] describes the preparation of a number of derivatives of the isomeric aminobenzotrifluorides, especially heterocyclic compounds. In conjunction with a study of certain azomethines being carried out in this Laboratory,[3] it was found desirable to prepare at

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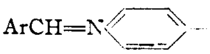
[1] Parts of this paper were taken from a thesis submitted by John L. Eisenmann to the Graduate School of Boston College in partial fulfillment of the requirements for the degree of Master of Science.

[2] P. M. Maginnity and C. A. Gaulin, THIS JOURNAL, **73**, 3579 (1951).

[3] *Cf.* P. M. Maginnity and T. J. Gair, *ibid.*, **74**, 4958 (1952).

TABLE I

SUBSTITUTED SCHIFF'S BASES ArCH=N—R

Ar	R	M.p. (or B.p.), °C.[a]	Description	Formula	Nitrogen, % Calcd.	Nitrogen, % Found	Picrate[b] M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
			A. Solid compounds						
C_6H_5	o-CF_3	61–62	Lt. brown needles	$C_{14}H_{10}F_3N$	5.62	5.43			
C_6H_5	m-CF_3	66–67	White platelets	$C_{14}H_{10}F_3N$	5.62	5.67	124–126	11.71	11.85
C_6H_5	p-CF_3	65	White needles	$C_{14}H_{10}F_3N$	5.62	5.31	121.5–123	11.71	11.96
m-$CH_3C_6H_4$	p-CF_3	19–21	Lt. tan crystals	$C_{15}H_{12}F_3N$	5.32	5.31	138–139	11.38	11.43
p-$CH_3C_6H_4$	p-CF_3	114–115	White platelets	$C_{15}H_{12}F_3N$	5.32	5.32	159–160	11.38	11.45
p-$C_6H_4CH{=}CH$	m-CF_3	102.5–103	Lt. yellow platelets	$C_{16}H_{12}F_3N$	5.09	5.09	153.5–154.5	11.11	11.38
p-$C_6H_4CH{=}CH$	p-CF_3	98.5–101	Yellow crystals	$C_{16}H_{12}F_3N$	5.09	5.37	140–141	11.11	11.20
o-$CH_3OC_6H_4$[c]	m-CF_3	43–44	White needles	$C_{15}H_{12}F_3NO$	5.02	5.15	144.5–145.5	11.02	10.96
p-$CH_3OC_6H_4$[c]	m-CF_3	41–41.5	White platelets	$C_{15}H_{12}F_3NO$	5.02	5.06	181.5–183.5	11.02	10.91
p-$CH_3OC_6H_4$	p-CF_3	84.5–85.5	White crystals	$C_{15}H_{12}F_3NO$	5.02	5.08	183.5–185	11.02	11.20
2,3-$(CH_3O)_2C_6H_3$	m-CF_3	44.0–44.5	Fine white needles	$C_{16}H_{14}F_3NO_2$	4.53	4.52	95–96.5[d]	10.41	10.59
2,3-$(CH_3O)_2C_6H_3$	p-CF_3	87–88	Lt. tan crystals	$C_{16}H_{14}F_3NO_2$	4.53	4.26	133.5–135	10.41	10.21
3,4-$(CH_3O)_2C_6H_3$	m-CF_3	76–76.5	White crystals	$C_{16}H_{14}F_3NO_2$	4.53	4.27	159.5–161	10.41	10.30
3,4-$(CH_3O)_2C_6H_3$	p-CF_3	90–90.5	Lt. yellow crystals	$C_{16}H_{14}F_3NO_2$	4.53	4.05	188.5–189	10.41	10.35
m-$CF_3C_6H_4$	o-CF_3	50–50.5	White platelets	$C_{15}H_9F_6N$	4.42	4.51			
m-$CF_3C_6H_4$	m-CF_3	53.5–54	White needles	$C_{15}H_9F_6N$	4.42	4.50			
p-HOC_6H_4	m-CF_3	170–171	White needles	$C_{14}H_{10}F_3NO$	5.28	5.30	203.5–205	11.34	11.21
o-HOC_6H_4	m-CF_3	82–83	Lt. yellow platelets	$C_{14}H_{10}F_3NO$	5.28	5.37	144.5–145.5	11.34	11.29
m-$CF_3C_6H_4$	H	47–47.5	Pale brown prisms	$C_{14}H_{10}F_3N$	5.62	5.81	159–161	11.71	11.78
m-$CF_3C_6H_4$	p-CH_3	39.5–40	Fine white needles	$C_{15}H_{12}F_3N$	5.32	5.19	164–166	11.38	11.51
m-$CF_3C_6H_4$	p-OCH_3	41–41.5	White platelets	$C_{15}H_{12}F_3NO$	5.02	5.16	159–160 with dec.	11.02	11.13
m-$CF_3C_6H_4$	p-OH	79–81	Fine light brown needles	$C_{14}H_{10}F_3NO$	5.28	5.20	188–189.5 with dec.	11.34	11.19
			B. Liquid compounds						
m-$CH_3C_6H_4$	o-CF_3	134–135 at 8 mm.	Lt. yellow oil	$C_{15}H_{12}F_3N$	5.32	5.30			
m-$CH_3C_6H_4$	m-CF_3	208–210 at 43 mm.	Lt. yellow oil	$C_{15}H_{12}F_3N$	5.32	5.13	132–133	11.38	11.20
p-$CH_3C_6H_4$	o-CF_3	134–139 at 8 mm.	Lt. yellow oil	$C_{15}H_{12}F_3N$	5.32	5.43			
p-$CH_3C_6H_4$	m-CF_3	171–173 at 17 mm.	Lt. yellow oil	$C_{15}H_{12}F_3N$	5.32	5.47	153.5–154.5	11.38	11.41
p-$C_6H_5CH{=}CH$	o-CF_3	165–168 at 8 mm.	Viscous yellow oil	$C_{16}H_{12}F_3N$	5.09	5.37	132–133.5	11.11	11.32
p-$C_6H_5CH_2CH_2$	o-CF_3	220–228 at 8 mm.	Viscous orange oil	$C_{16}H_{14}F_3N$	5.05	4.82			
p-$C_6H_5CH_2CH_2$	m-CF_3	287–289 at 43 mm.	Viscous orange oil	$C_{16}H_{14}F_3N$	5.05	4.96	114.5–116.5[e]	11.07	11.24
o-$CH_3OC_6H_4$	o-CF_3	152–154 at 8 mm.	Lt. yellow oil	$C_{15}H_{12}F_3NO$	5.02	5.21	87–88	11.02	11.18
p-$CH_3OC_6H_4$	o-CF_3	158–162 at 8 mm.	Viscous orange oil	$C_{15}H_{12}F_3NO$	5.02	5.02			
2,3-$(CH_3O)_2C_6H_3$	o-CF_3	164–167 at 8 mm.	Lt. yellow oil	$C_{16}H_{14}F_3NO_2$	4.53	4.54			
3,4-$(CH_3O)_2C_6H_4$	o-CF_3	176–180 at 8 mm.	Yellow oil	$C_{16}H_{14}F_3NO_2$	4.53	4.28			

[a] All melting points (corrected) determined on a calibrated Fisher–Johns melting point apparatus. [b] Picrates were recrystallized from glacial acetic unless otherwise noted. [c] These compounds prepared by L. P. Paradis. [d] Recrystallized from ethanol. [e] Recrystallized from benzene.

this time a new series of fluorinated azomethines from the three fluorine substituted toluidines.

In the present work, thirty-three new azomethines were prepared, each containing the trifluoromethyl group. The methods for their preparation in general followed those described for analogous compounds containing the methyl group in place of the trifluoromethyl group.[4–7] Table I summarizes the data obtained for the fluorinated azomethines.

Experimental

o- and m-Aminobenzotrifluoride.—The ortho isomer was prepared from the commercially available (Hooker) meta compound by methods previously described.[2,8]

p-Aminobenzotrifluoride was prepared by a procedure based on that of Jones.[2,8] It was previously noted that when the original method of Jones was used, the reaction was often violent and the crude p-nitrobenzal bromide was quite irritating to the skin. When smaller quantities were brominated over longer periods of time, according to the following procedure, the reaction became less violent and yields were increased.

Forty-eight grams of p-nitrotoluene was brominated at 190–200° as described by Jones, the p-nitrotoluene being stirred rapidly while 140 g. of bromine was added over a period of 4–5 hours. To avoid contact with the irritating crude products, the reaction mass was not poured into a dish but allowed to cool in the flask. About 500 ml. of hot petroleum ether was added to the solid material in the flask and stirred with additional heating until all but a black residue had dissolved. Evaporation of the solvent to one-half of its volume and cooling of the remainder to 0° produced a precipitate of crystalline p-nitrobenzal bromide. The crude product thus obtained was further brominated as described by Jones. The yield of pure p-nitrobenzotribromide was 90.3 g. by this method, corresponding to a yield of 68% (from p-nitrotoluene), compared to 58% by Jones' original method.

m-Trifluoromethylbenzaldehyde.[9]—m-Aminobenzotrifluoride was diazotized and converted into m-trifluoromethylbenzonitrile (b.p. 94–95° at 30 mm.) by the method described in "Organic Syntheses."[10] The nitrile (14.9 g.) was reduced to the aldehyde by the method of Stephen,[11,12] producing 10.9 g. (78%) of m-trifluoromethylbenzaldehyde, b.p. 93–94° at 52 mm.

Preparation of Azomethines.—The following procedure is based on those developed for syntheses of the corresponding non-fluorinated bases (*cf.* references 4–7). Equal weights (usually 1.5 to 2.5 g.) of the amine and aldehyde were mixed in a test-tube or small flask and heated either in an oil-bath or on a hot-plate until the reaction ceased. The reaction was considered completed when the gently boiling solution no longer expelled water and began to reflux smoothly on the sides of the vessel, the time for this generally being from 10–15 minutes. When this point was reached, the solution was allowed to cool slightly and was then poured into about 50 g. of an ice–water mixture. If the compound solidified, it was separated and recrystallized

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(4) C. K. Tinkler, *J. Chem. Soc.*, **103**, 885 (1913).

(5) T. C. James and C. W. Judd, *ibid.*, **105**, 1427 (1914).

(6) A. Senier and F. G. Shepheard, *ibid.*, **95**, 443, 1943 (1909).

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(9) This work was carried out by Mr. Leo P. Paradis, student at Boston College.

(10) H. T. Clarke and R. R. Read, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 514.

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(12) J. W. Williams, THIS JOURNAL, **61**, 2248 (1939).

from ethanol. If the substance remained liquid (generally a heavy oil), it was extracted with ether, the extract dried over magnesium sulfate, and warmed to remove the solvent. The resulting residue was distilled under diminished pressure.

Picrates.—The picrates of the azomethines were prepared by adding a saturated solution of picric acid in either ethanol or benzene to a solution of about 0.2 g. of the base in the same solvent. The crude picrates were recrystallized from glacial acetic acid (except as noted in the table).

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Correlation of Cl^{35} Nuclear Quadrupole Coupling Frequencies with Hammett's Sigma[1]

BY HARLAN C. MEAL

RECEIVED SEPTEMBER 4, 1952

The nuclear quadrupole resonance frequency for Cl^{35} has been measured for some chlorobenzene derivatives with a frequency modulated super-regenerative spectrometer[2] (Table I). Signals too weak to be detected with frequency modulation and oscilloscope display were observed using magnetic field modulation, phase-sensitive detection and pen recording. Temperature dependences of the frequencies were determined (Fig. 1) and extrapolated to absolute zero. These, together with the data of Dean and Pound similarly extrapolated, have been plotted against Hammett's substituent parameter sigma[3] (Fig. 2). Limits of error assigned are the mean deviations given by Hammett or arbitrarily taken to be 0.1 unit for sigma; for the frequencies the expected maximum error in the extrapolation is used. Where crystallographically non-equivalent chlorines give rise to multiple lines the frequencies of the several lines are plotted.

TABLE I

Cl^{35} NUCLEAR QUADRUPOLE INTERACTION FREQUENCIES OBSERVED IN VARIOUS SUBSTITUTED CHLOROBENZENE COMPOUNDS

Substituent	Cl^{35} frequency at 196°K.	77°K.	0°K. (extrapolated)	σ
o-NO$_2$	36.997 mc.[a]	37.260 mc.	37.47 mc.	+2.030
o-CF$_3$[b]	35.633			
o-Cl	35.496[a]	35.824	35.97	+1.260
	35.424[a]	35.755	35.92	
	35.278[a]	35.755	35.97	
	35.215[a]	35.580	35.75	
m-NO$_2$	35.225[a]	35.457	35.60	+0.710
m-COOH	35.053	35.227	35.26	+ .355
m-CF$_3$	34.632	35.073	35.23	+ .42[c]
m-Cl	34.732[a]	35.030	35.20	+ .373
	34.724[a]	35.030	35.20	
	34.523[a]	34.875	35.09	
	34.503[a]	34.809	34.96	
p-OH	34.672[a]	34.945[a]	35.19	− .317
	34.434[a]	34.700[a]	34.82	
m-N═C═O[b]	34.653			
p-OCH$_3$	34.433	34.753	34.94	− .268
o-N═C═O[b]	34.415			
None	34.026[a]	34.622[a]	34.90	0.00
p-Cl	34.562[a]	34.779[a]	34.88	+ .227
p-COOH	34.471	34.673	34.78	+ .728
p-COCH$_1$	34.327	34.618	34.73	+ .874
p-CHO	34.381	34.607	34.67	+1.126
	34.403	34.623	34.68	
p-CH$_2$Cl	34.303	34.567	34.69	+0.025
	32.840	33.754	34.24	
p-OC$_2$H$_5$	34.180	34.381	34.44	− .25
p-NH$_2$	33.974[a]	34.146[a]	34.20	− .660
p-CH═CHCOOH	34.227		34.40	+ .619
Benzyl chloride	32.417	33.630	34.14	

[a] Data from Dean and Pound (private communication).
[b] Observations not yet complete, also, no σ-values available.
[c] J. D. Roberts, R. L. Webb and E. A. McElhill, THIS JOURNAL, 72, 408 (1950).

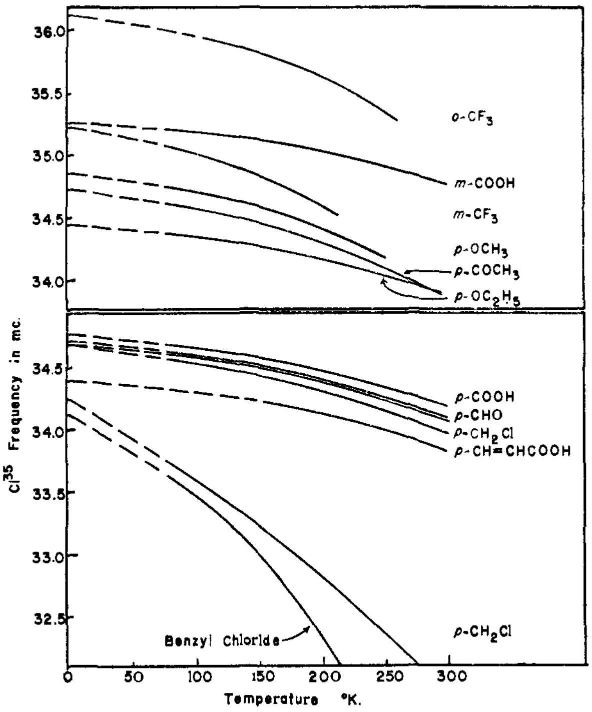

Fig. 1.

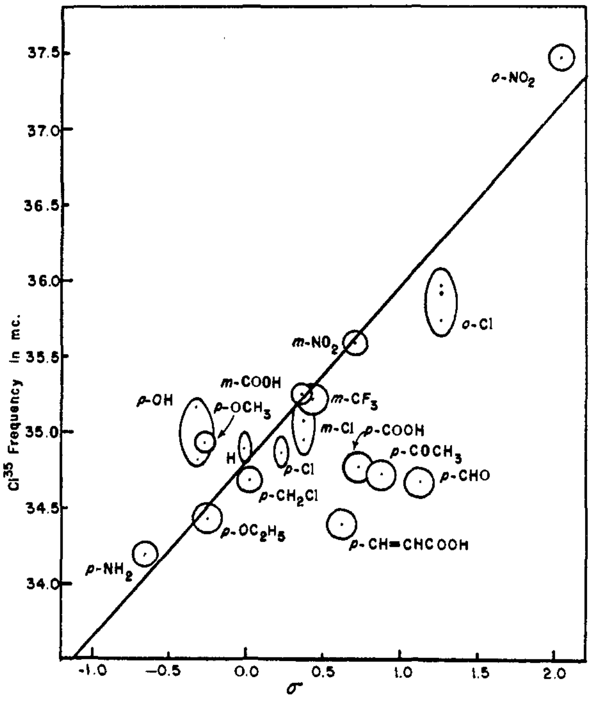

Fig. 2.

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[1] The research reported in this paper was made possible by support extended Harvard University by the ONR under Contract N5ori 76, Task Order V.

[2] C. Dean and R. V. Pound, *J. Chem. Phys.*, **20**, 195 (1952).

[3] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chap. VII.

In the case of p-chlorobenzyl chloride it is thought that the two lines arise from the two chemically different chlorines in the molecule. The higher frequency was assigned to the chlorine on the ring on the basis of the result obtained with benzyl chloride. σ-Values for the ortho substituents were calculated from the ionization constants of the corresponding benzoic acids,[4] for p-CH_2Cl from nuclear nitration data,[3,5] for p-OH from the ionization constant of p-hydroxybenzoic acid.[6] The work of Taft indicates that obtaining ortho σ-values in this fashion is a dubious procedure[7] although the fit is satisfactory. Further work with ortho substituted chlorobenzene compounds may help elucidate the polar effects of such substituents.

One might expect a relation to exist between the resonance frequency and sigma since the latter is a measure of the electron density at a given carbon atom in the ring[3] and the quadrupole frequency is closely related to the location of bonding electrons.[8] Solid state influences might upset this relation but these are apparently relatively constant in the present compounds. In iodine[8] and chloral hydrate[9] they cause larger deviations.

The σ-values assigned to the substituents p-CHO, p-$COCH_3$, p-COOH and p-CH=CHCOOH are probably too large as a result of resonance stabilization of the phenoxide ion in the experiments used to determine those values.[10] Hammett states that these values are probably only valid for phenol and aniline derivatives. There is a wider difference between the meta and para σ-values for these compounds than for compounds in which resonance is blocked. The same resonance effects in the chlorine substituted molecule might be expected to diminish the quadrupole frequency by increasing the double bond character of the C–Cl bond. The deviation of the p-OH substituent may arise from hydrogen bonding of the chlorine through the hydroxyl of an adjacent molecule as in chloral hydrate.[9] Also the σ-value assigned to the hydroxyl group is not well defined.[11] The deviation of the p-OCH_3 compound is unexplained.

The Cl^{35} quadruple frequency in p-deuterochlorobenzene has been observed to be equivalent, within experimental error (4 kc.), to that in chlorobenzene.

The author would like to express his appreciation to Professor E. Bright Wilson, Jr., who suggested this research and lent valuable assistance in discussions, to Professor J. D. Roberts of M. I. T., who supplied the p-chlorocinnamic acid, the o- and the m-chlorobenzotrifluorides, and for several valuable suggestions, to Dr. Christopher Dean for considerable help with the instrumentation, to Miss Janet Hawkins who supplied the p-deuterochlorobenzene, and to Dr. Harry C. Allen, Jr., for constant advice and encouragement.

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(4) J. F. J. Dippy and R. H. Lewis, *J. Chem. Soc.*, 343 (1935); J. F. J. Dippy, F. R. Williams and R. H. Lewis, *ibid.*, 1426 (1937).

(5) C. K. Ingold, *et al.*, *ibid.*, 575 (1949); 905, 918, 929 (1938); 1959 (1931).

(6) G. E. K. Branch and D. L. Yabroff, THIS JOURNAL, **56**, 2568 (1934).

(7) R. W. Taft, Jr., *ibid.*, **74**, 2729, 3120 (1952).

(8) C. H. Townes and B. P. Dailey, *J. Chem. Phys.*, **20**, 35 (1952).

(9) H. C. Allen, THIS JOURNAL, **74**, 6074 (1952).

(10) G. N. Burkhardt, C. Horrex and D. I. Jenkins, *J. Chem. Soc.*, 1654 (1936); G. N. Burkhardt, W. G. K. Ford and E. Singleton, *ibid.*, 17 (1936).

(11) E. Berliner and L. C. Monack, THIS JOURNAL, **74**, 1574 (1952).

Preparation of Radiohypophosphate Ion

BY THERALD MOELLER AND GLADYS H. QUINTY

RECEIVED JUNE 20, 1952

In conjunction with investigations on the hypophosphates of thorium and the rare earth elements,[1] hypophosphate ion ($P_2O_6^{-4}$) containing phosphorus-32 was required. This was best prepared as the disodium dihydrogen salt by the direct oxidation of elemental radiophosphorus with sodium chlorite by an adaptation of the procedure of Leininger and Chulski.[2] Attempted preparations involving exchange of inactive hypophosphate with radio-orthophosphate and with radiopyrophosphate gave negative results, in keeping with other observations[3-7] upon the general absence of exchange among the oxidation states of phosphorus.

Experimental

Chlorite Oxidation of Radiophosphorus.—One-gram samples of red phosphorus were sealed in evacuated quartz tubes and irradiated in the pile at the Oak Ridge National Laboratories. As received after irradiation, these samples had activities approaching 50 millicuries per gram of phosphorus. The tubes were opened in a dry-box in a carbon dioxide atmosphere by cutting grooves around the tips with a small emery wheel, continuing grinding until small holes developed to admit carbon dioxide, and then cracking off the tips. Each sample of active phosphorus was then mixed thoroughly with 25 g. of inactive red phosphorus.

The mixed solids were converted by chlorite oxidation to disodium dihydrogen hypophosphate 6-hydrate as described by Leininger and Chulski.[2] To obviate losses and reduce contamination hazards, the reaction vessel was of Pyrex with the central tube sealed in. Connection to the receiving flask was made with Tygon tubing. Both reaction vessel and receiving flask were surrounded by $^1/_8$-in. lead sheeting, and all operations were conducted in well-ventilated hoods with ample precautions taken to prevent radiation hazards. The preparations proceeded as described,[2] yielding products of high purity and activity. The high-activity waste liquors which accumulated were stored in lead-shielded containers until activities had decreased to safe levels before disposal.

Attempted Orthophosphate–Hypophosphate Exchange.—Radiophosphoric acid, obtained from the Oak Ridge National Laboratories, was diluted with 0.1 M sodium dihydrogen orthophosphate solution to an activity of some 5000 counts per minute per milliliter. Equal aliquots of this solution and of a 0.1 M disodium hypophosphate solution were mixed, adjusted to pH 1, 5 and 10 and temperature equilibrated at 25, 60 and 90°. At various time intervals, 2-ml. samples were withdrawn, diluted with 2 ml. of 12 M hydrochloric acid, and treated with a few drops of concentrated thorium nitrate solution (7 g. of the salt in 50 ml.). Under these conditions, only thorium hypophosphate is precipitated,[1] and precipitation of thorium is quantitative.

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(1) G. H. Quinty, Doctoral Dissertation, University of Illinois, 1951.

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(5) D. E. Hull, THIS JOURNAL, **63**, 1269 (1941).

(6) R. C. Vogel and N. Podall, *ibid.*, **72**, 1420 (1950).

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The precipitates were removed and washed five times by centrifuging with diluted hydrochloric acid containing sodium nitrate to prevent peptization. After being dried, the precipitates were counted, using a thin-wall beta counting tube. Inasmuch as activities in the precipitates (*ca.* 0–100 counts per minute) were negligible in comparison with the activity of the standards (4500–4600 counts per minute per milliliter) the absence of exchange is indicated. Extreme washing reduced activities in the precipitates still further, showing that observed activities were probably due only to adsorption and occlusion. Neither alteration of *p*H nor of temperature gave any evidences of exchange.

Attempted Pyrophosphate–Hypophosphate Exchange.—Radiophosphoric acid was converted to pyrophosphate by evaporating with disodium hydrogen orthophosphate solution and igniting the residue for 2 hr. at 600°. The active pyrophosphate was dissolved in water and diluted appropriately with tetrasodium pyrophosphate solution. The exchange procedure was identical with that described above except that concentrations were reduced to 0.01 *M* to avoid precipitation of thorium pyrophosphate.[8] Results exactly comparable with those mentioned above are again interpreted as indicating no exchange. Again some adsorption and occlusion effects were noted.

It should be pointed out that the counting rates noted for the solids were not absolutely correct because the weights of the precipitates used were not determined and because the layers counted were not of uniform thickness, but the values obtained were of the correct orders of magnitude and the interpretations logical.

Acknowledgment.—Support received from the Office of Naval Research is gratefully acknowledged.

[8] T. Moeller and G. K. Schweitzer, *Anal. Chem.*, **20**, 1201 (1948).

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Radiometric Determination of the Solubilities of Thorium and Certain Rare Earth Metal Hypophosphates

BY THERALD MOELLER AND GLADYS H. QUINTY

RECEIVED JUNE 20, 1952

Although the extremely small acid solubility of thorium hypophosphate has been used to advantage for the efficient removal of thorium from its admixtures with the rare earth elements,[1-6] no quantitative comparisons of hypophosphate solubilities which might lend support to the method have appeared. The availability of radiohypophosphate[7] provided a tool for solubility determinations. Neodymium and yttrium were selected as representative members of the cerium and yttrium sub-groups, respectively, for comparison with thorium.

Data summarized in Table I indicate that thorium hypophosphate remains essentially quantitatively insoluble in at least 4 *N* hydrochloric acid, whereas under comparable conditions the rare earth metal hypophosphates are sufficiently soluble to permit separations. Thorium hypophosphate is markedly less soluble than the pyrophosphate.[8]

TABLE I

SOLUBILITIES OF HYPOPHOSPHATES IN HYDROCHLORIC ACID SOLUTIONS

Sample	Hydrochloric acid concentration, *N*	Solubility, mole/liter × 10^4
ThP_2O_6	1.00	0.25
	2.00	.47
	4.00	1.65
	6.00	2.10
$Nd_4(P_2O_6)_3$	0.05	0.11
	.10	.48
	.20	1.60
	.30	2.00
	1.00	14.46
	2.00	34.70
$Y_4(P_2O_6)_3$	0.20	3.02
	0.30	5.52
	1.00	26.90

Experimental

Solubilities were determined by essentially the same procedure previously described for pyrophosphates.[8] Thorium, neodymium and yttrium hypophosphates were precipitated by adding suitable volumes of a standard sodium hypophosphate solution (26.4 mg. $P_2O_6^{-4}$ per ml.) of known radioactivity (*ca.* 4500 counts per minute per milliliter)[7] to excesses of the metal salt solutions. The precipitates were washed thoroughly, air-dried, and suspended in 50-ml. volumes of hydrochloric acid solutions of varying normalities. These suspensions were equilibrated for 5 days in a thermostat at 25 ± 0.1°, studies having shown that longer periods produced no significant changes. The suspensions were then filtered and the activities of the filtrates measured using an annular volume tube.[8] Comparisons of these activities with that of the standard indicated the solubilities. These are expressed in terms of anhydrous hypophosphates in Table I, the compositions of the precipitates having been determined by independent means.[9]

Although statistical errors at some of the low counting rates encountered and the probable presence of low activities of thorium decay products render these results not absolutely quantitative, the values are of the correct orders of magnitude and especially useful on comparative bases. The rare earth metal hypophosphates are too soluble at acidities above 1–2 *N* to permit accurate evaluations by this procedure.

Acknowledgment.—Support received from the Office of Naval Research is gratefully acknowledged.

[1] F. Wirth, *Z. angew. Chem.*, **25**, 1678 (1912).

[2] F. Wirth, *Chem. Ztg.*, **37**, 773 (1913).

[3] M. Koss, *ibid.*, **36**, 686 (1912).

[4] A. Rosenheim, *ibid.*, **36**, 821 (1912).

[5] F. Hecht, *Z. anal. Chem.*, **75**, 28 (1928).

[6] T. Moeller, G. K. Schweitzer and D. D. Starr, *Chem. Revs.*, **42**, 63 (1948).

[7] T. Moeller and G. H. Quinty, THIS JOURNAL, **74**, 6122 (1952).

[8] T. Moeller and G. K. Schweitzer, *Anal. Chem.*, **20**, 1201 (1948).

[9] G. H. Quinty, Doctoral Dissertation, University of Illinois, 1951.

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The Solid State Reaction between Magnesium and Chromium Oxides

BY G. PARRAVANO

RECEIVED JUNE 30, 1952

Chemical reactivity of inorganic materials is known to be structure-sensitive, being dependent on a variety of variables which are involved in the history and preparation of the reacting substances. Thus, ill-defined phase boundary effects are responsible for the empirical relations often deduced for the kinetics of solid state changes. These relations cannot be used for the direct establishment of a reaction mechanism.

It has been realized that in order to minimize the conditions under which phase boundary processes will affect the kinetics of the reaction it is necessary to work with well sintered specimens, showing a distribution of particle size and shape over a narrower range than powders obtained at low temperatures. Under these conditions it is possible to find a kinetic behavior of the reacting system conforming more closely to theoretical expectations.

The present note shows how this agreement can be approached quite well in the study of the solid state reaction between magnesium and chromium oxides. The same reaction was previously investigated by Huttig and co-workers.[1] Their results obtained on powder mixtures do not lend themselves to any kinetic treatment.

Experimental

Chromium oxide (Mallinckrodt) and magnesium oxide (reagent, sulfate-free) powders were heated separately at 750° for six hours, cooled to room temperature, pressed into pellets under 5000 lb./sq. inch pressure and sintered at 1100°. The resulting specimens had a cross section of 98.5 sq. mm.

The formation of the spinel, $MgCr_2O_4$, was followed using a technique similar to that of Bengtson and Jagitsch.[2] A chromium oxide and magnesium oxide pellet were gently pressed together; and at different time intervals the change in weight of both pellets was recorded. In order to avoid material transport between the two pellets other than through the contact layer, a flow of air was maintained around the reacting specimens.

Results and Discussion

It was soon realized that at the temperatures investigated some evaporation of chromium oxide took place. The rate of this process was therefore determined on separate pellets of chromium oxide, by recording the loss of weight of the pellets at different time intervals and at constant temperature. The decrease in weight was found to be a linear function of the time of heat treatment. From the plots of weight decrease *vs.* time the following rate constants, k_e, were evaluated (Table I).

From these data an activation energy of 36 kcal./mole was derived for the evaporation process.

It was found that during the reaction between magnesium and chromium oxides, the magnesium oxide specimen showed a continuous increase, while the chromium oxide specimen a continuous decrease in weight. The decrease in weight of the latter, after due allowance was made for the evaporation, was found to agree closely with the increase in weight of the magnesium oxide pellet.

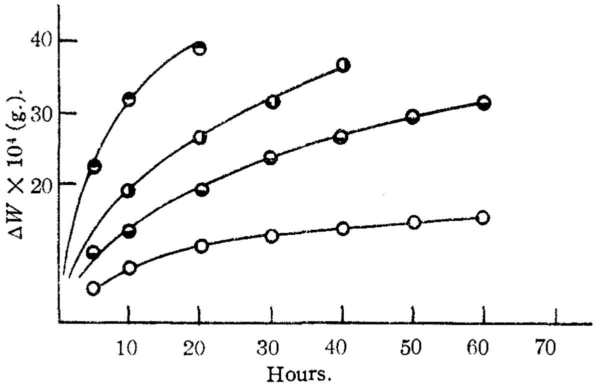

Fig. 1.—Weight increase of MgO pellet during reaction with Cr_2O_3: ○, t = 1000°; ◒, t = 1100°; ◑, t = 1200°; ◓, t = 1250°.

TABLE I

EVAPORATION OF CHROMIUM OXIDE

Temp., °C.	$k_e \times 10^6$ g. cm.$^{-2}$ hr.$^{-1}$
890	0.63
1000	15
1100	28
1200	105

Furthermore the area of this pellet which had reacted with chromium oxide became gray-brown in color. At the end of one run the gray-brown substance was collected and examined by X-rays. The resulting pattern was that of the spinel $MgCr_2O_4$.[3]

In Fig. 1 are presented the data for the weight increase of magnesium oxide specimens during the reaction with chromium oxide. These data can be fitted fairly well to a quadratic type of equation (Fig. 2)

$$d\Delta W/dt = k/\Delta W$$

where W is the weight increase and k is a constant. The values for the rate constant, $k_r = \Delta W^2/q \times$

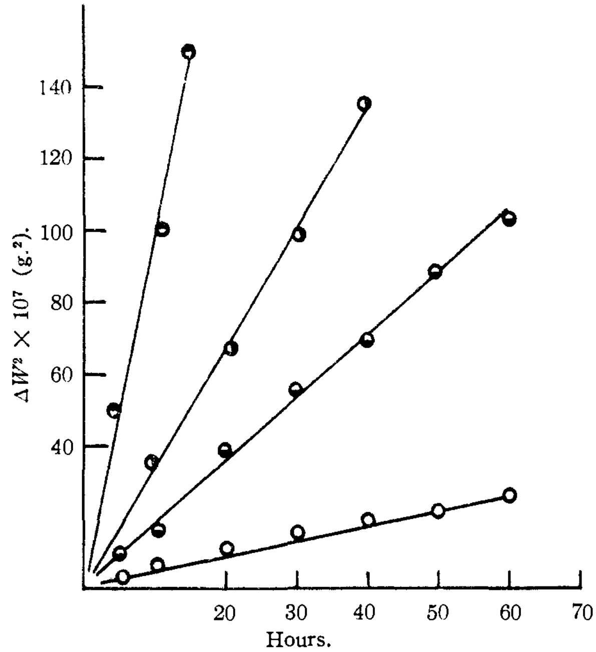

Fig. 2.—Weight increase of MgO pellet during reaction with Cr_2O_3, parabolic plot: ○, t = 1000°; ◒, t = 1100°; ◑, t = 1200°; ◓, t = 1250°.

TABLE II

REACTION BETWEEN MAGNESIUM AND CHROMIUM OXIDES

Temp., °C.	$k_r \times 10^7$, g.^{2} cm.$^{-4}$ hr.$^{-1}$
1000	0.226
1100	1.81
1200	3.54
1250	10.4

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(1) H. Kittel and G. F. Hüttig, *Z. anorg. Chem.*, **217**, 194 (1934); G. F. Hüttig, D. Zinker and H. Kittel, *Z. Elektrochem.*, **40**, 306 (1934); Th. Meyer and G. F. Hüttig, *ibid.*, **41**, 429 (1935).

(2) B. Bengtson and R. Jagitsch, *Arkiv. Kemi, Mineral. Geol.*, **24**, No. 18 (1947).

(3) M. Hamelin (*Rev. Met.*, **47**, 324 (1950)) has shown that the only compound formed by heating mixtures of magnesium and chromium oxides at temperatures between 1000 and 1400° is magnesium chromite.

1/*t* (*q* = reacting area) at different temperatures are collected in Table II.

These data could be plotted according to the Arrhenius equation, from which an activation energy of 50 kcal./mole was derived.

On the basis of these results it can be concluded that in the present case the solid state reaction between magnesium and chromium oxides occurred only at the contact area between the two specimens and not by means of material transport through the gas phase and that the rate of the process is determined by *the diffusion of chromium oxide particles through the spinel layer.* The nature of the diffusing particles however cannot be ascertained from the present data.

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The System Water-Dioxane-Hydrogen Chloride

By R. A. Robinson

Received July 7, 1952

In a recent note Grubb and Osthoff[1] published a study of the separation of water-dioxane mixtures at 25° into two layers on the addition of hydrogen chloride. They stated that this behavior had not been reported previously. It was, however, given brief mention in a review article 14 years ago[2] and has since[3] been studied quantitatively.

Figure 1a shows the tie-lines and the area corresponding to two-phase systems as determined by direct analysis of the conjugate solutions.[3] The points correspond to the data of Grubb and Osthoff.[1] (A few points on the lower right-hand side have been omitted to avoid over-crowding the graph.) In general the agreement between the two determinations is good; Grubb and Osthoff find that the region of partial miscibility is somewhat more extensive in the region of the water-rich mixtures but, considering the analytical difficulties inherent in this investigation, I think the agreement is satisfactory.

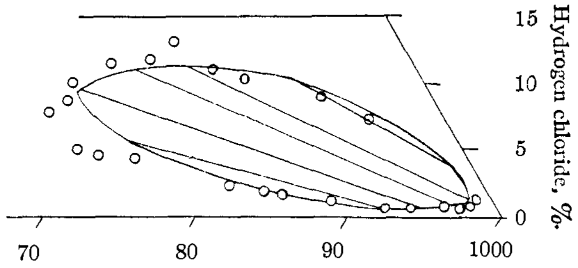

Fig. 1a.—Isotherm of the system water-dioxane-hydrogen chloride at 25°: O, data of Grubb and Osthoff; tie-lines from data of Robinson and Selkirk.

Some time ago, I made a few measurements on this system at 10° by the method I had used earlier at 25° and obtained the results given in Table I and Fig. 1b.

TABLE I

Upper layer			Lower layer		
HCl, %	H_2O, %	$C_4H_8O_2$, %	HCl, %	H_2O, %	$C_4H_8O_2$, %
4.68	3.8	91.5	9.56	9.6	80.8
2.84	2.5	94.7	10.02	14.5	75.5
1.49	1.4	97.1	9.50	18.0	72.5
0.76	2.0	97.2	8.33	21.8	69.9
.51	4.2	95.3	6.98	23.5	69.5
.57	5.6	93.8	5.03	23.8	71.2
.96	10.9	88.1	3.16	19.6	77.2

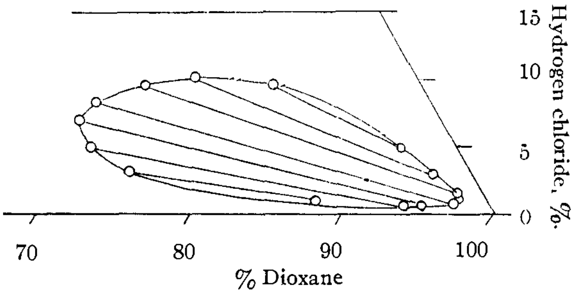

Fig. 1b.—Isotherm of the system water-dioxane-hydrogen chloride at 10°: O—O, tie-lines and composition of conjugate solution; present work.

Lowering the temperature by 15° causes the major axis of the (very approximately) elliptical curve to swing slightly in a counter-clockwise direction with, however, little change in composition of the conjugate solutions.

I have to thank Mr. Andrew Yeo Boon Hin and Mr. Oh Bak Kim for making some preliminary measurements on this system.

University of Malaya
Singapore

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[1] W. T. Grubb and R. C. Osthoff, This Journal, **74**, 2108 (1952).

[2] H. S. Harned, *J. Franklin Institute*, **225**, 623 (1938).

[3] R. A. Robinson and R. C. Selkirk, *J. Chem. Soc.*, 1460 (1948).

Potential Antivirals. I. Simple Analogs of Chloramphenicol (Chloromycetin)

By Arthur P. Phillips

Received August 8, 1952

The simple chemical structure[1] and broad antibiotic spectrum[2] of chloramphenicol have made it an interesting model for other possible chemotherapeutic agents. While a variety of new synthetic and biologically produced drugs have become available in recent years for combating effectively many of the more common diseases of bacterial or protozoal origin, few if any of these are useful in the treatment of the important diseases attributed to a virus cause. Since chloramphenicol is somewhat effective against certain organisms believed to be viruses it seemed worthwhile to seek additional chemotherapeutic substances against important virus infections among various analogs of this useful antibiotic.

Two chemical units, the aromatic nitro and the dichloroacetyl, had been identified[1] as part of the chloramphenicol structure although these groupings had not been previously recognized in natural products, nor had they been thought desirable for incorporation into synthetic drugs. These two

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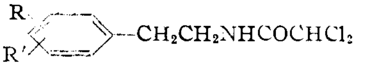
[1] M. C. Rebstock, *et al.*, This Journal, **71**, 2458 (1949).

[2] I. W. McLean, Jr., *et al.*, *J. Clin. Investigation*, **28**, 953 (1949).

TABLE I

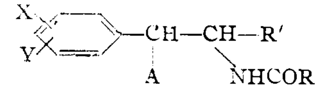


Compd. No.	R, R′	Cryst. solvent[a]	M.p., °C.[b] (uncor.)	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
			A. Simple phenethyl dichloroacetamides					
I	H	Ea.H	80–81	$C_{10}H_{11}ONCl_2$	51.7	51.8	4.8	4.8
II	2-CH_3O	Ea.H	86–87	$C_{11}H_{13}O_2NCl_2$	50.4 N 5.3	50.7 N 5.3	5.0	4.9
III	3-CH_3O	E.H or B.H	72–73	$C_{11}H_{13}O_2NCl_2$	N 5.3	N 5.5		
IV	3-C_2H_5O	E.H	70–71	$C_{12}H_{15}O_2NCl_2$	52.2	52.6	5.5	5.3
V	4-CH_3O	Ea.H	90–92	$C_{11}H_{13}O_2NCl_2$	50.4	50.3	5.0	5.0
VI	3-CH_3-4-CH_3O	Ea.H	101–102	$C_{12}H_{15}O_2NCl_2$	52.1	52.1	5.4	5.4
VII	3,4-$(CH_3O)_2$	M	127–128	$C_{12}H_{15}O_3NCl_2$	49.3	49.7	5.2	5.1
VIII	2,5-$(CH_3O)_2$	B.H or E	83–84	$C_{12}H_{15}O_3NCl_2$	49.3	49.2	5.2	5.2
IX	2,5-$(CH_3O)_2$-4-Br	M	141–142	$C_{12}H_{14}O_3NBrCl_2$	38.8	38.6	3.8	3.7
			B. Simple nitro phenethyl dichloroacetamides					
X	4-NO_2	Ea.H	98–99	$C_{10}H_{10}O_3N_2Cl_2$	43.3	43.2	3.6	3.7
XI	3-NO_2-4-CH_3O	Ea.H	108–109	$C_{11}H_{12}O_4N_2Cl_2$	43.0	43.0	3.9	3.9
XII	2-NO_2-4,5-$(CH_3O)_2$	HOAc	194–195	$C_{12}H_{14}O_5N_2Cl_2$	42.7	42.7	4.2	3.9
XIII	2,5-$(CH_3O)_2$-4-NO_2	M	155–156	$C_{12}H_{14}O_5N_2Cl_2$	42.7	43.0	4.2	4.2

[a] B = benzene; E = ether; Ea = ethyl acetate; H = Skellysolve B; HOAc = acetic acid; M = methanol. [b] Yields were usually greater than 80%.

TABLE II

MISCELLANEOUS PHENETHYLAMIDES

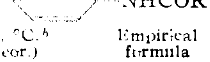


Compd. No.	X.Y.A.	R,R′	Cryst. solvent[a]	M.p., °C.[b] (uncor.)	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
XIV	H	R = CH_2Cl R′ = H	Ea.H	67–68	$C_{10}H_{12}ONCl$	60.7	60.9	6.1	5.8
XV	X = 4-CH_3O	R = CH_2Cl R′ = CH_3	Ea.H	79–80	$C_{12}H_{16}O_2NCl$	59.6	60.1	6.7	6.7
XVI	X = 3,4-$(CH_3O)_2$	R = CCl_3 R′ = H	Ea.H	109–110	$C_{12}H_{14}O_3NCl_3$	44.1	44.3	4.3	4.5
XVII	X = 4,5-$(CH_3O)_2$ Y = 2-NO_2	R = CCl_3 R′ = H	M.Aq	137–138	$C_{12}H_{13}O_5N_2Cl_3$	38.7	38.7	3.5	3.5
XVIII	A = OH	R = $CHCl_2$ R′ = 4-$CH_3OC_6H_4$	M	178–179	$C_{17}H_{17}O_3NCl_2$	57.6	57.6	4.8	4.8
XIX	H	R = $CHCl_2$ R′ = 3,4-$(CH_3O)_2C_6H_3$	M	130–131	$C_{18}H_{19}O_3NCl_2$	58.7	58.7	5.2	5.2
XX	H	R = $CHCl_2$ R′-2-NO_2-4,5-$(CH_3O)_2$-C_6H_2	HOAc	242–243	$C_{18}H_{18}O_5N_2Cl_2$	52.3	51.9	4.4	4.4

[a] Aq = water; see footnote (*a*) Table I. [b] See footnote (*b*) Table I.

TABLE III

ANILINE DERIVATIVES



Compd. No.	X	R	Cryst. solvent[a]	M.p., °C.[b] (uncor.)	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
XXI	COOH	$CHCl_2$	M	241–242	$C_9H_7O_3NCl_2$	43.5	44.0	2.9	3.0
XXII	$ClCH_2CONH$	CH_2Cl	HOAc or M	>315	$C_{10}H_{10}O_2N_2Cl_2$	45.9	45.8	3.9	4.2
XXIII	$Cl_2CHCONH$	$CHCl_2$	HOAc	252–253	$C_{10}H_8O_2N_2Cl_4$	36.4	36.4	2.4	2.4

[a] See footnote (*a*) Table I. [b] See footnote (*b*) Table I.

groups, either individually or together, have now been substituted in some simple phenethylamine derivatives (see Tables I and II). A few derivatives of aniline are shown in Table III.

The simple ring substituted phenethyl dichloroacetamides (Table IA) were prepared by warming of the appropriate amine with methyl dichloroacetate. The related nitro compounds (Table IB) from some of them were obtained by nitration of the dichloroacetamides with concentrated nitric acid in glacial acetic acid solution.

In Table II are shown a number of variations from the simpler substances of Table I. Included are some monochloroacetyl and trichloroacetyl amides as well as some variations on the phenethylamine skeleton. The trichloroacetyl amides were made from the methyl ester as were the dichloroacetyls. Use of the acid chloride or anhydride seemed to be necessary to introduce the monochloroacetyl group. The aniline derivatives shown in Table III were all made from the aniline and the corresponding acyl chloride.

Most of these compounds were examined for antiviral activity by Dr. D. J. Bauer of The Wellcome Laboratories of Tropical Medicine, Euston Road, London, England. Although several of the compounds showed some activity against one of the viruses used, that of Rift Valley Fever, on repetition of the experiments most of these proved to be inactive. Only one compound, N-(2,5-dimethoxy-4-nitrophenethyl)-dichloroacetamide (XIII of Table IB), gave a consistently positive result against Rift Valley Fever.

Acknowledgment.—The author is indebted to Samuel W. Blackman for the microanalyses included.

Experimental

A number of typical preparative procedures are outlined below.

N-(2,5-Dimethoxyphenethyl)-dichloroacetamide (VIII).—A mixture of 18 g. (0.1 mole) of 2,5-dimethoxyphenethylamine and 17 g. (0.12 mole) of methyl dichloroacetate was heated for two hours at 100°. The reaction mixture was cooled, 100 cc. of ether was added, and after scratching and chilling there was obtained 27 g. (93%) of white crystals. After recrystallization from benzene–hexane these melted at 83–84°.

N-(2,5-Dimethoxy-4-nitrophenethyl)-dichloroacetamide (XIII).—To 29 g. (0.1 mole) of the above amide (VIII) in 300 cc. of glacial acetic acid was added bit by bit with cooling and good stirring 15 cc. of concentrated nitric acid over a period of one hour. Yellow prisms start to precipitate near the end of the acid addition. After all acid had been added the mixture was left for two hours at room temperature, and then was diluted with 3 liters of cold water. The yellow crystalline product was collected and washed with water; yield 29 g. (87%); after recrystallization from methanol it melted at 155–156°.

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Spectrophotometric Study of the Tetrachloroiodide Complex in Acetonitrile

BY ALEXANDER I. POPOV AND JOHN N. JESSUP

RECEIVED JULY 7, 1952

In conjunction with a detailed investigation of the behavior of polyhalogen ions in solutions, it was found necessary to study the absorption spectrum of trimethylsulfonium tetrachloroiodide. While a large number of metallic salts of the tetrachlorohydroiodic acid have been reported in the literature,[1] these compounds were found unsuitable for this investigation since they are only soluble in water or aqueous alcohol, solvents which rapidly hydrolyze the polyhalogen complexes. In order to obtain compounds soluble in organic solvents, it was necessary to resort to the salts of large organic cations. Trialkyl sulfonium salts were chosen because of the ease with which they can be prepared.

Following the method given by Werner,[2] 2 g. of trimethylsulfonium iodide was dissolved in 200 ml. of glacial acetic acid containing about 8% of carbon tetrachloride, and a slow stream of dry chlorine was passed through the solution for several minutes. The solution was cooled to 0° and yellow crystals of the complex crystallized out. The product was filtered, washed with chloroform to remove excess chlorine, and dried in an oven at 50°. About 1.7 g. (50% yield) of the complex was obtained. The melting point of the final product was 180° which does not agree with the m.p. of 155° given by Werner. Analysis for chlorine gave 40.2% Cl, calculated for $(CH_3)_3SICl_4$, 41% Cl. The compound was quite stable when kept stoppered and out of contact with moisture. Odor of chlorine was noticeable, however, if it was exposed to humid air.

It was found impossible to recrystallize this compound even if the solvents were previously saturated with chlorine. Invariably a mixture of the tetrachloride and the dichloride complexes was obtained.

For comparison purposes it was necessary to prepare the analogous dichloroiodide complex. Method of preparation suggested by Dobbin and Mason[3] was used with some modifications. Dry trimethylsulfonium iodide was placed in an erlenmeyer flask and a current of chlorine was passed over it. A dark brown residue appeared in the first step of the reaction, being probably the iodine chloride formed: $(CH_3)_3SI + Cl_2 \rightarrow (CH_3)_3SCl + ICl$. After several minutes the dark color disappeared and a yellow crystalline product was obtained. Since in all cases the analysis showed an excess of chlorine present (due to the formation of some tetrachloroiodide complex), the complex was recrystallized from alcohol, dried in an oven at 50°, and analyzed. The amount of chlorine found was 25.2%, calculated for $(CH_3)_3SICl_2$, 25.8% Cl. The melting point was 103° which agreed with that given by Dobbin and Mason. The yield was 60%.

It was necessary to cool the erlenmeyer during the reaction, and to pass the chlorine only at a very slow rate; otherwise, iodine chloride formed in the first step of the reaction would be carried off with resulting poor yields.

Since the ultraviolet spectrum of these complexes was of particular interest, the choice of a suitable solvent was somewhat restricted. Alcohols could not be used for reasons already given, and the saturated aliphatic hydrocarbons did not possess sufficient polarity to dissolve appreciable amounts of the complex.

Acetonitrile solutions were found to be relatively stable for short periods of time and the solvent did possess the required transmittancy in the ultraviolet region. As in all previous work with the polyhalogen complexes,[4] the purity of the solvent was quite critical.

Acetonitrile was purified by shaking it for several hours with a concentrated solution of potassium hydroxide, drying over anhydrous sodium carbonate and then distilling from phosphorus pentoxide through a three-foot column. The b.p. was 81.0° at 760 mm. of pressure.

Solutions were prepared by dissolving the required amount of the complex in acetonitrile, just before the absorption measurements. Usually,

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[1] N. V. Sidgwick, "The Chemical Elements and Their Compounds," Vol. II, Oxford University Press, New York, N. Y., 1950, p. 1198 ff.

[2] E. A. Werner, *J. Chem. Soc.*, **89**, 1625 (1906).

[3] L. Dobbin and O. Mason, *ibid.*, **47**, 67 (1885).

[4] (a) R. E. Buckles, A. I. Popov, W. F. Zelezny and R. J. Smith, THIS JOURNAL, **73**, 4525 (1951); (b) R. E. Buckles, J. Yuk and A. I. Popov, *ibid.*, **74**, 4379 (1952); (c) A. I. Popov and E. H. Schmorr, *ibid.*, **74** 4672 (1952).

the concentration was checked by an iodometric titration, and a good agreement was obtained with concentrations calculated from the weight of the sample. Every precaution was taken not to expose the solution to atmospheric moisture more than it was absolutely necessary. Two concentration ranges were used, depending on the region investigated. The solutions were approximately 10^{-3} M for measurements in the 380–260 mμ range, and 10^{-5} M in the 260–210 mμ range.

Absorption measurements were made on a Beckman model DU spectrophotometer and the final runs were on a Cary recording spectrophotometer model 11. Matched silica cells of 1-cm. path length were used. The experiments were carried out at room temperature, which was approximately 25°.

Preliminary measurements showed that the absorption spectrum of the tetrachloroiodide complex did change with time. Fresh solutions of this complex gave two maxima, one at 214 mμ with a molar absorbancy index of 42000,[5] and a second at 340 mμ with a molar absorbancy index of 1280. In about 30 minutes it was noticed that the absorbancy of the first peak increased and the maximum was shifted toward longer wave lengths, while the second maximum remained at the same wave length, but decreased in absorbancy.

A time study of this change of absorption is illustrated in Fig. 1. After 24 hours the maxima were at 227 and 338 mμ with the molar absorbancy indices of 55000 and 410, respectively. No further change of the absorption spectrum with time was observed.

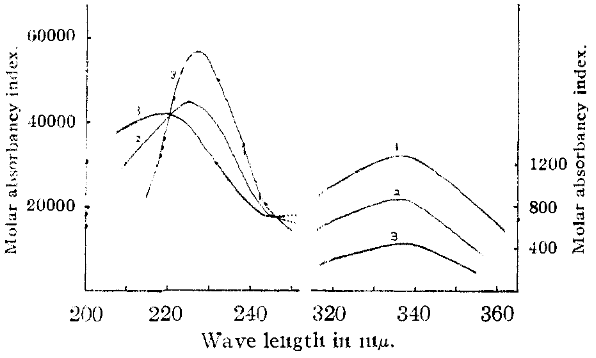

Fig. 1.—Absorption spectrum of trimethylsulfonium tetrachloroiodide in acetonitrile: curve 1, fresh solution; curve 2, after 2.5 hours; curve 3, after 24 hours.

The absorption curve of the dichloroiodide complex in acetonitrile is given in Fig. 2. The solution appeared to be stable and did not change the absorption spectrum with time. It is seen that this curve essentially coincides with the 24-hour old curve of the tetrachloroiodide complex. Presence of two isobestic points (Fig. 1) at 219 and 245 mμ shows that only two absorbing species were present in solution, and therefore the conclusion is warranted that the tetrachloroiodide ion dissociated in acetonitrile to the dichloroiodide and chlorine.

Undoubtedly, a fast equilibrium $(CH_3)_3SICl_4 \rightleftarrows (CH_3)_3SICl_2 + Cl_2$ is established, and curve 1, Fig. 1, illustrates the equilibrium conditions.

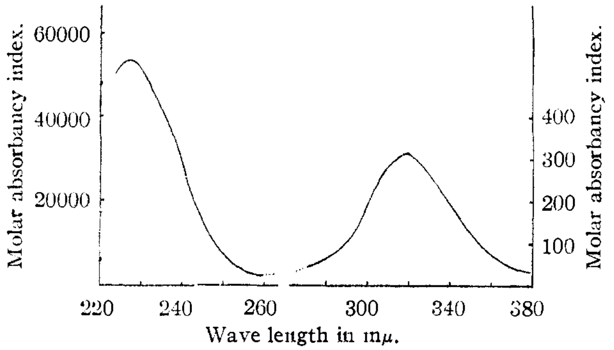

Fig. 2.—Absorption spectrum of trimethylsulfonium dichloroiodide in acetonitrile.

The slow reaction observed is very probably due to the shift in equilibrium because of removal of chlorine by the chlorination of the solvent.

Since the tetrachloroiodide ion can be considered as a complex of iodine trichloride with Cl^-, it seems interesting to note that apparently this complex formation stabilizes iodine trichloride to some extent. It has been fairly well established that iodine trichloride molecule is stable only in the solid state[6] and dissociated in solution, immediately and completely, to iodine chloride and chlorine. If this was the case with the tetrachloroiodide complex, the initial absorption curve should be a composite curve of ICl_2^- and Cl_2. That this is not the case is easily seen from the fact that the absorbancy increases with time at 227 mμ. Attempts were made to obtain absorption curves of iodine trichloride and of chlorine in acetonitrile, but the results were unsatisfactory, because, in order to obtain sufficient amount of absorption, comparatively concentrated solutions ($\geqslant 10^{-2}$ M) had to be prepared and under these conditions the chlorination of the solvent was quite rapid.

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[5] Nomenclature used in this paper follows the recommendations of the National Bureau of Standards, Letter Circular, LC-857 (1947).

[6] A. E. Gillam and R. A. Morton, *Proc. Roy. Soc.* (*London*), **A124**, 604 (1929).

DEPARTMENT OF CHEMISTRY
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IOWA CITY, IOWA

A Polarographic Study of Thallium Pyrophosphate Complexes

BY PASCHOAL SENISE[1] AND PAUL DELAHAY

RECEIVED MARCH 6, 1952

Polarographic studies of pyrophosphate complexes of various metals have been reported by Sartori,[2] Rogers and Reynolds,[3] Laitinen and Onstott[4] and Reynolds and Rogers.[5] In these investigations, no mention is made of the formation of thallium pyrophosphate complexes; and it is the purpose of the present paper to report a quantitative study of such compounds.

Experimental

Preliminary measurements were made with a Sargent model XI polarograph. Final waves were determined point

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[1] On leave from Faculdade de Filosofia, Ciencias e Letras da Universidade de Sao Paulo, Sao Paulo, Brazil.

[2] G. Sartori, *Gazz. chim. ital.*, **64**, 3 (1934).

[3] L. B. Rogers and C. A. Reynolds, THIS JOURNAL, **71**, 2081 (1949).

[4] H. A. Laitinen and E. I. Onstott, *ibid.*, **72**, 4729 (1950).

[5] C. A. Reynolds and L. B. Rogers, *Anal. Chem.*, **21**, 176 (1949).

by point by measuring the current and the voltage with a Sargent polarograph model III and a Leeds and Northrup student potentiometer, respectively. An H-cell[6] was used throughout the work. The rate of flow of mercury and the drop time, measured at −0.7 volt (*vs.* S.C.E.), were as follows: m = 2.31 mg. sec.$^{-1}$ and t = 3.10 sec. C.P. reagents were used without further purification. Except when otherwise indicated, the solutions were 0.2 molar with respect to potassium hydroxide and the ionic strength was adjusted at a value of 2.0 by addition of potassium nitrate. Gelatin was used as a maximum suppressor at a concentration of 0.01%. All measurements were made at 35 ± 0.1°.

In the study of the influence of pH, the pyrophosphate solutions were buffered with acetic acid for pH's below 6 and with boric acid for pH's between 6 and 8. In other experiments in which the pH was comprised between 7.5 and 8.5, the Kolthoff[7] buffer (monopotassium phosphate and borax) was used. For pH's between 8.5 and 11 the Britton and Welford[7] buffer of monopotassium phosphate and sodium hydroxide were employed. For higher pH's only potassium hydroxide was used.

Description and Discussion of Results

Influence of pH.—Experiments carried out in solutions buffered at different pH's but at the same ionic strength (μ 1.5) and constant sodium pyrophosphate concentration (0.1 M), showed that the diffusion current decreases as the pH is increased up to 9.5. With more alkaline solutions, the current is independent of pH. This variation of the diffusion current is probably caused by the progressive ionization of pyrophosphoric acid and pyrophosphate ions and the resulting changes in the nature of the thallium complexes. Extreme values of the diffusion current for a millimolar thallium solution were as follows: 5.66 microamp. at pH 4.5, and 3.64 microamp. at, and above, pH 9.5.

Influence of Concentration of Pyrophosphate.—The half-wave potentials and diffusion currents for various concentrations of pyrophosphate at a constant ionic strength of 2 (except for the highest concentration of pyrophosphate) are given in Table I.

TABLE I

DATA FOR 0.2 MILLIMOLAR THALLIUM SOLUTION IN 0.2 M POTASSIUM HYDROXIDE

$Na_4P_2O_7$, moles per l.	$E_{1/2}$,[a] volt *vs.* S.C.E.	i_d, microamp.
0.000	−0.4887	1.19
.012	− .4959	1.04
.033	− .5075	0.90
.057	− .5163	.82
.093	− .5257	.77
.116	− .5310	.74
.141	− .5387	.73
.166	− .5466	.70
.187	− .5520	.69

[a] $E_{1/2}$ reproducible within 0.001 volt.

By plotting $E_{1/2}$ against the logarithm of the concentration of pyrophosphate a curve is obtained. This indicates the formation of at least two complexes, and consequently the classical polarographic method of determining unstability constants[8] is not applicable. The formation constants for the various complexes, however, can be calculated by the method recently reported by DeFord and Hume.[9,10] In this treatment one calculates the functions

$$F_0 = \text{antilog}\left\{0.435\,\frac{nF}{RT}\,[(E_{1/2})_S - (E_{1/2})_C] + \log\frac{I_S}{I_C}\right\} \quad (1)$$

$$F_1 = [F_0 - K_0/f_S]C_Xf_X \quad (2)$$

$$F_j = [F_{j-1} - K_{j-1}/f_{MX}]/C_Xf_X \quad (3)$$

where $(E_{1/2})_S$ and $(E_{1/2})_C$, I_S and I_C are the half-wave potentials and the diffusion currents of the waves for the simple ion and the complexes, respectively; K_0 is equal to unity; K_j is the formation constant of the complex of jth order; and C_x is the concentration of the complex forming substance.

In the present case the complexes $Tl(P_2O_7)_j^{(4j-1)-}$ which could possibly exist correspond to the following values of j: $1/4$, $1/3$, $1/2$, 1, 2, ... In order to determine whether the complex corresponding to $j = 1/4$ is formed one should consider the function

$$F_{1/4} = [F_0 - K_0/f_S]/C_X^{1/4}f_X \quad (4)$$

whose limit is $K_{1/4}$ when C_X approaches zero. This function $F_{1/4}$ was calculated, and it was concluded by extrapolating its value to $C_X = 0$ that $K_{1/4} = 0$, *i.e.*, that the undissociated pyrophosphate $Tl(P_2O_7)_{1/4}$ virtually does not exist in solution. Likewise, by plotting $F_{1/3}$ *vs.* $C_X^{1/3}$, and $F_{1/2}$ *vs.* $C_X^{1/2}$, it was concluded that the complexes $Tl(P_2O_7)_{1/3}^{-1/3}$ and $Tl(P_2O_7)_{1/2}^{-}$ are not formed under the present conditions. On the other hand, by plotting F_1 *vs.* C_X (Fig. 1), the value $K_1 = 49 \pm 8$ was obtained for the formation constant corresponding to the complex $Tl(P_2O_7)^{-3}$. The extreme values of F_1 shown in Fig. 1 were calculated by assuming that the precision for the quantity $[(E_{1/2})_s - (E_{1/2})_c]$ of equation (1) was ±0.002 volt and that the currents I_s and I_c were measured within ±1%. Likewise, the function F_2 (Fig. 1) was calculated on the basis of the extreme values of F_1. By extrapolating F_2 to zero concentration of pyrophosphate one obtains $K_2 = 75 \pm 75$. The plot of F_2 *versus* the concentration of pyrophosphate still exhibits a marked curvature, and consequently at least the complexes of 3rd and 4th order should be considered.[9] The calculation of K_3 and K_4, however, is rather meaningless because the errors on F_3 and F_4 are too large.

It should be added that, in the above calculations, all the activity coefficients were assumed to be equal to unity, as was done by Hume, *et al.*, in the study of cadmium thiocyanate complexes. Therefore, the above formation constants should be regarded as formal constants for an ionic strength of 2. In the present case, the charges of the complex ions are large, and consequently the activity coefficients are undoubtedly much smaller than one. As a result, the discrepancies between the above formal constants and the corresponding thermodynamic data are probably quite pronounced. Furthermore, liquid junction potentials were assumed to be constant regardless of the concentration of pyrophosphate ion. It is true that the ionic strength was constant in our experiments, but nevertheless the composition of the medium

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[6] J. J. Lingane and H. A. Laitinen, *Ind. Eng. Chem., Anal. Ed.*, **11**, 504 (1939).

[7] H. T. S. Britton, "Hydrogen Ions," Vol. I, D. Van Nostrand Co., Inc., New York, N. Y., 1943, p. 307.

[8] I. M. Kolthoff and J. J. Lingane, "Polarography," Interscience Publishers, Inc., New York, N. Y., 1941, Chap. X.

[9] D. D. DeFord and D. N. Hume, THIS JOURNAL, **73**, 5321 (1951).

[10] D. N. Hume, D. D. DeFord and G. C. B. Cave, *ibid.*, **73**, 5323 (1951).

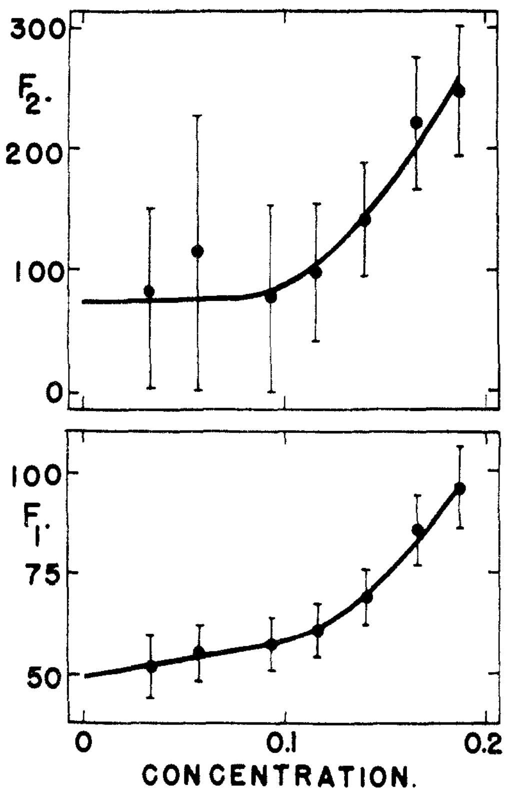

Fig. 1.—Variations of functions F_1 and F_2 with the concentration of pyrophosphate (in moles per l.). See data in Table I.

was changed, and this caused a variation of the liquid junction potential. However, the resulting error was probably small (less than 0.001 volt) since a saturated solution of potassium chloride was used in the junction.

Summarizing, the existence of various pyrophosphate complexes of $Tl(+1)$ was demonstrated. The species $Tl(P_2O_7)^{-3}$ is predominant in the neighborhood of pH 13, but complexes of a higher order also exist; their formation constants, however, can only be determined in a very approximate manner by the polarographic method.

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The Systems Ammonia-Sulfamide and Sulfuric Acid-Sulfamide

BY HARRY H. SISLER AND DANNY M. ROSENBAUM

RECEIVED AUGUST 20, 1952

Several studies[1,2] of the behavior of acid amides toward basic and acidic solvents have been carried out in recent years. As part of this program, we were interested in investigating the binary systems ammonia-sulfamide and sulfuric acid-sulfamide.

Experimental

Materials.—Anhydrous sulfuric acid was prepared by adding the calculated amount of fuming sulfuric acid to chemically pure concentrated sulfuric acid which had been checked to assure the absence of nitric acid. The purity of the anhydrous sulfuric acid thus obtained was checked by determining its freezing point. The freezing point of our product was 10.3° (lit. 10.31°). The freezing point was rechecked before each sample of the acid was taken.

Anhydrous ammonia of the synthetic grade with a stated purity of 99.9% was used. Its purity was also checked by its freezing point; found −77.8° (lit. −77.74°).

Sulfamide was prepared by the reaction of sulfuryl chloride with an excess of anhydrous ammonia in the vapor state. A stream of dry nitrogen was passed through a dilute solution of sulfuryl chloride in petroleum ether. The gas stream (containing entrained sulfuryl chloride) was then passed into a reaction flask into which a large excess of gaseous ammonia was being passed. The solid products of the reaction were dissolved in water which was made slightly acidic with hydrochloric acid. After the solution had stood for at least 48 hours, the solution was evaporated to a very small volume under an infrared lamp in a current of dry air. The height of the lamp was adjusted so as to maintain a temperature between 50 and 60° in the evaporating solution. The small volume of remaining solution was then placed in a vacuum desiccator over calcium chloride to crystallize. The dried crystals were extracted with ethyl acetate, the ethyl acetate evaporated, and the crystals obtained dried in a vacuum desiccator. The sulfamide was further purified by another recrystallization from ethyl acetate. The product melted sharply at 91.5° (uncor.) (lit. 91.5-93.0°). Yields approximating 30 to 35% based upon the sulfuryl chloride used were obtained.

The System Sulfuric Acid-Sulfamide.—It was observed immediately that when samples of anhydrous sulfuric acid and sulfamide are mixed a clear solution is obtained, but that, if the solution stands for from 15 to 30 minutes at room temperature, a white solid begins to appear. This crystalline white solid was removed and shown by analysis and determination of the melting point to be virtually pure sulfamic acid. The reaction was also carried out in pure nitromethane and it was shown that, in the presence of excess sulfuric acid, the solvolytic reaction represented by the equation

$$SO_2(NH_2)_2 + SO_2(OH)_2 \longrightarrow 2SO_2(NH_2)(OH)$$

takes place quantitatively to yield sulfamic acid, which may be filtered off and isolated. Typical analytical results are listed in Table I.

TABLE I

	Experimental	Calcd. for $SO_2(NH_2)(OH)$
Sulfur(VI), %	31.8, 32.2, 32.1	33.0
Equiv. wt.	96.3, 96.5, 96.4	97.1

Melting point 203° (uncorrected) (lit. 205).

The System Ammonia-Sulfamide.—This binary system was investigated by the cryoscopic method and a phase diagram for the system constructed. The freezing point cell used is shown in Fig. 1. The thoroughly cleansed and dried cell was flushed out with dry nitrogen and the two side arms stoppered. A weighed sample of sulfamide was introduced through side arm B, the side arm sealed, and the whole cell and contents weighed. The desired amount of ammonia was introduced into the cell through side arm A and condensed by a Dry Ice-$CHCl_3$-CCl_4 cooling mixture. The rate of condensation of ammonia was followed by means of a flowmeter in the line. After the desired quantity of ammonia had been condensed, the side arm A was sealed, and the cell allowed to come to room temperature and weighed. The freezing points of the mixtures thus obtained were determined by means of cooling curves recorded, as described in previous publications from this Laboratory, on a Micromax self-recording potentiometer connected to a copper-constantan thermocouple placed in the well (C) of the cell. Constant stirring was provided by an intermittently actuated solenoid around the neck of the cell and a glass stirrer (E) which contained an iron slug (D) in its upper end. The thermocouple was covered with 2,3-dimethylpentane to minimize convection effects in the thermocouple well. The precautions observed and the techniques used in taking the freezing points were essentially the same as described in previous publications from this Laboratory.[3] The freezing

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[1] H. H. Sisler, A. W. Davidson, R. Stoenner and L. Lyon, THIS JOURNAL, **66**, 1888 (1944).

[2] H. H. Sisler, C. A. VanderWerf and S. Stephanou, *ibid.*, **68**, 2538 (1946).

[3] B. Rubin, H. H. Sisler and H. Schechter, *ibid.*, **74**, 877 (1952).

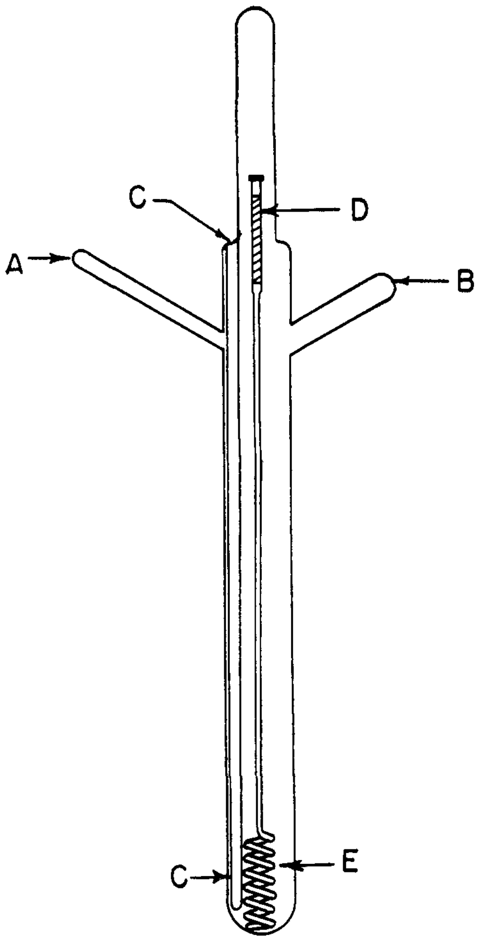


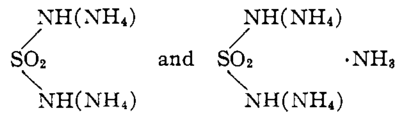
Fig. 1.—Freezing point cell.

points were each determined at least twice and are believed to be correct within 1.5°. Each portion of the curve was checked at least twice and no more than seven consecutive points were determined without cleaning out the cell completely.

The results of this phase study are represented graphically in Fig. 2. This figure indicates the formation of two previously unreported compounds, *viz.*, $SO_2(NH_2)_2\cdot 2NH_3$ and $SO_2(NH_2)_2\cdot 3NH_3$, with melting points of −15.8° and −12.5°, respectively. It came as something of a surprise that the 1:1 compound is not indicated. Eutectics were observed at −21.8° and 59.5 mole % of ammonia, at −19.0° and 69.1 mole % of ammonia, and at about −78.0° and about 97 mole % of ammonia.

Discussion and Conclusions

The complete solvolysis of sulfamide in solution in anhydrous sulfuric acid prevents (or at least makes very difficult) the determination of whether or not sulfamide acts as a base toward sulfuric acid. With reference to the sulfamide-ammonia system, one might be tempted to interpret the formation of the compounds $SO_2(NH_2)_2\cdot 2NH_3$ and $SO_2(NH_2)_2\cdot 3NH_3$ as indicating that sulfamide acts as an acid toward anhydrous ammonia. The two compounds would thus be formulated



$$SO_2\begin{array}{l}\diagup NH(NH_4)\\ \diagdown NH(NH_4)\end{array}\quad\text{and}\quad SO_2\begin{array}{l}\diagup NH(NH_4)\\ \diagdown NH(NH_4)\end{array}\cdot NH_3$$

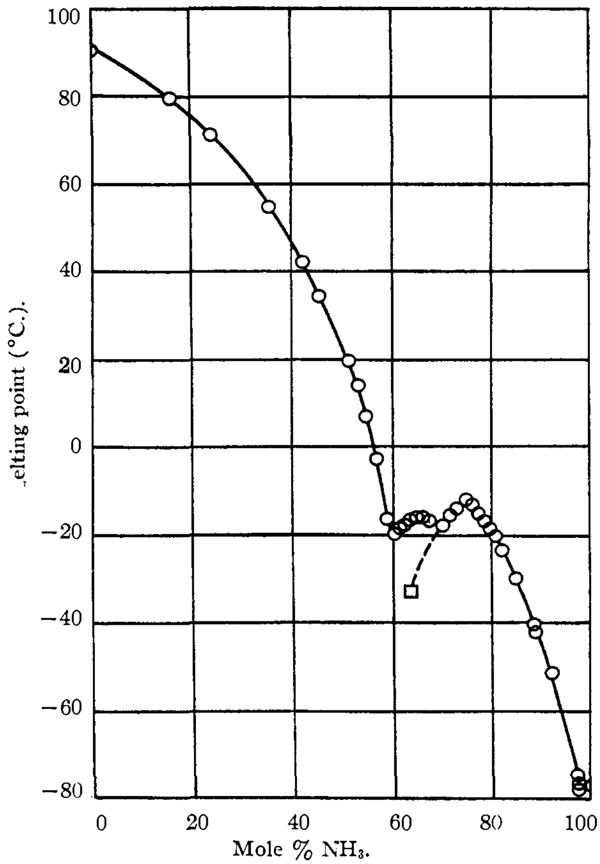
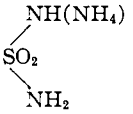


Fig. 2.—The system sulfamide–ammonia.

If this is the correct interpretation, however, it is difficult to understand why no evidence for the compound $SO_2(NH_2)_2\cdot NH_3$, or



$$SO_2\begin{array}{l}\diagup NH(NH_4)\\ \diagdown NH_2\end{array}$$

was obtained. There is no question, however, about the existence of the two new compounds, whatever may be the nature of their structures.

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Precipitate-Ion Exchange Reactions Using Nickel-63

By George K. Schweitzer and Parker B. Baum

Received July 7, 1952

A number of solid-fluid exchange reactions have been carried out in the past.[1] The purpose of these experiments was to investigate the exchange of nickel(II) ions in aqueous solution with nickel(II) in a number of insoluble compounds.

Experimental

Preparation of Compounds.—The insoluble nickel(II) compounds were prepared by the procedures described in the literature references cited in the footnotes of Table I.

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[1] A. C. Wahl and N. A. Bonner, "Radioactivity Applied to Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, pp. 351–364.

TABLE I

EXCHANGE RESULTS

Compound	Percentage exchange in 20 min.	40 min.	60 min.	Half time (min.)	Rate
Nickel(II) orthophosphate[a]	45	67	84	23	2.3×10^{-6}
Nickel(II) pyrophosphate[b]	32	62	81	25	2.2×10^{-6}
Nickel(II) sulfide[c]	34	57	79	26	2.1×10^{-6}
Nickel(II) hydroxide[d]	33	50	70	41	1.3×10^{-6}
Nickel(II) hexacyanoironate(II)[e]	16	37	55	53	1.0×10^{-6}
Tetrapyridine nickel(II) thiocyanate[f]	10	23	35	99	6.1×10^{-7}
Bis-diphenylthiocarbazide nickel(II)[g]	10	19	27	139	4.4×10^{-7}
Bis-salicyaldoxime nickel(II)[h]	5	17	20	173	3.5×10^{-7}
Bis-dimethylglyoxime nickel(II)[i]	No exchange				

[a] R. Tupputi, *Ann. chim. phys.*, [2] **78**, 133 (1840); J. W. Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. XV, Longmans, Green and Co., New York, N. Y., 1936, p. 494. [b] A. Schwarzenberg, *Ann.*, **65**, 158 (1848). [c] N. V. Sidgwick, "Chemical Elements and Their Compounds," Vol. II, Oxford University Press, New York, N. Y., 1950, p. 1432. [d] R. Tupputi, ref. *a*, p. 383. [e] P. Walden, *Z. physik. Chem.*, **10**, 710 (1892). [f] G. Spacu and J. Dick, *Z. anal. Chem.*, **71**, 442 (1927). [g] W. Parri, *Giorn. farm. chim.*, **73**, 207 (1924); *C. A.*, **19**, 223 (1925). [h] H. L. Riley, *J. Chem. Soc.*, 895 (1933). [i] L. Tschugaeff, *Compt. rend.*, **145**, 679 (1907).

Radioactive Nickel-63.—The radioactive nickel tracer employed was nickel-63, which emits a 0.057-Mev. beta particle with a half-life of 85 years.[2] This was obtained from the Oak Ridge National Laboratory as nickel(II) chloride in dilute hydrochloric acid.

Exchange Procedure.—All exchange reactions were carried out at 25°. Each reaction mixture consisted of 5.00 ml. of 0.0309 *M* radioactive nickel(II) chloride solution, 10.00 ml. of water and the insoluble nickel(II) compound under consideration. These were prepared by precipitating the nickel(II) ion from 4.05 ml. of 0.0381 *M* nickel(II) chloride solution. This gave equimolar quantities of nickel in the two species involved in each reaction. Reaction mixtures of each compound were vigorously stirred for periods of 20, 40 and 60 minutes. The precipitates were separated by suction filtration and the filtrates were treated with ammoniacal dimethylglyoxime solution to precipitate the nickel as bis-dimethylglyoxime nickel(II). These precipitates were mounted on fritted glass filter discs and the activity of each was measured. All samples were greater than infinite thickness for self absorption. A standard counting sample was prepared from the original radioactive solution.

Radioactivity Apparatus.—A Tracerlab SC-16 Windowless Flow Counter operating in the Geiger region was used in conjunction with a Tracerlab SC-2A Scaler to measure the activities of the samples. All samples were counted for a sufficiently long time to give a standard deviation equal to or less than 1%.

Results

The experimental results are shown in Table I. All systems except the bisdimethylglyoxime nickel(II) one showed exchange for the period of time of the reactions. Plots of the logarithm of one minus fraction exchange against time gave straight lines for all other exchange reactions. The rates of exchange were then calculated from the expression as given by Wahl and Bonner.[3] This equation is said to apply to heterogeneous reactions only if the mixing of isotopes in each phase is rapid as compared to the actual exchange process or to the diffusion across the interface.

Acknowledgment.—This work constitutes Contribution No. 112 from the Department of Chemistry of The University of Tennessee. The authors wish to thank the Research Corporation for the funds which made it possible.

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[2] "Isotopes," United States Atomic Energy Commission, Isotopes Division, March, 1951, p. 5.

[3] A. C. Wahl and N. A. Bonner, ref. 1, p. 34.

Dealkylation of Dialkylhydroquinone Diacetates with Aluminum Chloride[1]

BY JACK L. R. WILLIAMS

RECEIVED JULY 14, 1952

When hydroquinone diacetate is submitted to the Fries rearrangement, the product is acetylhydroquinone.[2] However, when 2,5-dimethylphenyl acetate is treated under similar conditions, 2-acetyl-4,6-dimethylphenol results.[3] The acetyl group displaces an ortho-methyl group, rather than taking the open para-position.

In the course of studying the behavior of alkylhydroquinone diacetates, it has been found that dealkylation took place in the case of 2,5-di-*t*-butylhydroquinone and 2,5-di-*t*-amylhydroquinone diacetates. The reactions were carried out using anhydrous aluminum chloride in the absence of a solvent; the products were acetylhydroquinone, instead of the expected dialkylacetohydroquinone, and much tar. The alkyl side chains were probably eliminated as the aluminum chloride complexes which would be expected to polymerize under the reaction conditions.

Experimental

2,5-Di-*t*-butylhydroquinone Diacetate.—To a mixture of 22.2 g. (0.1 mole) of 2,5-di-*t*-butylhydroquinone and 51.0 g. (0.5 mole) of acetic anhydride there was added, with shaking, 5 cc. of a solution of 5 drops of concentrated sulfuric acid in 10 cc. of acetic anhydride. The temperature rose immediately and the reaction mixture was allowed to stand for 1.0 hour, after which time it was poured into 1.0 liter of ice-water. The white crystals were filtered and dried to yield 28.8 g. (94%), m.p. 172–173°. A small sample was recrystallized from benzene and dried *in vacuo*, m.p. 173–174°.

Anal. Calcd. for $C_{18}H_{26}O_4$: C, 70.6; H, 8.6. Found: C, 71.1; H, 8.9.

2,5-Di-*t*-amylhydroquinone Diacetate.—From 25.0 (0.1 mole) of 2,5-di-*t*-amylhydroquinone and 51.0 g. (0.5 mole) of acetic anhydride there was obtained, by the above procedure, 33.0 g. (98%) of 2,5-di-*t*-amylhydroquinone diacetate, m.p. 114–115° (softened at 112–113°).

Anal. Calcd. for $C_{20}H_{30}O_4$: C, 71.8; H, 9.0. Found: C, 72.2; H, 9.4.

Rearrangement of 2,5-Di-*t*-butylhydroquinone Diacetate with Aluminum Chloride.—A mixture of 50 g. (0.16 mole)

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[1] Communication No. 1501 from the Kodak Research Laboratories.

[2] G. C. Amin and N. M. Shah, *Org. Syntheses*, **28**, 42 (1948).

[3] K. von Auwers, H. Bundesmann and F. Wieners, *Ann.*, **447**, 162 (1926).

of 2,5-di-*t*-butylhydroquinone diacetate and 109 g. (0.81 mole) of anhydrous aluminum chloride was divided into two portions. One portion was placed in a 1-liter beaker surrounded by an oil-bath maintained at 125–130°. The temperature of the periodically stirred mixture rose to 110° during 20 minutes, after which time the second portion was added, with stirring. After the addition was completed, the reaction mixture was heated at 115–120° (oil-bath 130°) for 0.75 hour. The reaction mixture was cooled rapidly by pouring it into a large enamel tray. The solid reaction residue was stirred with 400 cc. of concentrated hydrochloric acid and 1.0 liter of crushed ice. The ice–acid slurry was heated on the steam-cone until all of the lumps had melted to an oil, after which time the oil was solidified and removed by chilling the mixture in ice. The oil was stirred with 200 cc. of 20% sodium hydroxide. Acidification of the filtered alkaline solution yielded 4.8 g. of yellow solid, m.p. 195°, which, after recrystallization from 25 cc. of ethanol, gave 2.3 g. of pure acetylhydroquinone, m.p. 204–205°. The mixed melting point with an authentic sample of acetylhydroquinone was 204–205°. An additional 0.7 g. of crude acetylhydroquinone, m.p. 201–202°, was obtained from the aqueous mother liquors by further chilling the mixture to 0°. The total yield of acetylhydroquinone, m.p. 201–205°, was 3 g. (12.1%). All attempts to isolate other definite compounds from the tarry reaction product were unsuccessful.

Rearrangement of 2,5-Di-*t*-amylhydroquinone Diacetate with Aluminum Chloride.—When a mixture of 54.5 g. (0.16 mole) of 2,5-di-*t*-amylhydroquinone diacetate and 109 g. (0.81 mole) of anhydrous aluminum chloride was treated as described above for 2,5-di-*t*-butylhydroquinone diacetate, 3.3 g. of crude acetylhydroquinone, m.p. 190–192°, was obtained. Recrystallization gave 1.4 g., m.p. 202.5–203°, yield 5.5%.

KODAK RESEARCH LABS.
EASTMAN KODAK CO.
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Coconut Milk Factor: The Growth-promoting Substances in Coconut Milk[1]

BY E. M. SHANTZ AND F. C. STEWARD

RECEIVED AUGUST 1, 1952

Coconut milk is the fluid endosperm that nourishes an immature embryo which later produces a spongy mass of cotyledonary tissue that eventually fills the central cavity of the seed. The dramatic ability of this fluid to foster rapid and random division of otherwise mature cells of higher plants has recently attracted attention. This communication will show that the growth-promoting qualities of coconut milk are due to a number of growth substances. At least three of these substances can be recognized as chemical entities. They have been isolated in small amounts, in crystalline form, and their general characteristics can be described. However, the actual number of such substances in coconut milk that give a distinct growth response when added separately and in low concentration to the nutrient medium may well be considerably larger.

When whole coconut milk is added to a basal medium containing mineral salts, sugar and vitamins it causes a striking increase in the growth by cell division of explants of certain tissues, notably carrot root phloem.[2] This response, under suitably controlled conditions, furnishes an assay method for the active substances[3] Whole coconut milk produces an optimum growth response when added to the culture medium at a level of about 15% by volume, which represents a concentration of about 10,000 p.p.m. on a dry weight basis.

The initial enrichment of the activity was made by treating whole coconut milk with an excess of mercuric acetate after dilution by an equal volume of ethanol. After filtration, the precipitate was suspended in water, treated with H_2S, and filtered to remove the precipitated sulfide. The filtrate was concentrated to a heavy sludge under reduced pressure and the sludge was twice extracted by agitation with 90% ethanol. Removal of the solvent left a dark heavy sirup equivalent to approximately 0.6% of the initial dry material of the coconut milk. This sirup showed optimum activity in the tissue culture growth test when added to the basal medium at a level of about 200 p.p.m.

The above extract was fractionated further by differential solubility in various solvents and by partition chromatography on cellulose. At this stage, fractions were obtained which, although active at much lower concentrations, failed to produce at any concentration a total response which approached that given by the addition of whole coconut milk. The full response, however, could be restored by recombination with certain other fractions which were known to contain, among other things, the bulk of the free amino acids present in the crude extract. A similar effect could be obtained by adding an enzymatic hydrolysate of casein to the basal medium at a level of 500 p.p.m., and to a somewhat lesser extent by the addition of pure amino acid mixtures. The addition of casein hydrolysate alone to the basal medium has but a relatively slight effect upon growth; a pronounced response is obtained only in combination with certain fractions from coconut milk. Extensive work has shown, however, that the degree of dependence upon casein hydrolysate varies somewhat among individual carrot roots from the same stock and to a slightly greater extent among roots from different stocks.

Following the discovery of this effect of added casein hydrolysate, various fractions of the coconut milk concentrate were re-examined to determine which ones, ineffective in themselves, became active when tested in the presence of casein hydrolysate. This was done by measuring the growth of aseptic carrot tissue explants in an otherwise synthetic medium. From fractions which proved to be active in this assay procedure small amounts of three substances have now been isolated which, when tested in the presence of casein hydrolysate, induce a rate of growth which approaches that obtained by the use of whole coconut milk.

Compound A.—This was obtained directly upon evaporation of the alcohol extract described above. The alcohol-soluble portion of the mercury-freed precipitate from 800 gallons of coconut milk was reduced to three liters of aqueous solution. This was filtered to remove a small amount of insoluble residue. Upon drying the filter paper a number of small white crystals could be seen and these were mechanically separated from extraneous material. The 78 mg. of crude crystals thus obtained were twice recrystallized from 2 ml. of hot absolute ethanol, giving a final yield of 56 mg. of fine white needles melting at 240.5° (uncor.). The maximum solubility of this compound in water at room temperature was approximately 40 mg./l. The ultraviolet absorption curve in absolute ethanol is shown in Fig. 1 and the infrared absorption curve in a Nujol mull is shown in Fig. 2. This material gave no color reaction with ninhydrin. *Anal.* C, 75.22; H, 6.93; N, 14.19. The growth response in the carrot tissue bioassay test is shown in Fig. 6.

Further Fractionation Procedure.—An amount of the crude concentrate equivalent to approximately 200 gallons of the original coconut milk was further enriched by several solvent fractionation procedures to yield 2.8 g. of material active in the growth assay at 20 p.p.m. This concentrate was chromatographed in *n*-butanol–acetic acid–water mixture on a column containing 800 g. of finely powdered cellulose and was divided into 300 fractions of 25 ml. each. Each fraction was examined for its ultraviolet absorption, fluorescence under ultraviolet, and intensity of its reaction, if any, with ninhydrin.

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(1) This work commenced at the University of Rochester and has been continued at Cornell University. It has been supported by grants to one of us (F. C. S.) from the National Institute of Health. Access to the large bulk of coconut milk was made possible through the generous help of the Grasselli Chemicals Division of the du Pont Co. Mrs. Alice Peabody assisted with the growth assays by tissue culture methods.

(2) S. M Caplin and F. C. Steward, *Science* **108**, 655 (1948).

(3) (a) S. M. Caplin and F. C. Steward, *Nature*, **163**, 920 (1949); (b) F. C. Steward, S. M. Caplin and F. K. Millar, *Ann. Botany*, **16**, 57 (1952).

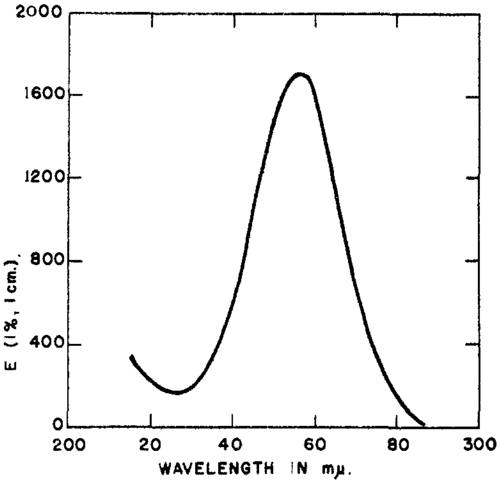

Fig. 1.—Ultraviolet absorption spectrum of compound A in absolute ethanol: E (1%, 1 cm.) at the maximum (256 mμ) = 1700.

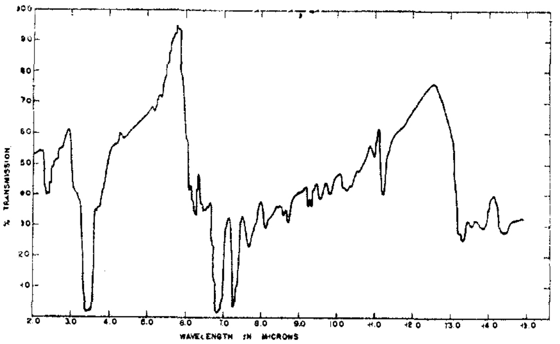

Fig. 2.—Infrared spectrum of compound A in a Nujol mull. The strong absorption bands at 3.45 and 7.26 μ and part of the band at 6.90 μ are due to the Nujol.

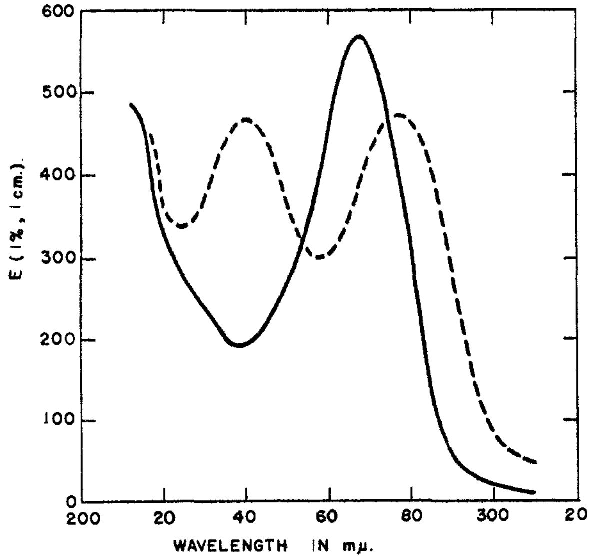

Fig. 3.—Ultraviolet absorption curve of compound B in 0.001 N HCl (solid line) and in 0.001 N NaOH solution (dotted line). The values of E (1%, 1 cm.) at the maxima are 568 at 267 mμ in acid solution, and 470 at 240 mμ and 475 at 277 mμ in alkaline solution.

About 50% of the material preceded the first strong ninhydrin reacting region. Strong biological activity was found distributed throughout these early fractions, and further fractionation of material from this region indicates that there are undoubtedly several active substances, not yet obtained pure but identifiable by differences in ultraviolet absorption or, in at least one instance, by an intense blue fluorescence.

From the fastest-moving ninhydrin-reacting region, crystalline phenylalanine was obtained and its identity established by paper chromatography. From a later region of fractions, showing both a strong ninhydrin test and ultraviolet absorption at 275 mμ, crystalline tyrosine was obtained. Between the phenylalanine and tyrosine regions there were fractions which absorbed strongly at 260–275 mμ but did not react with ninhydrin. From these fractions B and C were isolated.

Compound B.—Crystalline compound B was obtained in very small amount from the fractions immediately preceding the tyrosine upon evaporating to a small volume. The crystals were filtered, washed with alcohol, redissolved in water, and ultimately recrystallized from 0.3 ml. of absolute alcohol One and two-tenths milligrams of small white needles were obtained after filtering, washing and drying. From the adjoining fractions an additional 0.7 mg. was obtained. The distinctive ultraviolet absorption curve of this compound with its pronounced shift between acid and alkaline solution (Fig. 3) made it possible to determine that very little of this substance remained in the mother liquors. The small yield precluded any extensive chemical tests but two separate growth assays, one of which is shown in Fig. 6, demonstrated that this substance possessed definite growth-promoting power at very low concentrations.

Compound C.—This substance was obtained from the fractions immediately following phenylalanine in the cellu-

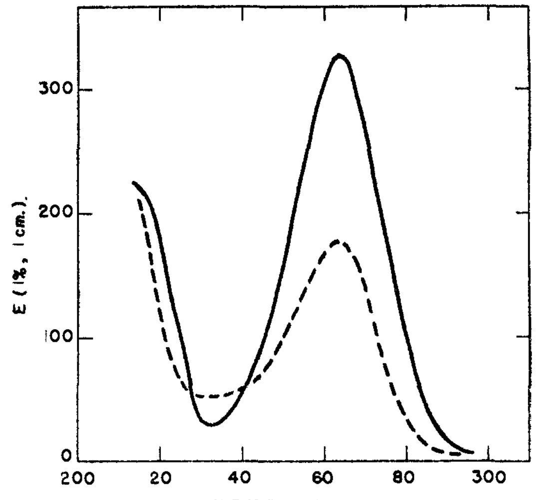

Fig. 4.—Ultraviolet absorption curve of compound C in 0.001 N HCl (solid line) and in 0.001 N NaOH (dotted line). The values of E (1%, 1 cm.) at the maximum (263 mμ) are 326 in acid solution and 177 in alkaline solution.

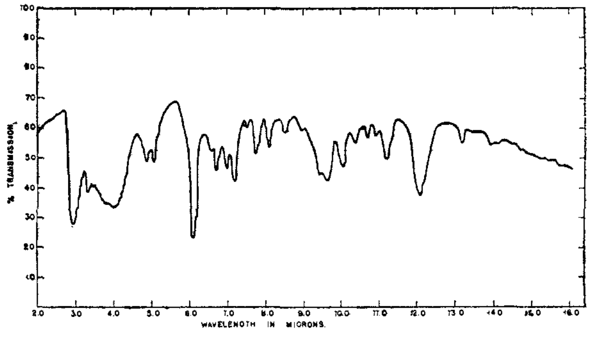

Fig. 5.—Infrared spectrum of compound C in the form of a thin semi-crystalline glass.

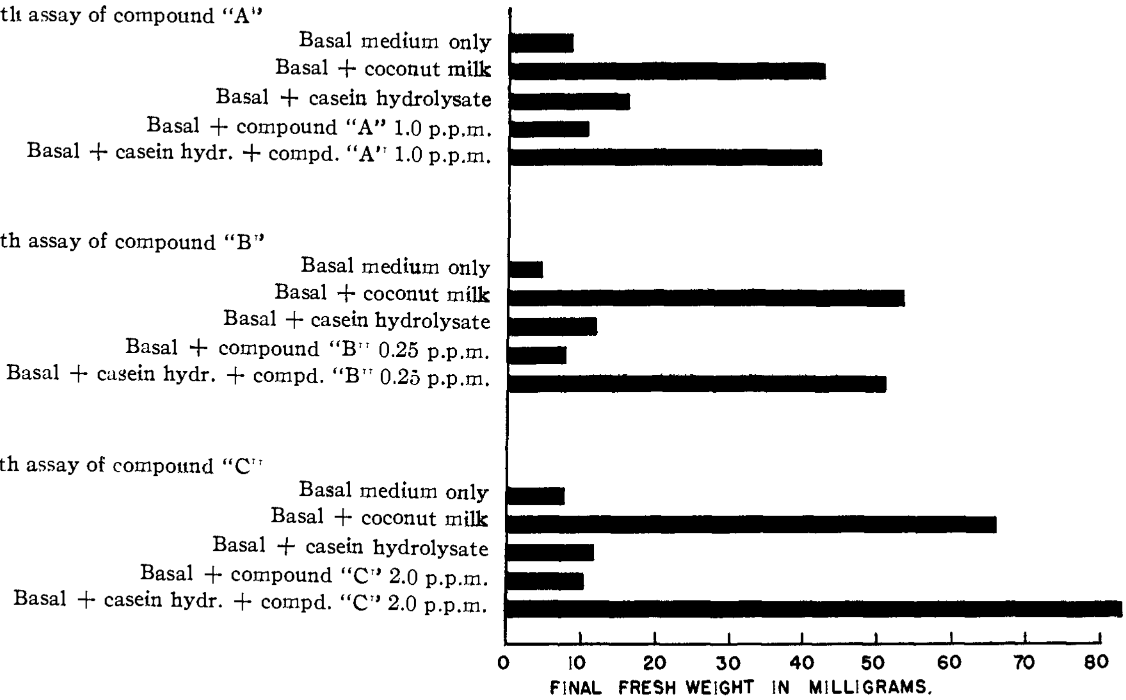

Fig. 6.—Tissue culture growth assays of compounds A, B and C. Each bar represents the average weight of 4 carrot phloem explants after a 14 day test period. Original weight of each explant = 2.6 mg. These tests were not done concurrently and therefore each of the three groups depicts the growth of explants from a different carrot root.

lose column partition chromatography procedure. These fractions (210 mg.) were dissolved in 50 ml. of hot acetone, the volume reduced to 10 ml. and the solution stored for 2 days at −20°. Clusters of prismatic white crystals were obtained which were filtered, washed with cold acetone, recrystallized twice at room temperature from 5 ml. of hot acetone, washed, and dried under vacuum giving a final yield of 19.9 mg.

When determining the melting point it was observed that the material sublimed at 200–210° and condensed in a crystalline state on the cool portions of the capillary. By ultraviolet and infrared absorption, the sublimed material was found to be apparently unchanged and its biological activity in the growth test also withstood this procedure.

The ultraviolet absorption curve of compound C in acid and alkaline solution is shown in Fig. 4. In alkaline solution the absorption maximum at 263 mμ is markedly depressed but unchanged in position. The infrared absorption curve is shown in Fig. 5.

An elementary analysis (single determinations only) showed C, 56.42; H, 8.11; N, 7.67. The growth promoting power of this substance in the carrot phloem explant tissue culture test is shown in Fig. 6.

In summary, the growth-promoting qualities of coconut milk are due in part to a substance or group of substances replaceable by casein hydrolysate. Over and above this, however, there are distinct substances, not contained in casein hydrolysate, which do not appear to be identical with other known vitamin-like compounds. Three such substances have been isolated in crystalline form and the almost certain occurrence of several others has been detected through the use of a carrot tissue culture bioassay procedure. The coconut milk growth factor (C.M.F.) is, therefore, not a single substance but a number of substances, possibly closely related, the identity of which still remains unknown. In view of their dramatic ability to incite random cell division in plant tissues, the isolation of these substances in greater quantity is now being undertaken and their nature and interactions with casein hydrolysate investigated further.

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The Composition of "Cycloheptanol" Produced by the Demianov Rearrangement

BY PETER A. S. SMITH AND DONALD R. BAER

RECEIVED AUGUST 14, 1952

The Demianov rearrangement of hexahydrobenzylamine with nitrous acid has been used as an example[1] of facile ring-expansion, and the product of the reaction has been and is being used as an intermediate in synthesis with the explicit assumption that it is pure cycloheptanol, free from other substances of similar boiling point.[2] We have found that the product consists surely of four and perhaps six, components, of which cycloheptanol constitutes not more than 65%. The other components are cyclohexylcarbinol, 1-methylcyclohexanol and the acetates of one or all of these alcohols. The sequestering of much of the product as acetate is presumably responsible for the failure of Ruzicka and Brugger to detect the cyclohexylcarbinol by reaction with phthalic anhydride.[2]

We have prepared ester-free "cycloheptanol" using sodium dihydrogen phosphate instead of acetic acid; its infrared absorption spectrum (Fig. 1, C) differs from that (Fig. 1, B) of the product ob-

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[1] For example, see R. C. Fuson in H. Gilman's "Treatise on Organic Chemistry," Vol. I, John Wiley and Sons, New York, N. Y., 1943, p. 97.

[2] L. Ruzicka and W. Brugger, *Helv. Chim. Acta*, 9, 399 (1926).

tained by Ruzicka and Brugger's method by the absence of the strong band at 5.8 μ due to carbonyl absorption from the presence of about 30% of ester. A presumably pure reference sample of cycloheptanol was prepared by the lithium aluminum hydride reduction of the heart-cut of a 400-ml. sample of suberone.[3] In the spectra of both samples produced by the Demianov reaction there are bands, notably at 8.5, 9.1 and 11.2 μ, not present in the spectrum of pure cycloheptanol (Fig. 1, A). These bands appear in the spectra of cyclohexylcarbinol (Fig. 1, G) and 1-methylcyclohexanol (Fig. 1, F), and from a synthetic mixture of 62% cycloheptanol, 33% cyclohexylcarbinol and 5% 1-methylcyclohexanol a nearly exact match (Fig. 1, D) is obtained for the spectrum of "cycloheptanol" produced in phosphate solution. The "cycloheptanol" produced in acetate solution after being freed of ester by saponification[4] gives a spectrum (Fig. 1, E) showing only small, quantitative differences (estimated proportions 50:40:10). In confirmation of these results, the permanganate oxidation of the Demianov "cycloheptanol" yielded cyclohexanecarboxylic acid, isolated as its anilide.

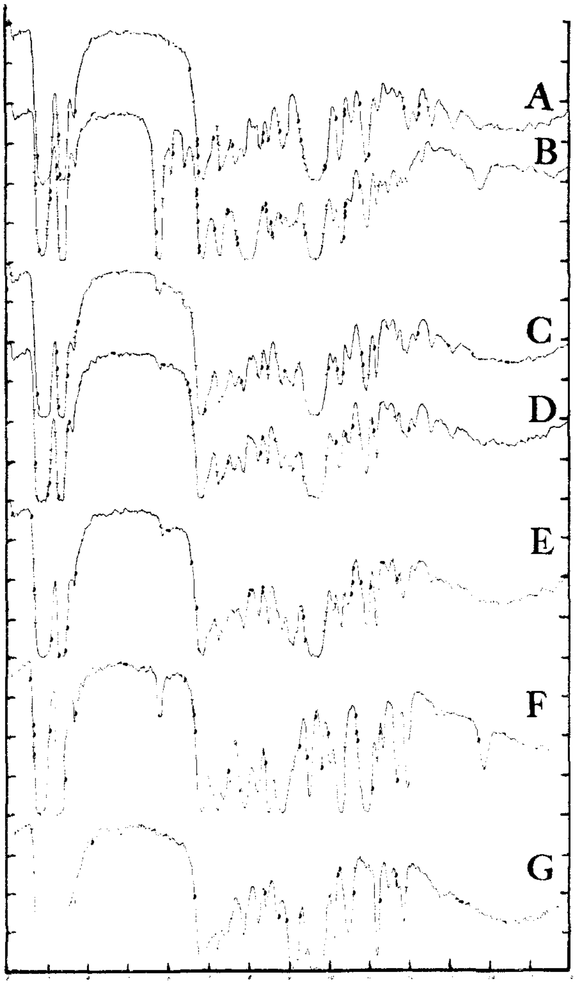

Fig. 1.—Infrared absorption spectra, undiluted liquids, Baird spectrophotometer: A, cycloheptanol; B, Demianov "Cycloheptanol" prepared with acetic acid; C, as B, but prepared with sodium dihydrogen phosphate; D, 63% cycloheptanol, 32% cyclohexylcarbinol, 5% 1-methylcyclohexanol; E, as B, after saponification; F, 1-methylcyclohexanol; G, cyclohexylcarbinol.

Inasmuch as the alcohols and their acetates all boil close to each other, the Demianov rearrangement should no longer be taken as a reliable route to cycloheptanol and the purity of substances already prepared from such "cycloheptanol" should be held in doubt.

Experimental

Hexahydrobenzylamine.—To a solution of 142 g. (1 mole) of cyclohexylacetic acid in 320 ml. of concd. sulfuric acid, heated to 50° and covered by about a half-inch layer of chloroform, was added 80 g. (1.25 moles) of sodium azide in portions with stirring, at such a rate as to keep the temperature between 50 and 60°. The mixture was then heated on a steam-bath for 30 minutes and poured onto 1200 g. of ice. The resulting aqueous solution was cautiously alkalized with concd. sodium hydroxide solution and the amine layer was separated and dried over potassium hydroxide. The distilled product, b.p. 159–161° (740 mm.), weighed 99.4 g. (88%).[5]

Cycloheptanol.—A 7.7-g. sample of suberone, b.p. 68–70° (18 mm.), was reduced with 0.92 g. of lithium aluminum hydride according to the standard procedure of Nystrom and Brown.[6] The product distilling at 87–88.5° (18 mm.) was collected as cycloheptanol; wt. 3.9 g. (50%), $n^{20}D$ 1.4757.[7]

Hexahydrobenzyl Alcohol.—The reduction of 15 g. of cyclohexanecarboxylic acid with lithium aluminum hydride gave 6.8 g. (56%) of alcohol, b.p. 181–182° (740 mm.).[8]

1-Methylcyclohexanol was prepared by the action of methylmagnesium iodide on cyclohexanone.[9] The weak absorption band at 5.8μ in its infrared spectrum (Fig. 1, F) indicates the presence of traces of ketone.

"Cycloheptanol" from Hexahydrobenzylamine. A. In Acetic Acid Solution.—The procedure of Ruzicka and Brugger[2] was applied to 10.0 g. (0.088 mole) of amine, and yielded 2.5 g. of olefins, b.p. 85–120° (740 mm.) and 6.0 g. of alcohols, b.p. 145–180° (740 mm.); 0.3 g. of unreacted amine was recovered. This material gave infrared spectrum B (Fig. 1); repeated fractional distillation reduced the intensity of the carbonyl absorption band (5.8 μ), but a carbonyl-free material could not be thus obtained.

B. In Phosphate Solution.—A saturated aqueous solution of 7.1 g. of sodium nitrite (0.11 mole) was added to a solution of 11.3 g. (0.10 mole) of amine and 55 g. (0.4 mole) of sodium dihydrogen phosphate in 150 ml. of water, and heated on a steam-bath for four hours; a brown oil separated. The mixture was then steam distilled and the distillate was extracted with three portions of ether. The combined extracts were fractionally distilled after drying over magnesium sulfate and yielded 2.6 g. (27%) of olefins, b.p. 95–104° (740 mm.), and 5.2 g. (46%) of alcohols, b.p. 158–184° (740 mm.), 2.2 g. (15%) of amine was recovered. The alcohol fraction gave infrared spectrum C (Fig. 1).

Oxidation of Saponified "Cycloheptanol."—Ten grams of the alcohol mixture (footnote 5) was stirred overnight with a solution of 11.4 g. of potassium permanganate in 225 ml. of

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[3] Kindly supplied by Dr. F. F. Blicke and Mr. Juan Azuara.

[4] This was done by Mr. Juan Azuara by refluxing 57 g. of "cycloheptanol" overnight with alcoholic potassium hydroxide, which yielded 28.8 g. of distilled alcohols, b.p. 178–184° (740 mm). His "cycloheptanol" was an aliquot of the distilled product obtained from 5 moles of amine, 5 moles of acetic acid and 6 moles of sodium nitrite.

[5] O. Wallach, *Ann.*, **353**, 299 (1907), reports b.p. 162–164°.

[6] R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 1197 (1947).

[7] I. Vogel, *J. Chem. Soc.*, 1336 (1938), reports $n^{20}D$ 1.4747; J. Böeseken and C. J. A. Hanegraaff, *Rec. trav. chim.*, **61**, 69 (1942), report $n^{20}D$ 1.4753; L. Ruzicka, P. A. Plattner and H. Wild, *Helv. Chim. Acta*, **28**, 395 (1945), report $n^{20}D$ 1.4705.

[8] P. Sabatier and A. Mailhe, *Ann. chim.*, [8] **10**, 527 (1907), report b.p. 181° (755 mm.) for this substance prepared in another manner.

[9] O. Wallach, *Ann.*, **359**, 287 (1908).

water. The filtered solution was extracted with benzene and then acidified with dilute sulfuric acid. The liberated cyclohexanecarboxylic acid was taken up in several portions of benzene, freed of solvent and warmed with 5 ml. of thionyl chloride. Treatment with 4 g. of aniline in benzene solution yielded the anilide, which was recrystallized from aqueous ethanol; yield 1.4 g., m.p. 147–148°.[10]

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[10] A. M. Schwartz and J. R. Johnson, THIS JOURNAL, **53**, 1065 (1931), report m.p. 146° for cyclohexanecarboxanilide.

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Preliminary Investigations on the Preparation of Optically Active Peptides Using Mixed Carbonic–Carboxylic Acid Anhydrides

BY JAMES R. VAUGHAN, JR.

RECEIVED JULY 2, 1952

The use of mixed carbonic–carboxylic acid anhydrides for the synthesis of peptides has been reported recently from this Laboratory[1] and independently from two European laboratories.[2] The general over-all equation for the reaction may be given by

$$\text{X-NHCH(R)COOCOOR}''' + \text{H}_2\text{NCH(R}'\text{)COOR}'' \longrightarrow$$

$$\text{X-NHCH(R)CONHCH(R}'\text{)COOR}'' + \text{R}'''\text{OH} + \text{CO}_2\uparrow$$

In our latest publication, the general nature of the reaction was demonstrated and it was reported that no racemization was observed in the preparation of simple, optically active dipeptide derivatives. The behavior of larger, optically active peptides, however, in which racemization may occur by mechanisms not operative in the case of dipeptides was not studied.

In the present work, the investigation of the retention of optical activity by this method of synthesis has been extended to a study of the reaction of amino acid esters with the mixed anhydrides of carbobenzoxy dipeptide acids in which the terminal amino acid having the free carboxylic function is optically active.

As model compounds, two dipeptide derivatives, carbobenzoxyglycyl-L-leucine and carbobenzoxyglycycl-L-phenylalanine, were examined. The first of these formed a toluene-soluble triethylamine salt and was caused to react with isobutylchlorocarbonate and then with methyl glycinate, by a modification of the method previously described,[1] to give methyl carbobenzoxyglycyl-L-leucylglycinate in 60% yield after purification. A 7% yield of the DL-isomer was also isolated.

The triethylamine salt of carbobenzoxyglycyl-L-phenylalanine, however, was only slightly soluble in toluene, and it was necessary to add a second solvent to effect solution. The use of toluene as the main solvent was desirable in order to obtain reaction temperatures of about −5° for the anhydride-forming step. When chloroform was used for this purpose and the reaction was carried through using isobutyl chlorocarbonate and ethyl glycinate in the usual manner, almost complete racemization occurred. Ethyl carbobenzoxyglycyl-DL-phenylalanylglycinate was obtained in 64% yield, whereas only 4% of the L-isomer was formed.

On further investigation, it was found that the amount of racemization observed could be greatly reduced by using the minimum amount of chloroform (1:8) necessary to solubilize the salt starting material and by reducing the time allowed for mixed anhydride formation to about 5 minutes. A summary of this work appears in the Experimental section.

When the use of chloroform in the anhydride-forming step was avoided and dioxane or tetrahydrofuran was used in its place, practically no racemization occurred. Thus, using a toluene–dioxane (5:2) solvent system in the above preparation, a 77% yield of ethyl carbobenzoxyglycyl-L-phenylalanylglycinate and only 2% of the DL-isomer was obtained after purification of all fractions. The use of dioxane alone as the solvent necessitated a slightly higher reaction temperature for the anhydride-forming step and resulted in a 64% yield of the L-isomer and 7% of the DL-form. The use of tetrahydrofuran alone, on the other hand, caused no detectable racemization and the pure L-isomer was isolated in 60% yield.[3]

As a check on the optical purity of ethyl carbobenzoxyglycyl-L-phenylalanylglycinate, the tripeptide was also prepared from a mixed isobutylcarbonate–carbobenzoxyglycine anhydride and ethyl L-phenylalanylglycinate. The product obtained was more difficult to purify than the one prepared from the carbobenzoxy dipeptide acid, but its optical rotation and melting point were in good agreement with those previously observed.

In connection with the above work, it was found that the over-all reaction time could be greatly shortened from that previously reported. Optimum time for anhydride formation at −5° is in the neighborhood of 5 to 10 minutes. However, this varies with the individual preparation. Also, after addition of an amino acid or peptide ester to a solution of the preformed mixed anhydride, the amide-forming reaction may be completed rapidly by heating the reaction mixture to reflux and then cooling.

Experimental[4]

Methyl Carbobenzoxyglycyl-L-leucylglycinate.—A solution of 3.22 g. (0.01 mole) of carbobenzoxyglycyl-L-leucine,[5] m.p. 99–100°, $[\alpha]^{25}\text{D}$ −9.5 ± 0.4° (c 5, ethanol), and 1.02 g. (0.01 mole) of triethylamine in 100 cc. of toluene was cooled to −5° and 1.37 g. (0.01 mole) of isobutyl chlorocarbonate added with stirring. After 10 minutes at this temperature, an 0.89-g. (0.01 mole) sample of methyl glycinate[6] was added with good stirring and the mixture was then heated rapidly to reflux and immediately cooled. Some of the product separated as a colorless oil. The reaction mixture, therefore, was stirred vigorously with 75 cc. of saturated sodium bicarbonate solution and the resulting heterogeneous mixture allowed to stand overnight at room temperature. The product separated from the toluene phase as colorless crystals, wt. 2.75 g. (70%), m.p. 131.5–132°. The material was recrystallized by dissolving it in

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[1] J. R. Vaughan, Jr., THIS JOURNAL, **73**, 3547 (1951); J. R. Vaughan, Jr., and R. L. Osato, *ibid.*, **74**, 676 (1952).

[2] R. A. Boissonnas, *Helv. Chim. Acta*, **34**, 874 (1951); T. Wieland and H. Bernhard, *Ann.*, **572**, 190 (1951).

[3] The yield before recrystallization was 83%, m. p. 112–115°.

[4] All melting points were taken on a Fisher–Johns block and are corrected.

[5] M. A. Stahmann, J. S. Fruton and M. Bergmann, *J. Biol. Chem.*, **164**, 759 (1946).

[6] M. Frankel and E. Katchalski, THIS JOURNAL, **64**, 2264 (1942).

TABLE I

PREPARATION OF ETHYL CARBOBENZOXYGLYCYL-L-PHENYLALANYLGLYCINATE UNDER VARYING CONDITIONS

Reaction time for anhydride formation (−5°), min.	Form in which glycine ester was used	Solvent system used	Reaction conditions after addition of the ester	Total yield of pure isomers, %	Racemization, %
5	Base	Tetrahydrofuran	Refluxed	60	0
5 (10°)	Base	Dioxane	Refluxed	71	10
5	Base	Toluene–chloroform (8:1)	Refluxed	65	30
3	Base	Toluene–chloroform (8:1)	Refluxed	68	28
10	Base	Toluene–chloroform (8:1)	Refluxed	70	51
5	HCl	Toluene–chloroform (8:1)	Refluxed	53	17
5	HCl	Toluene–chloroform (2:1)	Refluxed	82	56
5	HCl	Toluene–chloroform (2:1)	Room temp.	69	47
25	HCl	Toluene–chloroform (2:1)	Room temp.	69	93
25	HCl	Chloroform	Room temp.	31	100

The term "refluxed" refers to rapidly heating the reaction mixture to the point of reflux after the addition of the ethyl glycinate and then immediately cooling and working up the mixture. The term "room temperature" refers to allowing the reaction mixture to stand overnight before working it up. The amount of racemization observed in each experiment is expressed as the percentage of the total yield of material which crystallized from a 2% solution of the mixed isomers in alcohol as described above. In all cases, this product had a melting point in the range of 130–133°.

20 cc. of ethyl acetate and diluting this solution with 100 cc. of petroleum ether; wt. 2.35 g. (60%), m.p. 132.5–133°, $[\alpha]^{25}D$ −36.2 ± 0.5° (*c* 2, methanol).[7]

On diluting the original toluene reaction solution with petroleum ether, a small amount of optically inactive material slowly crystallized, wt. 0.25 g. (7%), m.p. 106–108°. The recorded m.p. of methyl carbobenzoxyglycyl-DL-leucylglycinate is 107°.[6]

Ethyl Carbobenzoxyglycyl-L-phenylalanylglycinate. A. By Coupling Carbobenzoxyglycyl-L-phenylalanine with Ethyl Glycinate.—A solution of 1.78 g. (0.005 mole) of carbobenzoxyglycyl-L-phenylalanine,[8] m.p. 125–126°, $[\alpha]^{25}D$ +38.8 ± 0.4° (*c* 5, ethanol), and 0.50 g. (0.005 mole) of triethylamine in a mixture of 40 cc. of toluene and 20 cc. of dioxane was cooled to −5° and a solution of 0.69 g. (0.005 mole) of isobutyl chlorocarbonate in 10 cc. of toluene added. After 5 minutes at this temperature, during which time triethylamine hydrochloride separated, a second solution of 0.52 g. (0.005 mole) of ethyl glycinate in 25 cc. of toluene was added with good stirring. The reaction mixture was then heated rapidly to reflux and immediately cooled and washed with 100 cc. of 1% sodium bicarbonate solution. On standing, the product crystallized from the heterogeneous mixture as colorless needles, wt. 1.60 g. (73%), m.p. 117–119°. Dilution of the organic phase from the filtrate with petroleum ether caused crystallization of a small second crop of material, wt. 0.25 g. (11.5%), m.p. 112–114°. The first crop was dissolved in 80 cc. of alcohol to make a 2% solution and seeded with the DL-isomer of the tripeptide derivative. After 2 hours in the refrigerator only a trace of ethyl carbobenzoxyglycyl-DL-phenylalanylglycinate[9] had separated, wt. 0.05 g. (2%), m.p. 131–132°. The solution was then concentrated to about 25 cc. and diluted hot with water (50 cc.) until cloudy. On cooling, the pure L-isomer crystallized, wt. 1.50 g. (68%), m.p. 118–119°, $[\alpha]^{25}D$ −11.5 ± 0.5° (*c* 2, ethanol). The second crop of product from the original reaction mixture was crystallized separately from ethyl acetate–petroleum ether to give an additional 0.20 g. (9%) of product also melting at 118–119°. The literature records a melting point of 117–118° and $[\alpha]^{24}D$ −12.3° (*c* 2, ethanol) for this compound.[10]

Before these conditions were established for the above reaction a number of experiments were run to determine the effect of changes in the time allowed and the solvent system used for anhydride formation, the effect of heating *versus* room temperature standing after amino acid ester addition, and the results of using pure ethyl glycinate *versus* the base prepared from the hydrochloride plus triethylamine in chloroform solution on the yield and per cent. racemization of the tripeptide derivative. In all cases the anhydride-forming reaction was carried out at −5°, except when dioxane was used as the solvent and a temperature of about 10° was required to prevent freezing. The results of this survey are summarized in Table I.

B. By Coupling Carbobenzoxyglycine with Ethyl L-Phenylalanylglycinate.—A solution of 2.09 g. (0.01 mole) of carbobenzoxyglycine and 1.02 g. (0.01 mole) of triethylamine in a mixture of 50 cc. of toluene and 5 cc. of chloroform was cooled to −5° and a solution of 1.37 g. (0.01 mole) of isobutyl chlorocarbonate in 10 cc. of toluene added with stirring. After 5 minutes at this temperature, a second solution of 3.31 g. (0.01 mole) of ethyl L-phenylalanylglycinate hydrobromide and 1.02 g. (0.01 mole) of triethylamine in 25 cc. of chloroform was added with good stirring and the reaction mixture was then heated rapidly to reflux and immediately cooled. The solution was washed with water and with 3% sodium bicarbonate and concentrated to about 25 cc. on a steam-bath under an air jet. The concentrate was diluted with 150 cc. of petroleum ether to precipitate the product as a colorless oil which slowly solidified. The solvent was decanted and the residue was redissolved in 50 cc. of ethanol and allowed to stand overnight. No crystallization occurred, and therefore, the DL-form of the tripeptide derivative apparently was not formed. The solution was next diluted with 100 cc. of petroleum ether to give a cloudy mixture from which the product slowly crystallized as colorless needles, wt. 3.35 g. (76%), m.p. 114–116°. Recrystallization of this material from alcohol–petroleum ether as above followed by crystallization from 12 cc. of ethanol gave 2.35 g. (54%) of material having a melting point of 116–118° and $[\alpha]^{25}D$ −12.6 ± 0.5° (*c* 2, ethanol). Additional crystallization from ethyl acetate–petroleum ether mixture followed by fractional crystallization from ethanol failed to purify completely this product. Both the melting point and optical rotation remained unchanged.

Ethyl Carbobenzoxy-L-phenylalanylglycinate.—A solution of 5.98 g. (0.02 mole) of carbobenzoxy-L-phenylalanine,[11] m.p. 130–132°, $[\alpha]^{24}D$ + 4.8 ± 0.2° (*c* 2, glacial acetic acid) and 2.04 g. (0.02 mole) of triethylamine in 50 cc. of toluene was cooled to −5° and 2.74 g. (0.02 mole) of isobutylchlorocarbonate added with stirring. After 10 minutes at this temperature, a second solution of 2.06 g. (0.02 mole) of ethyl glycinate in 5 cc. of toluene was added with good stirring and the reaction mixture was heated rapidly to reflux and then immediately cooled. Washing this solution with water caused crystallization of the product. This was filtered off, washed with dilute sodium bicarbonate solution and dried, wt. 5.10 g. (66.5%), m.p. 108–110°. The organic phase was separated from the filtrate, washed as above, dried and diluted with petroleum ether to crystallize a second crop of product, wt. 1.00 g. (13%), m.p. 93–98°. The two crops were combined, dissolved in 40 cc. of hot ethyl acetate and the solution filtered. Dilution of the hot filtrate with 125 cc. of petroleum ether gave a clear solu-

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[7] G. W. Anderson and R. W. Young, *ibid.*, **74**, 5307 (1952), give m.p. 132–133° and $[\alpha]^{25}D$ −36.1° (*c* 5, methanol).

[8] K. Hofmann and M. Bergmann, *J. Biol. Chem.*, **134**, 225 (1940).

[9] J. R. Vaughan, Jr., and R. L. Osato, THIS JOURNAL, **73**, 5553 (1951).

[10] G. W. Anderson, J. Blodinger and A. D. Welcher, *ibid.*, **74**, 5309 (1952).

[11] M. Bergmann, *et al.*, *Z. physiol. Chem.*, **224**, 36 (1934), give m.p. 126–128° (cor.) and $[\alpha]^{21}D$ +4.9° (acetic acid).

tion from which the product rapidly crystallized as colorless needles, wt. 5.50 g. (71.5%), m.p. 109–110°, $[\alpha]^{25}D$ −17.3 ± 0.5° (*c* 2, ethanol). The literature melting point is 111°.[12]

When the preparation was repeated using the "standard" conditions previously reported,[1] a 72% yield of recrystallized material was also obtained; m.p. 109–110°.

Ethyl L-Phenylalanylglycinate Hydrobromide.—A 7.69-g. (0.02 mole) sample of ethyl carbobenzoxy-L-phenylalanylglycinate, 300 mg. of palladium black[13] and 1.5 cc. of glacial acetic acid were placed in 150 cc. of absolute alcohol and hydrogen was bubbled through the mixture at room temperature. Carbon dioxide evolution began immediately and was complete within 1 hour. The catalyst was filtered off and the solution concentrated to about 25 cc. and acidified with a slight excess of 1 *N* alcoholic hydrogen bromide. The solution was then reconcentrated to 25 cc. by vacuum distillation and diluted with 50 cc. of ether to precipitate a small amount of "gel-like" material. This impurity was filtered off and the filtrate was diluted with an additional 200 cc. of ether to give a clear solution from which the product crystallized as colorless plates on standing, wt. 4.05 g. (61%). m.p. 135–136°; $[\alpha]^{27}D$ +40.2 ± 0.5° (*c* 2, water). Recrystallization did not change the melting point or rotation.[14]

A second crop of material was obtained from the filtrate by concentration to dryness and recrystallization of the solid residue as above, wt. 0.65 g. (10%), m.p. 131–134°.

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(12) M. Bergmann and J. S. Fruton, *J. Biol. Chem.*, **118**, 414 (1937).

(13) R. Willstätter and E. Waldschmidt-Leitz, *Ber.*, **54**, 128 (1921).

(14) Reference 10 gives m.p. 135–136° and $[\alpha]D$ +40° (*c* 2, water) for this compound.

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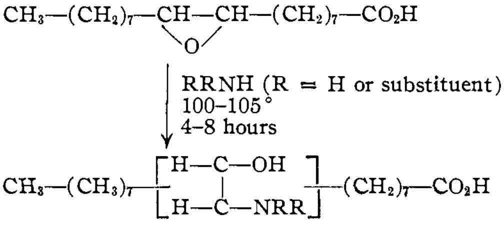
Chemistry of Epoxy Compounds. XIV.[1] Reaction of *cis*-9,10-Epoxystearic Acid with Ammonia and Amines[2]

BY DANIEL SWERN AND THOMAS W. FINDLEY

RECEIVED JULY 17, 1952

This note reports the opening of the oxirane ring of *cis*-9,10-epoxystearic acid with ammonia and amines (equation 1), the isolation of pure 9,10(10,9)-aminohydroxystearic acid and moderately pure N-substituted aminohydroxystearic acids, and potentiometric titration curves for several of these amino acids in the presence and absence of formaldehyde.



$$CH_3—(CH_2)_7—\underset{\diagdown O \diagup}{CH—CH}—(CH_2)_7—CO_2H \xrightarrow[\substack{100–105° \\ 4–8\ hours}]{RRNH\ (R\ =\ H\ or\ substituent)} CH_3—(CH_3)_7—\left[\begin{array}{c} H—C—OH \\ | \\ H—C—NRR \end{array}\right]—(CH_2)_7—CO_2H \qquad (1)$$

Experimental

Materials Used.—*cis*-9,10-Epoxystearic acid, m.p. 59.5°, was prepared from oleic acid by epoxidation with perbenzoic acid.[3] A.C.S. reagent grade concentrated aqueous ammonia was used. The Eastman Kodak Co. White Label Grades of 25% aqueous methylamine, 33% aqueous ethylamine, 33% aqueous dimethylamine and diethylamine were used without further purification. Diethylamine was diluted with approximately two parts of water to yield a 33% solution. Aniline was freshly distilled before use.

Preparation of 9,10(10,9)-Aminohydroxystearic Acid.—A typical experiment is described. Six grams (0.02 mole) of 9,10-epoxystearic acid and 14 ml. of 14.5 *N* aqueous ammonia (0.20 mole) were placed in a Pyrex glass combustion tube sealed at one end and partially constricted at the other. The tube was immersed in Dry Ice–acetone for several minutes and the constricted end of the tube was sealed off. The tube was then placed within a steel pipe which was closed with threaded caps at each end, and the whole assembly was heated and rotated in an oil-bath at 100–105° for four hours. The steel pipe was removed from the bath and allowed to cool to room temperature. The glass tube was again immersed in Dry Ice for several minutes and the tube was opened. The contents were transferred quantitatively to an evaporating dish and 205 ml. of 0.1 *N* aqueous sodium hydroxide was added. The solution was boiled until the odor of ammonia could not be detected and the vapors gave no test for alkalinity with test paper (about one to two hours were required). Sufficient (approximately 205 ml.) 0.1 *N* hydrochloric acid was then added to neutralize the sodium hydroxide and yield a mixture whose *p*H was about 6. A viscous oil precipitated which solidified on standing overnight; weight 6.1 g. The crude 9,10(10,9)-aminohydroxystearic acid was crystallized twice from 95% ethanol (8 ml./g.) at 0°, yielding 3.5 g. (55%) of pure material, m.p. 153–155°. In duplicate experiments, yields ranging from 30–62% were obtained. *Anal.* Calcd. for $C_{18}H_{37}O_3N$: C, 68.6; H, 11.8; N, 4.44; neut. equiv., 315.5. Found: C, 68.9; H, 11.7; N, 4.51; neut. equiv. (formaldehyde present), 316.

Preparation of N-Substituted 9,10(10,9)-Aminohydroxystearic Acids.—The reaction of aqueous methylamine (12.4 g.) with *cis*-9,10-epoxystearic acid (6.0 g.) for eight hours at 100–105° yielded a viscous oil which did not solidify after removal of excess methylamine and acidification, as described in the preceding section under 9,10(10,9)-aminohydroxystearic acid. The reaction product was evaporated to dryness and separated from sodium chloride by solution in 40 ml. of boiling absolute ethanol. The ethanol solution was cooled to −50° for one week, yielding 1 g. of 9(10)-N-methylamino-10(9)-hydroxystearic acid, m.p. 100–103°. *Anal.* Calcd. for $C_{19}H_{39}O_3N$: N, 4.25; neut. equiv., 329.5. Found: N, 4.59; neut. equiv. (formaldehyde present), 331.5. The filtrate was evaporated to dryness yielding 5 g. of viscous oil; N, 4.19; neut. equiv., 348. It was evident, therefore, that the reaction yielded mainly 9(10)-N-methylamino-10(9)-hydroxystearic acid.

Aqueous ethylamine (13.7 g.) and *cis*-9,10-epoxystearic acid (6.0 g.) yielded 7.3 g. of a viscous oil after separation of the sodium chloride as described above. *Anal.* Calcd. for 9(10)-N-ethylamino-10(9)-hydroxystearic acid, $C_{20}H_{41}O_3N$: N, 4.08. Found: N, 4.36. No precipitate was obtained when a solution of this product in absolute ethanol was cooled to −50°.

Aqueous dimethylamine (13.7 g.) and *cis*-9,10-epoxystearic acid (6.0 g.) yielded 7.7 g. of yellow viscous oil from the alcohol solution. *Anal.* Calcd. for 9(10)-N,N-dimethylamino-10(9)-hydroxystearic acid, $C_{20}H_{41}O_3N$: N, 4.08. Found: N, 3.67. This product showed appreciable water solubility; a 5% solution was only slightly turbid.

Aqueous diethylamine (21 g.) and *cis*-9,10-epoxystearic acid (6.0 g.) yielded 7.1 g. of a semi-solid. *Anal.* Calcd. for 9(10)-N,N-diethylamino-10(9)-hydroxystearic acid, $C_{22}H_{45}O_3N$: N, 3.77. Found: N, 2.64.

cis-9,10-Epoxystearic acid (24 g., 0.08 mole) and aniline (72 g., 0.8 mole) were heated on the steam-bath for six hours in a nitrogen atmosphere. The reaction mixture was poured into 1 liter of 1.5 *N* hydrochloric acid in a separatory funnel and the aqueous layer was discarded. The upper oil layer was washed with four 500-ml. portions of 1.5 *N* hydrochloric acid, then with 5% sodium chloride until the wash was neutral, and twice with distilled water. The upper layer was dissolved in ethyl acetate and the solution was dried over anhydrous calcium sulfate. Filtration and evaporation of solvent yielded 16–25 g. of reddish-brown oil. Analysis indicated that it contained about 80% 9(10)-N-phenylamino-10(9)-hydroxystearic acid and about 20% of the anilide of this substance. *Anal.* Calcd. for 9(10)-N-phenylamino-10(9)-hydroxystearic acid, $C_{24}H_{41}O_3N$: N, 3.57; neut. equiv., 391.5; calcd. for the anilide, $C_{30}H_{46}O_2N_2$: N, 6.0. Found: N, 4.05; neut. equiv., 475–481.

Surface Active Properties of N-Substituted 9,10(10,9)-Aminohydroxystearic Acids.—Although 9(10)-N,N-di-

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(1) For paper XIII, see THIS JOURNAL, **74**, 1655 (1952).

(2) Article not copyrighted.

(3) D. Swern, T. W. Findley and J. T. Scanlan, THIS JOURNAL, **66**, 1925 (1944).

methylamino-10(9)-hydroxystearic acid was the only compound studied which showed appreciable water solubility, 9(10)-N-methylamino- and 9(10)-N-ethylamino-10(9)-hydroxystearic acids showed slight solubility. Surface tensions of 0.2% solutions of these compounds under neutral, acidic and alkaline conditions are shown in Table I. Measurements were made with the Du Nouy Interfacial Tensiometer.

TABLE I

SURFACE TENSION OF 0.2% SOLUTIONS OF N-SUBSTITUTED 9,10(10,9)-AMINOHYDROXYSTEARIC ACIDS

Aminohydroxystearic acid	t, °C.	pH[a]	Surface tension, dynes/cm.
Dimethyl-	19	4	36
Dimethyl-	19	7	33
Dimethyl-	19	9	38
Dimethyl-	19	11	37
Methyl-	24	4	36
Methyl-	24	7	33
Methyl-	24	9	38
Methyl-	24	11	39
Methyl-[b]	24	7	34
Ethyl-	24	5	37
Ethyl-	24	7	33
Ethyl-	24	10	36

[a] The pH values other than 7 were obtained by the addition of a sufficient quantity of aqueous sodium hydroxide or hydrochloric acid. [b] Half-saturated with sodium chloride.

Potentiometric Titrations.—Approximately 0.3–0.6 g. of N-substituted or unsubstituted aminohydroxystearic acids were dissolved in 100 ml. of 70% aqueous ethanol and the titration curves were determined using a pH meter with external electrodes. With the exception of the titration of 9(10)-N-phenylamino-10(9)-hydroxystearic acid, the compounds studied showed no sharp inflection in the titration curves if formaldehyde was absent from the titration mixture. To obtain satisfactory titration curves, it was necessary to employ formaldehyde. Approximately 10 ml. of 35% aqueous formaldehyde, neutralized with dilute aqueous alkali to phenol red, was used in the solvent system. Figure 1 shows the titration curves for pure 9(10),10(9)-aminohydroxystearic acid in the absence (A) and presence (B) of formaldehyde, and the crude reaction product of *cis*-9,10-epoxystearic acid with aqueous ammonia prior to recrystallization (C, formaldehyde present). Figure 2 shows the titration curves for 9(10)-N-methylamino-10(9)-hydroxystearic acid in the absence (A) and presence (B) of formaldehyde and Fig. 3, curves A and B, show similar data for 9(10)-N-phenylamino-10(9)-hydroxystearic acid.

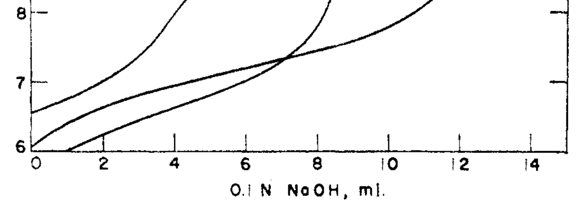

Fig. 1.—Titration curves for 9,10(10,9)-aminohydroxystearic acid: A, 0.3270 g. of pure sample, formaldehyde absent; B, 0.2720 g. of pure sample, formaldehyde present; neut. equiv., 316 (8.61 ml. of 0.1 N NaOH required); C, 0.4162 g. of crude reaction product, formaldehyde present; neut. equiv., 340 (12.24 ml. of 0.1 N NaOH required).

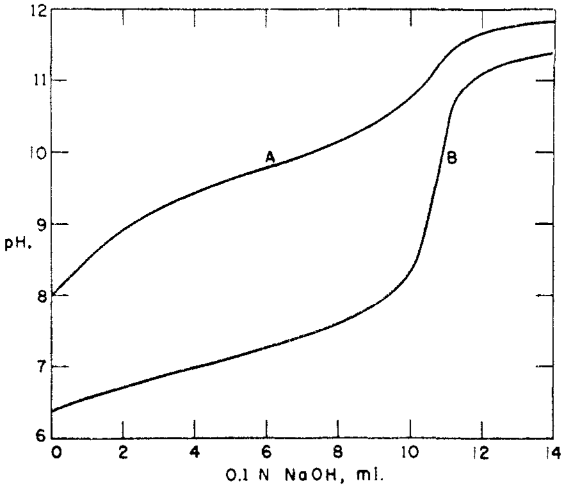

Fig. 2.—Titration curves for 9(10)-N-methylamino-10(9)-hydroxystearic acid: A, 0.3722 g. of sample, formaldehyde absent; B, 0.3563 g. of sample, formaldehyde present; neut. equiv., 330 (10.80 ml. of 0.1 N NaOH required).

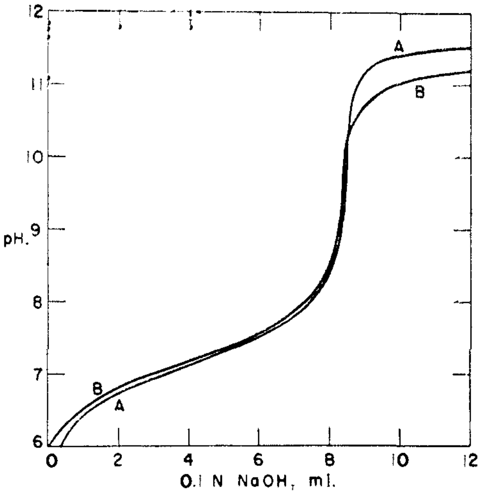

Fig. 3.—Titration curves for 9(10)-N-phenylamino-10(9)-hydroxystearic acid: A, 0.4014 g. of sample, formaldehyde absent; neut. equiv., 475 (8.45 ml. of 0.1 N NaOH required); B, 0.4024 g. of sample, formaldehyde present; neut. equiv., 481 (8.37 ml. of 0.1 N NaOH required).

Discussion

With the exception of 9(10)-N-phenylamino-10-(9)-hydroxystearic acid, the titration curves in the absence of formaldehyde show that substituted and unsubstituted aminohydroxystearic acids behave as typical amino acids, namely, they exist in solution as salts even in 70% ethanol. Formaldehyde, since it suppresses the basic properties of the nitrogen, permits a typical titration curve to be obtained. The failure of 9(10)-N-phenylamino-10(9)-hydroxystearic acid to show any difference in behavior in the absence or presence of formaldehyde is attributed to the lower basic strength of nitrogen containing a phenyl substituent, thereby preventing salt formation from occurring.

The relatively high water-solubility of 9(10)-N, N-dimethylamino-10(9)-hydroxystearic acid is attributed to the higher basic strength of the dimethylamino moiety, which would enhance salt formation and, consequently, solubility in water. The surface-active properties of the compounds are to be expected in view of their salt formation and structural relationship to amine salts of long-chain fatty acids in which properly balanced hydrophilic and hydrophobic groups are present. Sinking time measurements on canvas disks immersed in aqueous solutions of these substances show that the canvas is penetrated rapidly but not nearly so rapidly as in aqueous solutions of the sodium salt of dioctyl sulfosuccinate of the same concentration.

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Further Aspects of the Schmidt Reaction

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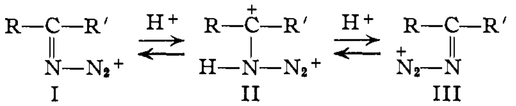
The Schmidt reaction of *p*-methylbenzophenone has been studied both by Smith and Horwitz[1] and Sherk, *et al.*[2] Smith and Horwitz, using trichloroacetic acid as the solvent and only a relatively small amount of sulfuric acid as the catalyst, obtained benz-*p*-toluidide and *p*-toluanilide in a ratio of 54:46. Sherk, *et al.*, by passing hydrogen azide slowly through a mixture of the ketone in an excess of sulfuric acid, with benzene as the solvent, obtained benz-*p*-toluidide in a yield of 82%. The divergent results suggested that product ratios might be very sensitive to the experimental conditions in this reaction.

Inasmuch as the Schmidt reaction of aldehydes gives rise to different product ratios as the sulfuric acid concentration is altered,[3] it seemed reasonable to suppose that the same might hold true for the Schmidt reaction of ketones. Specifically, it was thought that the geometrically isomeric cations, I and III, first proposed by Smith[4] as product controlling intermediates (*trans* rearrangement) in the Schmidt reaction of ketones, might undergo an acid-catalyzed interconversion, possibly *via* the conjugate acid, II. As Smith and Horwitz[1] have suggested, it is possible for "migration aptitudes"[5] to influence the product ratio, if the rate of interconversion of the *syn* and *anti* forms of the intermediate compares in magnitude with the rate of migration of either R (phenyl) or R′ (*p*-tolyl). In this connection, it has been established[6,7] that in the Schmidt reaction of 1-phenyl-1-*p*-tolylethylene, the *p*-tolyl group migrates about five times as fast as the phenyl group.



$$\underset{\text{I}}{R{-}\underset{\overset{\|}{N-N_2^+}}{C}{-}R'} \overset{H^+}{\rightleftharpoons} \underset{\text{II}}{R{-}\underset{\overset{|}{H-N-N_2^+}}{\overset{+}{C}}{-}R'} \overset{H^+}{\rightleftharpoons} \underset{\text{III}}{R{-}\underset{\overset{\|}{\overset{+}{N_2}-N}}{C}{-}R'}$$

The Schmidt reaction of *p*-methylbenzophenone has been repeated under two different sets of conditions in order to determine any possible change in product ratio with increase in the sulfuric acid concentration. By use of an 8:1 molar ratio of sulfuric acid to the ketone, there was obtained a product ratio of 51% benz-*p*-toluidide to 49% *p*-toluanilide. The conditions of Sherk, *et al.*,[2] were employed in a second run. Here also there was obtained a ratio of benz-*p*-toluidide to *p*-toluanilide of 53:47. Since our method of analysis (see the experimental section) is probably accurate to not more than ± 5%, these results are in agreement with that of Smith and Horwitz,[1] who used a different method of analysis of the products.

Since the *p*-anisyl group migrates at a faster rate than the *p*-tolyl group in the Schmidt reaction of 1,1-diarylethylenes,[6,7] and since the methoxyl group is a stronger base strengthening substituent than the methyl group, both effects should enhance the possibility of a change in product ratio with change in sulfuric acid concentration in the Schmidt reaction of *p*-methoxybenzophenone. Even in this case, however, in the presence of a large excess of sulfuric acid, there was obtained a ratio of benz-*p*-anisidide to anisanilide of 66:34, in substantial agreement with the ratio of 61:39 reported by Smith and Horwitz.[1,8] Hence we conclude that a change in sulfuric acid concentration does not affect product ratios in the Schmidt reaction of *p*-substituted benzophenones.

Prior to the publication of Boyer's[9] work on conjugate addition reactions of hydrazoic acid, we had investigated the Schmidt reaction of 2-vinylpyridine. The rearrangement usually exhibited by arylethylenes was not detected, and only 1-α-pyridyl-2-azidoethane was isolated, the product obtained by Boyer in the absence of sulfuric acid.

Experimental[10]

Azeotropic Esterification of a Known Mixture of *p*-Toluic Acid and Benzoic Acid.—To a solution of 6.80 g. (0.05 mole) of *p*-toluic acid and 6.10 g. (0.05 mole) of benzoic acid in 75 cc. of absolute ethanol and 75 cc. of benzene was added 1 cc. of concentrated sulfuric acid. The mixture was slowly distilled through an 18″ electrically heated Vigreux column, to which an azeotropic head was attached. When the temperature of the overhead vapor reached 72°, the distillation was stopped and the remaining alcohol and benzene removed *in vacuo*.

A small amount of water was added to the residual mixture, which was then neutralized with powdered sodium carbonate. The mixture was extracted with ether, dried over anhydrous sodium sulfate, filtered and the ether evaporated. Distillation of the residue through a Todd column

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[1] P. A. S. Smith and J. P. Horwitz, THIS JOURNAL, **72**, 3718 (1950).

[2] J. K. Sanford, F. T. Blair, J. Arroya and K. W. Sherk, *ibid.*, **67**, 1941 (1945).

[3] W. E. McEwen, W. E. Conrad and C. A. VanderWerf, *ibid.*, **74**, 1168 (1952).

[4] P. A. S. Smith, *ibid.*, **70**, 320 (1948).

[5] There is growing evidence that the term "migratory aptitude" has little meaning. A superior interpretation is based on the concept of a driving force due to the participation of the migrating group in the attainment of the transition state. See S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1113 (1952), and other recent papers by Winstein, *et al.*, for the elaboration of this theory.

[6] W. E. McEwen, M. Gilliland and B. I. Sparr, *ibid.*, **72**, 3212 (1950).

[7] W. E. McEwen and N. B. Mehta, *ibid.*, **74**, 526 (1952).

[8] *Cf.* P. A. S. Smith and B. Ashby, *ibid.*, **72**, 2503 (1950).

[9] J. H. Boyer, *ibid.*, **73**, 5284 (1951).

[10] Analyses by Oakwold Laboratories, Alexandria, Va. All m.ps. are corrected.

afforded 6.70 g. (89%) of ethyl benzoate, b.p. 95–96° (15 mm.), $n^{20}_{\rm D}$ 1.5048; reported b.p. 87° (10 mm.),[11] $n^{20}_{\rm D}$ 1.5057.[12] A second fraction consisted of 7.40 g. (90%) of ethyl *p*-toluate, b.p. 107° (11 mm.), $n^{20}_{\rm D}$ 1.5082; reported b.p. 110°(12 mm.),[13] $n^{18}_{\rm D}$ 1.5089.[13] Acenaphthene was used as a "chaser."

Reaction of Hydrazoic Acid with *p*-Methylbenzophenone. A.—To a mixture of 51.5 cc. (0.92 mole) of concentrated sulfuric acid, 19.6 g. (0.1 mole) of *p*-methylbenzophenone and 200 cc. of benzene was added 7.8 g. (0.12 mole) of sodium azide, in small portions, during two hours, at room temperature. The mixture was then warmed to 45–55° until the theoretical volume of nitrogen had evolved (8 hours). The reaction mixture was poured on crushed ice, partially neutralized with 10% sodium hydroxide solution, then made basic with saturated sodium carbonate solution. The mixture was extracted with ether, and the ether solution washed with dilute hydrochloric acid and 10% sodium carbonate solution. The ether solution was dried over anhydrous magnesium sulfate, filtered and the ether evaporated. There remained 18.7 g. of solid material, which was hydrolyzed by refluxing for five days with a mixture of 400 cc. of glacial acetic acid and 100 cc. of 40% hydrobromic acid. The mixture was diluted and extracted with ether. The ether solution was washed with water, dried over anhydrous sodium sulfate, filtered and the ether evaporated. There remained 12.8 g. of mixed solids containing benzoic and *p*-toluic acids.

The acids were esterified and fractionated as described above for the known mixture. There was obtained 4.00 g. (31%) of ethyl benzoate, b.p. 96–97° (17 mm.), $n^{20}_{\rm D}$ 1.5066 and 4.25 g. (33%) of ethyl *p*-toluate, b.p. 115–116° (17 mm.), $n^{20}_{\rm D}$ 1.5090.

B.—The procedure of Sherk, *et al.*,[2] was employed on 19.6 g. (0.1 mole) of *p*-methylbenzophenone. The reaction mixture was handled as in A. There was obtained 6.2 g. (41.3%) of ethyl benzoate, b.p. 96–98° (18 mm.), $n^{20}_{\rm D}$ 1.5048 and 6.0 g. (36.6%) of ethyl *p*-toluate, b.p. 118–119° (19 mm.), $n^{20}_{\rm D}$ 1.5083.

Schmidt Reaction of *p*-Methoxybenzophenone.—*p*-Methoxybenzophenone, 22.7 g. (0.1 mole), was reacted in the same manner as that described for *p*-methylbenzophenone, part A, except that the temperature was maintained at 25–30° throughout the reaction, and a benzene solution of hydrazoic acid was used instead of sodium azide. There was a large amount of tar formed, which was ether insoluble. From the ether solution there was obtained 18.7 g. of mixed neutral solids. On digestion with a small amount of ether, 8.0 g. of *p*-methoxybenzophenone was recovered from the ether solution. The remaining 10.7 g. of neutral solids was refluxed for five days in a solution of 90 g. of potassium hydroxide in 500 cc. of ethanol. The ethanol was distilled *in vacuo*, the residual solid dissolved in water and extracted with ether. Addition of hydrochloric acid to the aqueous layer precipitated the carboxylic acids, which were taken up in ether and dried over anhydrous sodium sulfate. Evaporation of the ether afforded 3.3 g. of mixed acids.

Anal. Found: methoxyl, 6.83, 7.04.

The analytical results indicate the presence of about 34% of *p*-anisic acid and 66% of benzoic acid.

1-α-Pyridyl-2-azidoethane.—Under the same conditions as employed in the Schmidt reaction of unsymmetrical diarylethylenes,[6] there was obtained a 17% yield of 1-α-pyridyl-2-azidoethane, b.p. 91° (8.5 mm.), 84–85° (4.5 mm.), 58° (0.6 mm.). The same substance was obtained in 97% yield by use of Boyer's procedure.[9]

Mercuric Chloride Addition Product.—Crystallized from 95% ethanol, the colorless addition product melted at 117°.

Anal. Calcd. for $C_7H_8N_4HgCl_2$: C, 20.13; H, 1.45; N, 13.41. Found: C, 19.91, 19.64; H, 1.60, 1.75; N, 13.14.

Catalytic Reduction of 1-α-Pyridyl-2-azidoethane.—A solution of 8.90 g. (0.06 mole) of 1-α-pyridyl-2-azidoethane in 30 cc. of absolute ethanol was hydrogenated at three atmospheres in a Parr apparatus for 24 hours over 0.10 g. of platinum oxide catalyst. The solution smelled of ammonia. Distillation afforded 3.1 g. (35%) of β-2-pyridylethylamine, b.p. 76–78° (4 mm.), reported[14] b.p. 92–93° (12 mm.).

Picrate.—Yellow needles were obtained from ethanol, m.p. 213–215°; reported[14] 215–216°.

Dihydrochloride.—Colorless crystals were obtained, m.p. 186–189°; reported m.p. 185–186°,[15] 189°.[16]

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[11] I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Vol. II, Oxford University Press, New York, N. Y., 1936, p. 20.

[12] J. Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publishing Co., Inc., New York, N. Y., 1950, p. 484.

[13] Reference 11, Vol. III, p. 777.

[14] K. Loffler, *Ber.*, **37**, 161 (1904).

[15] L. A. Walter, W. H. Hunt and R. J. Fosbinder, THIS JOURNAL, **63**, 2771 (1941).

[16] F. K. Kirchner, J. R. McCormick, C. J. Cavallito and L. C. Miller, *J. Org. Chem.*, **14**, 388 (1949).

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Molecular Refractions of the SO_3 and SO_2Cl Groups in *p*-Ethylbenzenesulfonyl Chloride and the Methyl, Ethyl and *n*-Butyl Esters of *p*-Ethylbenzenesulfonic Acid

BY RICHARD H. WILEY AND RICHARD P. DAVIS[1]

RECEIVED JULY 17, 1952

During a study of *p*-ethylbenzenesulfonyl chloride and its derivatives we have prepared three new esters derived from the sulfonyl chloride and obtained previously unrecorded constants for the compounds. The density and refractive index data gave molecular refraction values for the SO_3 and SO_2Cl groups showing deviations from the rather narrow range of values previously recorded for these groups in other compounds. We wish to record at this time the results of these observations.

p-Ethylbenzenesulfonyl chloride was prepared by the action of phosphorus pentachloride on the crude sulfonic acid.[2] The sulfonic acid was prepared by reaction of excess ethylbenzene with concd. sulfuric acid under conditions which permitted removal of the water formed during the reaction as the ethylbenzene–water azeotrope. The reaction was continued until the theoretical amount of water was collected. The sulfonyl chloride was obtained in 47% yield based on the amount of sulfuric acid used. It was characterized as the previously described[2b,2d,3] amide, m.p. 108°.

The fact that the amide prepared from this sulfonyl chloride consists chiefly of the isomer which melts at 108° is considered good evidence that the material is substantially pure *p*-ethylbenzenesulfonyl chloride. Also, it is known that mixtures of ortho and para isomers are obtained from low temperature (0°) sulfonations[3b] and that the ortho isomer rearranges to the para isomer at 100°.[2d] The pure amide of the ortho isomer melts at 126°.[3b] The sulfonation was run at 115° in our experiments. The crude amide, m.p. 97–106°, was obtained in 95% yield from the sulfonyl chloride.

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[1] This work was supported in part under Contract No. AT-(40-1)-229 between the Atomic Energy Commission and the University of Louisville. Taken from a thesis submitted by R. P. D. in partial fulfillment of the requirements for the M.S. degree.

[2] (a) P. Chruschtschow, *Ber.*, **7**, 1164 (1874); (b) L. Semptowski, *ibid.*, **22**, 2673 (1889); (c) A. Tohl and O. Eberhard, *ibid.*, **26**, 2940 (1893); (d) G. T. Moody, *ibid.*, **29R**, 663 (1896).

[3] (a) J. Moschner, *ibid.*, **34**, 1257 (1901); (b) R. Fricke and G. Spilker, *ibid.*, **58**, 1589 (1925).

The total yield of recrystallized amide m.p. 108° from the crude amide is 4.2 g. or 89% of the theoretical. No evidence of the amide of the ortho isomer reported[3b] to melt at 126° and to have a different crystalline form was observed.

The methyl, ethyl and *n*-butyl esters of *p*-ethylbenzenesulfonic acid were prepared in 61–71% yields by reactions of the sulfonyl chloride with the alcohol in the presence of sodium hydroxide[4] or pyridine[5] using previously described techniques.

Attempts were made to prepare other esters from the sulfonyl chloride and the following alcohols: isopropyl, *n*-amyl, *s*-butyl, benzyl and 2-ethylhexyl. In all cases liquids were obtained which did not solidify at low temperatures and decomposed on attempted distillation presumably to give olefins and the sulfonic acid. The latter was isolated and identified as a product of the decomposition of the amyl ester. These data suggest that the *p*-ethylbenzenesulfonates decompose more readily on heating and melt lower than the corresponding *p*-toluenesulfonates.

Molecular refraction data obtained from our density and refractive index measurements gave values of 9.95 to 10.72 for the SO_3 group in the *p*-ethylbenzenesulfonates and 16.77 for the SO_2Cl group in *p*-ethylbenzenesulfonyl chloride. Preliminary comparison of these values with those previously reported in the literature indicated rather wide deviations. For comparison, values from several sources are given in Table I along with our data for the *p*-ethylbenzene derivatives, some previously unrecorded data for *p*-toluenesulfonates, and our redetermination of the value for benzenesulfonyl chloride. In these calculations the values for the group increments given by Eisenlohr[6a] were used.

TABLE I

MOLECULAR REFRACTIVITY DATA

Compound	Sp. gr.[a]	n_D[a]	M_D (obsd.)	Group increments[b]
Benzenesulfonyl chloride	1.378 (23°)[c]	1.5505 (23°)[c]	40.93	15.72[c,d]
	1.3778 (23°)	1.5507 (23°)	40.94	15.73[d]
p-Ethylbenzenesulfonyl chloride	1.268	1.5469 (20°)	51.22	16.77[d]
Alkane and alkenesulfonyl chlorides	...	....	...	15.33–15.52[c,d]
Methyl PEBS[e]	1.193	1.5181 (20°)	50.88	10.72[f]
Ethyl PEBS[e]	1.178	1.5150 (20°)	54.73	9.95[f]
n-Butyl PEBS[e]	1.114	1.5051 (20°)	64.53	10.54[f]
n-Propyl PTS[e]	1.144	1.4998	55.00	10.12[f]
n-Butyl PTS[e]	1.120	1.5050	60.38	10.99[f]
n-Amyl PTS[e]	1.100	1.5028	65.02	11.01[f]
Allyl PTS[e]	1.175	1.5242	56.51	12.20[f]
Alkyl ethylenesulfonate[g]	...	....	...	8.99–9.83[f]

[a] Data obtained in the present studies except as otherwise indicated; sp. gr. at 20°/20° and n_D at 20° except as noted. [b] Based on Eisenlohr constants given in reference 6a. [c] From reference 8. Revised using Eisenlohr constants. [d] For SO_2Cl group. [e] PEBS = *p*-ethylbenzenesulfonate; PTS = *p*-toluenesulfonate. [f] For SO_3 group. [g] From reference 9. Revised using Eisenlohr constants.

The value for the SO_3 group, obtained as the difference between the observed molecular refraction and the sum of the group refractions including double bond exaltations, varies from 8.99 to 12.20. The value varies from 9.95–10.72 in three *p*-ethylbenzenesulfonates; from 10.12 to 12.20 in four *p*-toluenesulfonates; and from 8.99 to 9.83 in seven alkyl[7] ethylenesulfonates. The values for the *p*-toluenesulfonates not previously reported were obtained from density and refractive index values given previously.[7] The highest value of 12.20 is obtained from the data for allyl *p*-toluenesulfonate. Allyl structures are known to cause anomalies[6b] and if this value is omitted, as has been done in previous studies, the variation is from 9.95 to 11.01.

The value for the SO_2Cl group, also obtained by difference, varies from 15.31 to 16.77. Much less information is available for evaluation of the variation in the increment for this group. In four alkane and alkene sulfonyl chlorides the value varies from 15.33 to 15.52[8]; our value for *p*-ethylbenzenesulfonyl chloride is 16.77 and the previously reported[8] value for benzenesulfonyl chloride is 15.73. Our redetermination of the density and refractive index for the latter was in good agreement with previously recorded values and gives the same value for the SO_2Cl group increment.

The variations in values for these two groups—SO_3 and SO_2Cl—appear to fall within recognized limits. Variations of this order have been observed in the increments for other groups. Examples are the variations from 0.68 to 1.60 for fluorine and from 1.53 to 1.94 for the carbon–carbon double bond. The significance of such variations has been discussed previously.[6b] It is apparent, however, that the variations in the values for SO_3 and SO_2Cl are considerably greater than has been indicated in previous evaluations[8–10] of the values for these increments.

The ultraviolet absorption curves for the *p*-ethylbenzenesulfonic acid esters and chloride all show an absorption maximum at 264 ± 2 mμ. This appears to be the 255 mμ peak usually associated with the benzene nucleus shifted to slightly longer wave lengths by the sulfonate or sulfonyl chloride group. The four curves are similar and do not indicate the individuality of the chloride observed in the molecular refraction data.

Experimental[11]

_p_-Ethylbenzenesulfonyl Chloride.—Ethylbenzene was sulfonated with concentrated sulfuric acid at reflux in a continuous process. The crude acid was converted to the sulfonyl chloride by reaction with phosphorus pentachloride. Refractionation through a column packed with helices gave a fraction, b.p. 143° at 16 mm., $n^{20}D$ 1.5469, sp. gr. 20/20 1.268.

Reaction of the sulfonyl chloride with cold concd. ammonium hydroxide gave a precipitate of crystals. The dried crude product, m.p. 97–106°, weighed 4.5 g., 95% of the theoretical. One recrystallization from aqueous alcohol gave 3.3 g., 69.7% of the theoretical amount, of *p*-ethylbenzenesulfonamide, m.p. 108°. The total yield of pure amide, m.p. 108°, obtained by recrystallization of the crude amide was 4.2 g., 89% of the theoretical.

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(4) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 145.

(5) V. C. Sekera and C. S. Marvel, THIS JOURNAL, **55**, 345 (1933).

(6) K. Fajans in A. Weissberger, Ed., "Physical Methods of Organic Chemistry," 2nd Ed., Vol. I, Part II, Interscience Publishers, Inc., New York, N. Y., 1949: (a) p. 1163; (b) p. 1168–1169.

(7) H. Gilman and N. J. Beaber, THIS JOURNAL, **47**, 518 (1925).

(8) E. F. Landau, *ibid.*, **69**, 1219 (1947).

(9) W. F. Whitmore and E. F. Landau, *ibid.*, **68**, 1797 (1946).

(10) R. Boudet and R. Rambaud, *Bull. soc. chim. France*, 793 (1948).

(11) Sulfur analyses by Micro Tech Laboratories, Skokie, Illinois.

Methyl *p*-Ethylbenzenesulfonate.—A solution of 53 g. of *p*-ethylbenzenesulfonyl chloride in 63.5 ml. of methanol was placed in a reaction flask and cooled to 20° by immersion of the flask in a salt-ice-bath. The solution was stirred continuously while a solution of 40 g. of sodium hydroxide in 30 ml. of water was added slowly. The temperature was held at 23–25° during the addition. The reaction mixture was cooled to 0° and let stand for two hours. Sufficient water was added to dissolve the precipitated sodium chloride. The ester layer was decanted, washed with two 20-ml. portions of water and then with 40 ml. of a 5% sodium carbonate solution, dried over anhydrous sodium sulfate, and distilled to give 31.4 g. or 61% of the theoretical amount of methyl *p*-ethylbenzenesulfonate, b.p. 125–135° at 2 mm. Refractionation through a column packed with helices gave a sample, b.p. 128° at 2 mm., n^{20}_{D} 1.5181, sp. gr. 20/20 1.193, which was used for analysis.

Anal. Calcd. for $C_9H_{12}O_3S$: S, 16.0. Found: S, 15.85.

Ethyl *p*-Ethylbenzenesulfonate.—This ester was prepared using the procedure described for the methyl ester except that the reaction was run at 10°. The yield of ester b.p. 120–137° at 2 mm. was 20.9 g. or 67% of the theoretical amount. Refractionation through a column packed with helices gave a sample b.p. 142–150° at 4 mm., n^{20}_{D} 1.5150, sp. gr. 20/20 1.178, which was used for analysis.

Anal. Calcd. for $C_{10}H_{14}O_3S$: S, 14.95. Found: S, 14.70.

***n*-Butyl *p*-Ethylbenzenesulfonate.**—A mixture of 30 g. of *p*-ethylbenzenesulfonyl chloride and 18 ml. of *n*-butanol was cooled to 5°. To this solution, 23 ml. of pyridine was added over a three-hour period while maintaining the reaction mixture at a temperature of 8–18°. The reaction mixture was cooled to 3° and treated with sufficient dil. hydrochloric acid to neutralize the pyridine. The ester layer was separated and taken up in ether. The ether solution was washed with water and with 5% sodium carbonate and dried over anhydrous sodium sulfate. On fractionation 25.3 g. or 71.6% of the theoretical amount of *n*-butyl *p*-ethylbenzenesulfonate, b.p. 148–150° at 2 mm., was obtained. Refractionation through a column packed with helices gave a sample, b.p. 159° at 4 mm., n^{20}_{D} 1.5051; sp. gr. 20/20 1.114.

Anal. Calcd. for $C_{12}H_{18}O_3S$: S, 13.22. Found: S, 13.38.

Ultraviolet Absorption Data.—Ultraviolet absorption measurements were made with a Beckman DU photoelectric spectrophotometer using 1.00-cm. silica cells and hydrogen and tungsten discharge lamps as light sources. In all measurements 95% ethanol was used as a solvent. The esters and chloride showed an absorption maximum at 264 ± 2 mμ.

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The Charge Transfer Reaction between Molybdo- and Molybdioctacyanides[1]

BY RICHARD L. WOLFGANG

RECEIVED JULY 23, 1952

The high coördination number and the apparently very close structural similarity of the octacyanides of Mo(IV) and Mo(V) as well as, to a lesser extent, their high net charges lends interest to the charge transfer process between these two complexes. In particular, this case should be a significant indication of the validity of Libby's proposal[2] that the Franck–Condon principle is of primary importance in determining the rates of oxidation–reduction reactions in solution.

$K_4Mo(CN)_8$ and $K_3Mo(CN)_8$ were prepared by the method described by Willard and Thielke.[3] The same compounds containing 66-hr. Mo^{99} were made from MoO_3 irradiated in the Brookhaven reactor. The purity of the $K_4Mo(CN)_8$ was found by titration with $KMnO_4$ to be 99.9%. Decomposition of $K_3Mo(CN)_8$ to $K_4Mo(CN)_8$—a photo-induced reaction—was found to be negligible in the time of the runs.

Three different separations of the two complexes were developed: (1) Several organic solvents miscible with water were found to precipitate $Mo(CN)_8^{-4}$ while leaving $Mo(CN)_8^{-3}$ in solution. This method is effective at concentrations greater than $\sim 10^{-3} f$. In practice separations were carried out by adding five volumes of absolute alcohol to one volume of reactant solution. (2) Cd(II) gives good precipitates with $Mo(CN)_8^{-4}$ at concentrations down to $\sim 10^{-3} f$ while leaving $Mo(CN)_8^{-3}$ in solution. (3) Tetraphenylarsonium chloride was found to give filterable precipitates with concentrations of $Mo(CN)_8^{-3}$ down to 10^{-4}–$10^{-5} f$. In basic solution $Mo(CN)_8^{-4}$ gave no precipitate, while in acid solution the concentration of $Mo(CN)_8^{-4}$ had to be kept below $\sim 10^{-3} f$ to prevent precipitation.

After separation by one of the above techniques, the second species was precipitated by a suitable method. Following a one-day wait to allow equilibration of the daughter Tc^{99m} both fractions were counted.

Using the above techniques over a wide range of *p*H and of anions present in solution, all experiments showed complete exchange, within the experimental error of 10%, in the approximately 5 seconds required for separation. Table I gives the conditions under which some typical experiments were carried out. All runs were made in very dim light at a temperature of 2 ± 1°.

The exchange between one of the species freshly precipitated by the separating agent and the other species was also measured in a series of runs analogous to those in Table I. In all cases a definite but incomplete heterogeneous exchange was found.

The possibility exists that in the homogeneous reaction the complete exchange found is induced by the separation.[4] The likelihood of this is decreased by the use of three distinct separation methods (although in this connection it would have been advantageous if a rapid non-precipitation technique could also have been used). It may be concluded that the charge exchange between $Mo(CN)_8^{-3}$ and $Mo(CN)_8^{-4}$ in aqueous solution is probably an extremely rapid process with a rate constant, if a second-order rate law is obeyed, greater than 10^3 f^{-1} sec.$^{-1}$ at 2°.

It has been shown that the cyanides attached to the central Mo do not exchange.[5] This fact in conjunction with the high degree of coördination involved makes it very unlikely that this charge transfer reaction proceeds by a radical or ion-exchange mechanism. It seems probable then that a true homogeneous electron transfer process is involved here.

Magnetic susceptibility measurements show that $K_4Mo(CN)_8$ is diamagnetic while $K_3Mo(CN)_8$ has a paramagnetism corresponding to one unpaired

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[1] Research carried out under the auspices of the U. S. Atomic Energy Commission.

[2] W. F. Libby, Symposium on Electron Transfer and Isotopic Reactions, *J. Phys. Chem.*, **56**, 863 (1952).

[3] H. H. Willard and R. C. Thielke, THIS JOURNAL, **57**, 2609 (1935).

[4] A. C. Wahl and N. Bonner, "Radioactivity Applied to Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 16.

[5] A. W. Adamson, J. P. Welker and M. Volpe, THIS JOURNAL, **72**, 4033 (1950).

TABLE I

TYPICAL CONDITIONS FOR $Mo(CN)_8^{-3}$-$Mo(CN)_8^{-4}$ EXCHANGE

Mo(IV), *f*	Mo(V), *f*	Other species, *f*	*p*H	Separation agent	Extent of exchange, %
5.0×10^{-2}	1.5×10^{-2a}	ClO_4^-, 2×10^{-2}; NH_4^+, 1×10^{-2}	2	C_2H_5OH	94
1.7×10^{-3}	1.2×10^{-4a}	ClO_4^-, 4×10^{-4}; NH_4^+, 1×10^{-4}	4–5	$Cd(NO_3)_2$ 0.1*f*	100
5.0×10^{-5a}	1.5×10^{-4}	Cl^-, 7×10^{-4}; NH_4^+, 3×10^{-3}	10–11	$(C_6H_5)_4AsCl$ 0.2*f*	100
9.6×10^{-4a}	1.1×10^{-3}	Cl^-, 1×10^{-2}; NH_4^+, 1×10^{-3}	1–2	$(C_6H_5)_4AsCl$ 0.2*f*	106
5.0×10^{-5}	4.0×10^{-5a}	NO_3^-. 1×10^{-4}; NH_4^+, 3×10^{-5}	6–8	$(C_6H_5)_4AsCl$ 0.2*f*	116

[a] Denotes initially active species.

electron.[6] This implies that both complexes have d^4sp^3 binding and should thus have a very similar configuration and internuclear spacing. It follows that the Franck–Condon principle should not impose any considerable barrier to electron transfer—a prediction which is in accord with the experimental findings. The results, furthermore fit well into an empirical correlation proposed by Adamson,[7] according to which exchange is rapid between species both having a low magnetic susceptibility.

The author greatly appreciates the helpful discussions of Dr. R. W. Dodson who first pointed out to him the interest which might be attached to this research. The advice of Dr. Joan Welker on the method of preparation and the kindness of Dr. A. W. Adamson in supplying the author with a sample of $K_4Mo(CN)_8 \cdot 2H_2O$ are gratefully acknowledged.

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[6] P. W. Selwood, "Magnetochemistry," Interscience Publishers, Inc., New York, N. Y., 1943, p. 150.

[7] A. W. Adamson, *J. Phys. Chem.*, in press (1952).

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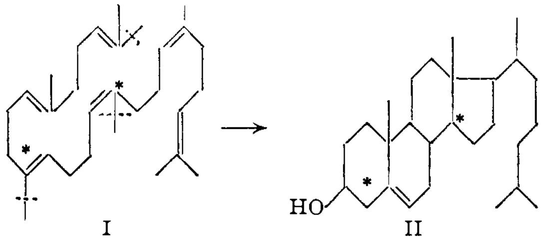
Synthetic C^{14}-"Squalene": Concerning its Incorporation into Cholesterol by Liver[1]

BY G. M. TOMKINS,[2] I. L. CHAIKOFF, W. G. DAUBEN, H. L. BRADLOW AND P. A. SRERE

RECEIVED JUNE 24, 1952

In 1926 and again in 1937, Channon[3] reported that the feeding of the hydrocarbon squalene (I) to rats resulted in an increase in the cholesterol (II) contents of their livers. In 1934, Robinson[4] suggested that by the following cyclization of the dihydrotriterpene, this compound might serve as a direct precursor of cholesterol.



I II

Subsequent work utilizing labeled acetate[5] has yielded results which can readily be interpreted in terms of this hypothesis[6] and, indeed, recently Langdon and Bloch[7] demonstrated the conversion of labeled squalene to this sterol.

Independently, we had undertaken[8] to study this conversion and should like to report our results employing specifically labeled, synthetic "squalene."[9] The metabolic fate of this compound was studied both *in vitro* and *in vivo*. The former type of experiment was conducted in two distinct fashions, (1) the compound, dispersed in saline with the aid of Tween 80, was incubated with liver slices and (2) liver slices of animals previously injected with the labeled material were incubated. In the *in vivo* experiment, the "squalene" was introduced by stomach tube into fasted rats. The results of these experiments are given in Tables I, II and III.

TABLE I

Liver slices incubated in the presence of labeled substrate for 3 hours at 37.5°

Expt.	Wt. of slices, g.	Contents of flask: Substrate	μM.	C^{14}, c.p.m.	Per cent. of added C^{14} recovered as CO_2	Cholesterol
I	1	Acetate-1-C^{14}	5	6.85×10^5	31.0	0.82
	1	Squalene-C^{14}		7.5×10^5	0.40	0
II	1	Acetate-1-C^{14}	5	6.85×10^5	36.0	0.68
	1	Squalene-C^{14}		7.5×10^5	0.62	0
III	1	Acetate-1-C^{14}	5	6.85×10^5	34.0	0.62
	1	Squalene-C^{14}		7.5×10^5	0.46	0

TABLE II

The labeled substrate was injected into the portal vein at time of sacrifice, and liver slices were incubated for 3 hours at 37.5°

Activity injected per 2 g. of liver, c.p.m.	Weight of liver slices per flask, g.	Per cent. of added C^{14} recovered as CO_2	Cholesterol
5.0×10^5	2	0.11	0.0
	2	.20	.0

TABLE III

The labeled substrate was administered enterally

Animal	Total activity administered, c.p.m.	Total activity in liver at end of 24 hr., c.p.m.	Per cent. C^{14} administered recovered as cholesterol
1	9.0×10^5	2.4×10^4	0.0
2	1.7×10^6	5.7×10^4	.0

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[1] Aided by a grant from the U. S. Public Health Service and the Life Insurance Medical Research Fund.

[2] Life Insurance Medical Research Fellow.

[3] H. J. Channon, *Biochem. J.*, **20**, 400 (1926); H. J. Channon and B. R. Tristam, *ibid.*, **31**, 738 (1937).

[4] R. Robinson, *J. Soc. Chem. Ind.*, **53**, 1062 (1934).

[5] H. N. Little and K. Bloch, *J. Biol. Chem.*, **183**, 33 (1950), and earlier papers.

[6] P. Srere (Dissertation, Univ. of California, 1951), in this Laboratory, has demonstrated that livers from animals kept for 30 days on a 1% squalene diet, show a decreased ability to incorporate C^{14}-labeled acetate into cholesterol but not into carbon dioxide. Such a result is compatible with the concept that an intermediate metabolic pool in the conversion acetate to cholesterol has been diluted or that squalene might act as a specific precursor of the sterol.

[7] R. G. Langdon and K. Bloch, THIS JOURNAL, **74**, 1869 (1952).

[8] "Ciba Foundation Conference on Isotopes in Biochemistry," J. and A. Churchill, Ltd., London, W. 1, England, p. 24 ff.

[9] The term "squalene" is used to indicate that the synthetic product is a dihydrotriterpene with six double bonds and is a mixture of double bond isomers (see W. G. Dauben and H. L. Bradlow, THIS JOURNAL, **74**, in press (1952)).

The data show that synthetically prepared squalene fails to be incorporated into cholesterol under all three conditions. Since in the *in vitro* experiment, the "squalene" was dispersed in Tween 80, it was essential to verify that this agent had not interfered with the biological synthesis of cholesterol. This was tested by incubating slices from the same liver with C^{14}-labeled acetate and amounts of Tween 80 equal to that employed in the "squalene" study. It was found that 0.6–0.8% of the acetate activity was incorporated into cholesterol and from 31–36% was oxidized to carbon dioxide. It is therefore clear that the failure in the incorporation of the labeled "squalene" under our experimental conditions cannot be due to interference by the Tween 80. It is of interest that the C^{14}-squalene was oxidized to carbon dioxide by liver slices. The recovery of radioactivity in the crude nonsaponifiable fraction of the liver of the rats fed the labeled material indicates that absorption of the unchanged "squalene" had occurred.

The results employing synthetic squalene are in contrast to those reported by Langdon and Bloch[7] in which it was demonstrated that *biologically* prepared squalene is a more active precursor of cholesterol than acetate. The failure of the synthetic material to be incorporated into the sterol could be due to the fact that the labeled "squalene," which is a mixture of double bond isomers, contains no molecules of the identical natural configuration. It should be recalled, however, that this synthetic material is apparently identical with the squalene obtained by the purification of the natural triterpene through its solid hexahydrochloride.[9] The high degree of stereospecificity of the conversion reported by Langdon and Bloch[8] is of interest since Hubbard and Wald[10] have shown that in the intact animal, inactive isomers of vitamin A are readily isomerized to the biological active form. Another possible explanation of this failure to be incorporated into cholesterol is that the presence of nonnatural squalene molecules might block the conversion of any natural material which might have been present in the synthetic material.

Experimental

C^{14}-Labeled "Squalene."—The material was prepared as described in reference 9 and was labeled with C^{14} in the carbon atoms indicated by the asterisks in I.

***In Vitro* Experiments.**—Two types of *in vitro* experiments were conducted. In one, liver slices approximately 0.5 mm. thick were incubated in a bicarbonate buffer containing the labeled "squalene." The "squalene" was dispersed in 1 ml. of 0.85% sodium chloride solution with the aid of 3–4 drops of Tween 80, and this solution was added to the medium. In the second type of experiment the labeled hydrocarbon, dispersed in saline and Tween 80 as described above, was injected directly into the portal vein of rats immediately after they had been stunned by a blow on the head. This injection procedure ensured entrance of the radioactive "squalene" into the liver. The livers were excised and sliced, and weighed portions of slices were incubated in the bicarbonate buffer medium as previously described. Incubation lasted three hours in both types of experiments. At the end of the run, the carbon dioxide was collected and its C^{14} content determined as described elsewhere.[11] Cholesterol was isolated from the contents of the flask and its C^{14} content measured in the manner reported earlier.[11]

***In Vivo* Experiment.**—The labeled triterpene was administered as a Tween dispersion by stomach tube to two rats that had been fasted for 10 hours. They were allowed to eat a stock diet *ad libitum* for 24 hours and then were sacrificed. The livers of these rats were removed and hydrolyzed overnight with alcoholic potassium hydroxide. The alkaline solution so obtained was extracted repeatedly with petroleum ether until radioactivity was no longer obtained. The residual hydrolysate was then acidified and reextracted in the same manner with petroleum ether. The lipid-free residue was finally extracted with warm water. The C^{14} content of the non-saponifiable fraction, the saponifiable fraction and the aqueous extract of the residue was then determined. Measurable amounts of radioactivity were found only in the non-saponifiable fraction. The cholesterol was isolated from this latter fraction and its radioactivity determined as described elsewhere.[11]

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[10] R. Hubbard and G. Wald, *Science*, **115**, 60 (1952).

[11] G. M. Tomkins and I. L. Chaikoff, *J. Biol. Chem.*, **196**, 569 (1952).

The Preparation and Some Properties of Ruthenocene and Ruthenicinium Salts

BY GEOFFREY WILKINSON

RECEIVED JUNE 12, 1952

A structure for the compound bis-cyclopentadienyliron $(C_5H_5)_2Fe$[1] has been suggested,[2] in which the central metal atom is symmetrically placed between the planes of two cyclopentadienyl rings, the π-electrons of which are involved in the filling of the 3d orbitals of the metal. With this scheme, it can be expected that ruthenium and osmium, both of which, like iron, have electronic structures for the atom ten electrons short of that of the next inert gas, will form π-complexes analogous to $(C_5H_5)_2Fe$.

The ruthenium compound, $(C_5H_5)_2Ru$, has now been made. Since the iron compound bis-cyclopentadienyliron has been named ferrocene[3] on account of its chemical behavior as an aromatic system, the ruthenium analog may be referred to as ruthenocene. Its systematic name is bis-cyclopentadienylruthenium. The unipositive ions $[(C_5H_5)_2Fe]^+$ and $[(C_5H_5)_2Ru]^+$ which are formed on oxidation of the neutral compounds, are, respectively, designated the ferricinium and the ruthenicinium ions.

Experimental

Ruthenocene has been prepared by the reaction of ruthenium(III) acetylacetonate with a fivefold excess of cyclopentadienylmagnesium bromide. The acetylacetonate was made by heating ruthenium chloride with acetylacetone in potassium bicarbonate solution[4]; the complex was extracted with benzene and purified by crystallization from benzene. Although the reaction mixture was held at 80° for 24 hours, subsequent experiments suggest that this procedure is unnecessary and that the reaction is almost immediate. After the reaction period, the Grignard mixture was decomposed with ice-water, and the product extracted with ether. The solvent was then removed and the residue extracted with petroleum ether, which in turn was removed. This residue

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[1] First reported by T. J. Kealy and P. L. Pauson, *Nature*, **168**, 1039 (1951). See also Miller, Tebboth and Tremaine, *J. Chem. Soc.*, 632 (1952).

[2] G. Wilkinson, M. Rosenblum, M. C. Whiting and R. B. Woodward, THIS JOURNAL, **74**, 2125 (1952).

[3] M. Rosenblum, M. C. Whiting and R. B. Woodward, *ibid.*, **74**, 3458 (1952).

[4] G. A. Barbieri, *Atti accad. Lincei*, **23**, [5] 336 (1914).

was sublimed at 120° in high vacuum, and the sublimate, which contained yellowish crystals in addition to gummy hydrocarbon polymers, was dissolved in ether and crystallized. The product was resublimed and was finally repeatedly crystallized from carbon tetrachloride. The yield of ruthenocene was about 20% of the theoretical yield to be expected when based on ruthenium(III) acetylacetonate.

Ruthenocene crystallizes in transparent, plate-like crystals, quite similar to those formed by ferrocene; the compound has only a very slight yellow color. The melting point is 195.5°, but the compound will sublime at lower temperatures. Analyses gave C, 51.68; H, 4.36, Ru, 43.8 (calcd. for $(C_5H_5)_2Ru$: C, 51.83; H, 4.31; Ru, 43.5). The ruthenium was determined by destruction of the compound by repeated evaporation with strong nitric acid, followed by careful ignition and reduction by hydrogen of the blue ruthenium dioxide thus obtained, to metallic ruthenium. Check analysis was made by the thiourea colorimetric method[5] using a ruthenium chloride reference solution; this in turn was standardized by conversion of an aliquot to the metal. The molecular weight determined by camphor melting point depression micromethod is 237 ± 5 (calcd. for $(C_5H_5)_2Ru$, 231.88). Ruthenocene closely resembles ferrocene in its general properties; it is soluble in organic solvents, sublimes readily, is unaffected by bases and by sulfuric and hydrochloric acids in absence of oxygen. The infrared absorption spectrum (Fig. 1), measured both in carbon tetrachloride and in carbon disulfide solution, has a remarkable resemblance to that of ferrocene, showing only the single sharp band at 3.23 μ attributable to C–H stretching and indicating the presence of only one type C–H bond. The ultraviolet absorption spectrum (Fig. 2, curve A) is again rather similar to that of ferrocene except for the non-existence of the second peak which is found in the ferrocene spectrum at 440 mμ.

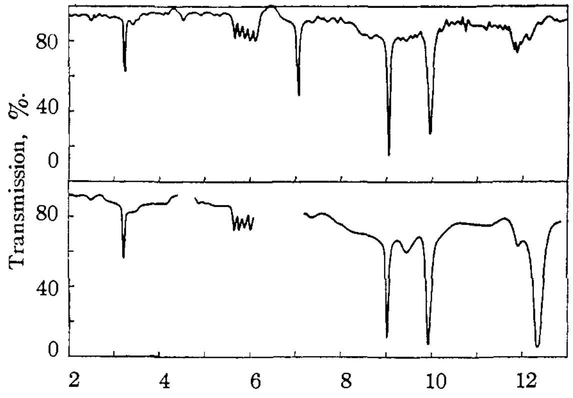

Fig. 1.—Infrared absorption spectrum of ruthenocene: top, carbon tetrachloride solution; bottom, carbon disulfide solution; Baird recording spectrophotometer, NaCl cell.

Ruthenocene can be oxidized to a unipositive ion $[(C_5H_5)_2Ru]^+$. Polarographic measurements[6] show that the oxidation of ruthenocene is a one-electron step. Unlike the deep blue color of solutions containing the ferricinium ion, the ruthenicinium salts give pale yellow aqueous solutions. The ultraviolet absorption spectrum of ruthenicinium perchlorate in 0.01 *N* perchloric acid solution is shown in Fig. 2, curve B.

Ruthenicinium perchlorate $[(C_5H_5)_2Ru]ClO_4$ has been prepared as a yellow crystalline solid, by controlled potential anodic oxidation of ruthenocene in 90% alcohol solution containing perchloric acid. On oxidation, the perchlorate separates and can be centrifuged and dried with absolute alcohol. Analysis for ruthenium gave 30.62%, calculated 30.69%. The salt dissolves in water to give a yellow solution; the only moderate solubility in water (~ 1 mg./ml.) and insolubility in alcohol is in contrast to the much greater solubility of ferricinium and cobalticinium[7] perchlorates in water. Measurement of the ultraviolet absorption spectrum of ruthenicinium perchlorate shows that the solutions of the salt in dilute perchloric acid are stable for an hour or two, but that partial decomposition of neutral solutions occurs fairly rapidly within half an hour with the formation of some ruthenocene; this behavior is similar to that of the ferricinium solutions which partially decompose within a few minutes to give some ferrocene, ferric hydroxide and unidentified organic hydrolysis products.

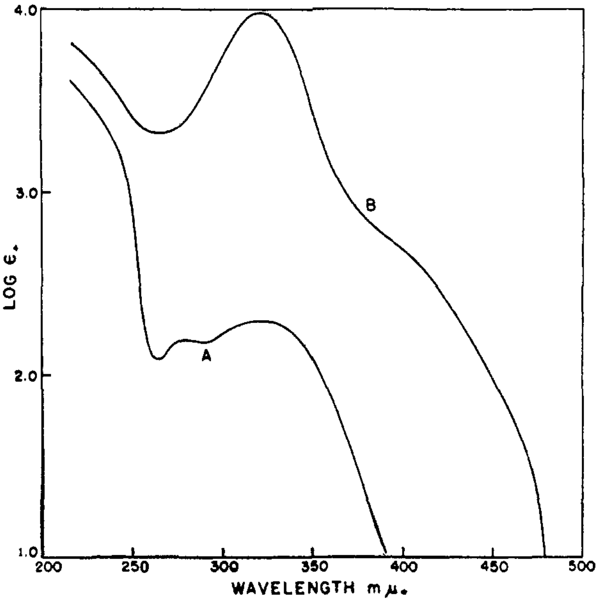

Fig. 2.—Ultraviolet spectra: A, ruthenocene in cyclohexane solution; B, ruthenicinium perchlorate in 0.01 *N* perchloric acid; Beckman spectrophotometer, silica cells. 25°.

The solution reactions of the ruthenicinium ion are those that might be expected for a large unipositive ion. From hydrochloric acid solutions silicotungstic acid precipitates a pale yellow silicotungstate. On addition of saturated solutions of sodium picrate, sodium 2,4-dinitrophenolate, sodium 7-iodo-8-hydroxyquinoline-5-sulfonate or sodium 6-chloro-5-nitrotoluene-3-sulfonate, to neutral solutions containing ~ 0.8 mg./ml. of ruthenicinium perchlorate, yellow colored precipitates are obtained. Analysis of the recrystallized picrate gave 21.95% Ru, calculated 22.12%. Ruthenicinium triiodide $[(C_5H_5)_2Ru]I_3$, is precipitated as a reddish solid on mixing solutions of iodine and ruthenocene in carbon tetrachloride. An excess (50 ml.) of a solution of iodine in carbon tetrachloride (equivalent to 26.10 ml. of 0.0153 *N* thiosulfate solution) was added to 21.10 mg. of ruthenocene in carbon tetrachloride; after centrifugation of the ruthenicinium triiodide and washing, the excess iodine was titrated with thiosulfate, 8.30 ml. being required. The iodine consumed in the reaction was thus in accord with the formation of ruthenicinium triiodide. Direct analysis of the compound gave Ru, 16.52; I, 62.23 (calcd. Ru, 16.60; I, 62.15). The compound is insoluble in water and most organic solvents; it is soluble in acetonitrile, alcohol and acetone. The behavior of ruthenocene with iodine closely resembles that of ferrocene, and the two triiodides have very similar properties.

Like ferrocene, ruthenocene can be oxidized with various chemical reagents such as bromine water and aqueous silver sulfate, but dilute nitric acid and stronger oxidizing agents destroy the ruthenicinium ion first formed, giving red solutions of tri- or tetravalent ruthenium.

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[5] E. B. Sandell, "Colorimetric Determination of Traces of Metals," 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1950.

[6] J. A. Page and G. Wilkinson, THIS JOURNAL, **74**, 6149 (1952).

[7] G. Wilkinson, *ibid.*, **74**, 6148 (1952).

The Preparation and Some Properties of the Cobalticinium Salts

BY GEOFFREY WILKINSON

RECEIVED JUNE 12, 1952

In view of the unusual stability of "ferrocene," bis-cyclopentadienyliron, $(C_5H_5)_2Fe$,[1] it would seem that the sandwich structure suggested[2] for the compound is a very stable one, and that other transitional metals with suitable electronic structures might well adopt a similar configuration to form either neutral compounds analogous to ferrocene, or metal hydrocarbon ions, depending on the oxidation state of the metal in the complex.

The methods of formation of ferrocene and of ruthenocene, the value for the oxidation potentials of these compounds to the unipositive ions, and the magnetic susceptibilities of ferrocene and the ferricinium salts, suggest that the metals in the neutral compounds are in the +2 oxidation state while in the ions, they are in the +3 oxidation state. The reaction of cyclopentadienylmagnesium bromide with a +3 cobalt or rhodium compound might therefore be expected to lead to a unipositive cobalt hydrocarbon ion isoelectronic with ferrocene. Salts of the ion $[(C_5H_5)_2Co]^+$ have now been prepared; they are designated cobalticinium salts by analogy with the ferricinium and ruthenicinium salts, although they might more properly be called salts of bis-cyclopentadienylcobalt(III).

Experimental

The metal acetylacetonate was used in the preparation of ruthenocene[3] and this technique is again used. Cobaltic acetylacetonate was prepared by treating the black hydrated oxide resulting from alkaline bromine oxidation of cobaltous chloride with acetylacetone; after standing for two days the mixture was centrifuged and the product crystallized from benzene. The addition of the dark green acetylacetonate in benzene to cold cyclopentadienylmagnesium bromide in benzene, produces instantaneously a bright yellow precipitate; an excess of the Grignard reagent, sufficient to react with all the carbonyl groups present in the acetylacetone was used. On addition of ice water to the product, the yellow precipitate dissolves giving a yellow solution; the yellow compound is a cobalticinium salt which is produced by an apparently simple metathetical reaction such as

$$2Co(C_5H_7O_2)_3 + 4(C_5H_5)MgBr = 2[Co(C_5H_5)_2]Br + MgBr_2 + 3Mg(C_5H_7O_2)_2$$

The mixture was extracted several times with ether and the large quantities of insoluble matter removed by centrifugation. The hot aqueous solution was then freed from magnesium salts by addition of barium hydroxide solution; after removal of magnesium hydroxide, the excess barium was removed by addition of an equivalent amount of dilute sulfuric acid. Using cobaltic acetylacetonate labeled with Co^{60}, it is found that the compound reacts completely to give the cobalticinium ion, all of which appears in the aqueous solution; no activity appeared in the ether extracts or in the aqueous solution in a form other than the metal hydrocarbon ion.

Final purification of the cobalticinium salt solution was made by precipitation of the picrate, by addition of a saturated solution of picric acid to the solution containing about 0.15 g./ml. of cobalticinium ion. The picrate was recrystallized from dilute picric acid solution; a yield of about 65% was obtained at this state. The recovery of all solutions and precipitation of the ion from neutral or faintly acid solutions by sodium 2,4-dinitrophenolate has given yields of about 95% based on the amount to be expected from complete reaction of the acetylacetonate. Conversion of the picrate or the 2,4-dinitrophenolate to other salts in aqueous solution is made by ether extraction of the organic acid after addition of the appropriate amount of mineral acid, and by anion exchange resin (Dow A2) columns.

In aqueous solution cobalticinium salts are exceedingly stable, in contrast to the ferricinium and ruthenicinium salts. The ion is unaffected by boiling with either aqua regia or concentrated sulfuric acid for 15 minutes or so, or with dilute alkalies alone or even in the presence of hydrogen peroxide. Fuming with perchloric acid however rapidly destroys the ion and analysis of cobalticinium salts and of solutions has been made by destruction in this manner. The cobalt was then determined either polarographically, or by the volumetric method involving the alkaline perborate oxidation of cobaltous solutions.[4] The chemical behavior of the cobalticinium ion in aqueous solution is much like that of a large alkali metal ion. The salts of common acids are very soluble in water, but have eluded attempts to crystallize them; on evaporation of chloride, bromide or sulfate solutions, only viscous liquids result, and some decomposition occurs. With large anions, crystalline salts are more easily obtained.

From hydrochloric acid solutions containing as little as 0.1 mg./ml. of cobalticinium ion, silicotungstic acid gives a pale yellow precipitate, resembling in this respect cesium and the ferrocinium and ruthenicinium ions. This precipitate can be metathesized with hot mercurous nitrate solutions, the excess of which can be removed by hydrochloric acid leaving a pure cobalticinium salt solution; a separation from ammonium salts is thus possible.

With sodium 2,4-dinitrophenolate and sodium 2,4-dinitro-1-naphthol-7-sulfonate, solutions of ~ 0.1 mg./ml. concentration give yellow crystals in about 10 minutes, and at higher concentrations, immediate precipitates; both these precipitates are much less soluble than the picrate. The analysis of the 2,4-dinitrophenolate, when precipitated from faintly acid solution and recrystallized twice, corresponds to a molecular complex of the formula $[(C_5H_5)_2Co](C_6H_3O_5N_2)\cdot 2C_6H_4O_5N_2$. Sodium α-naphthol-β-sulfonate gives a yellow precipitate with the cobalticinium ion, but there is no reaction with sodium 6-chloro-5-nitrotoluene-3-sulfonate. A further similarity to rubidium and cesium is the formation of a yellow ferric chloride–antimony chloride complex on addition of antimony trichloride in glacial acetic acid to ferric chloride solutions containing as little as 0.01 mg. of cobalticinium ion. The addition of a saturated solution of potassium permanganate to a fairly concentrated solution of cobalticinium salt (1–2 mg./ml.) gives a brown precipitate sparingly soluble in water and dilute acids.

The ultraviolet absorption spectrum of cobalticinium perchlorate in aqueous solution is shown in Fig. 1. The solutions used were prepared from the picrate by anion exchange

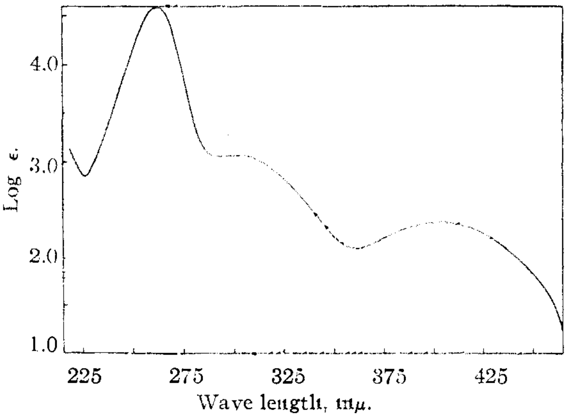

Fig. 1.—Ultraviolet absorption spectrum of cobalticinium perchlorate in water; Beckman spectrophotometer, silica cells, 25°.

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[1] First reported by T. J. Kealy and P. L. Pauson, *Nature*, **168**, 1039 (1951). See also Miller, Tebboth and Tremaine, *J. Chem. Soc.*, 632 (1952).

[2] G. Wilkinson, M. Rosenblum, M. C. Whiting and R. B. Woodward, THIS JOURNAL, **74**, 2125 (1952).

[3] G. Wilkinson, *ibid.*, **74**, 6146 (1952).

[4] E. H. Swift, "System of Chemical Analysis," Prentice-Hall, Inc., New York, N. Y., 1939, p. 344.

and were determined polarographically. Measurements taken at 242 and 278 mμ show that Beer's law is obeyed over a concentration range of 0.03 to 0.3 millimolar and at 336 mμ from 0.3 to 3.0 millimolar.

Attempts at reduction in aqueous solution by chemical reagents failed, which is not surprising in view of the reduction potential for the cobalticinium ion.[5] Cobalticinium hydroxide has been made in aqueous solution by the action of freshly prepared silver oxide on the chloride solution; from titration curves of the base with 0.1 *N* hydrochloric acid, *p*H measurements being made with a Beckman Model G instrument with glass and saturated calomel electrodes, the ionization constant of the base has been determined to be 8.2×10^{-3}.

Cobalticinium picrate $[(C_5H_5)_2Co](C_6H_2N_3O_7)$, is obtained as orange needle crystals which explode readily on heating, making carbon and hydrogen analysis difficult. Analyses gave C, 45.51; H, 3.36; N, 9.88; Co, 14.07; (calcd. C, 46.1; H, 2.88; N, 10.06; Co, 14.11). The solubility of the picrate in water at 25° is 3.0 g./liter.

The chloroplatinate $[(C_5H_5)_2Co]_2PtCl_6$ has been made by evaporation almost to dryness of cobalticinium chloride and chloroplatinic acid solutions and precipitation of the salt with absolute alcohol; the salt was then crystallized from water. Analyses gave C, 30.61; H, 2.81; Co, 15.01; Pt, 24.80; Cl, 27.10 (calcd. C, 30.55; H, 2.55; Co, 14.95; Pt, 24.85; Cl, 27.14).

The addition of a solution of potassium triiodide to a dilute solution of a cobalticinium salt gives a brown precipitate of cobalticinium triiodide; the ion thus resembles the ferricinium and ruthenicinium ions in forming triiodides very sparingly soluble in water. Analyses gave Co 10.30, I 66.77 (calcd. Co 10.32, I 66.71).

Since the cobalticinium ion is isoelectronic with ferrocene, its salts should be diamagnetic. The magnetic susceptibility of cobalticinium picrate has been measured by the Gouy split tube method using air ($\kappa = +0.029 \times 10^{-6}$ c.g.s. unit) and water (-0.72×10^{-6} c.g.s. unit) as standards. The values obtained were independent of field strength; the measurements were repeated after recrystallization of the picrate, and two packings of the tube with the powdered picrate were made in each case. The molar susceptibility χ^{25}_{mol} for cobalticinium picrate is $-194 \pm 2 \times 10^{-6}$ c.g.s. unit.

I am indebted to Mr. J. A. Page for polarographic measurements, and to Prof. R. B. Woodward, Dr. M. C. Whiting and Mr. M. Rosenblum for helpful discussions.

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[5] J. A. Page and G. Wilkinson, THIS JOURNAL, **74**, 6149 (1952).

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The Polarographic Chemistry of Ferrocene, Ruthenocene and the Metal Hydrocarbon Ions

BY JOHN A. PAGE AND GEOFFREY WILKINSON

RECEIVED JUNE 12, 1952

In a previous communication, a structure for "ferrocene," bis-cyclopentadienyliron $(C_5H_5)_2Fe$,[1] has been given,[2] in which the iron atom is symmetrically placed between two cyclopentadienyl rings; it was further shown that on oxidation salts of the unipositive ion $[(C_5H_5)_2Fe]^+$, which is designated the ferricinium ion, are formed. The analogous ruthenium compounds, ruthenocene, $(C_5H_5)_2Ru$, and the ruthenicinium salts have also been prepared,[3] as have salts of the ion $[(C_5H_5)_2Co]^+$ which is referred to as the cobalticinium ion.[4]

The polarographic behavior of these compounds has now been studied. Polarograms were obtained using a Sargent Model 11 instrument, and a divided H-cell with a saturated calomel reference electrode; chloride ion was excluded from the polarographic solution by means of a potassium nitrate–agar plug. This was necessary because the chloride ion gives an anodic wave in the alcohol solutions employed, which interferes with the polarographic waves of ferrocene and ruthenocene.

The Ferrocene–Ferricinium Ion System.—Ferrocene has been found to give a well defined reversible anodic wave at the dropping mercury electrode in a 90% ethanol, 0.1 *M* sodium perchlorate and 0.01 *M* perchloric acid supporting electrolyte. The half-wave potential is +0.31 *versus* the S.C.E. No change in the potential was observed between neutral and 0.01 *M* perchloric acid solutions, but the presence of perchloric acid improves the definition of the polarographic wave. The value of the polarographic constant in the supporting electrolyte, $i_d/Cm^{2/3}t^{1/6}$, was found to be 1.27 μa./m*M*./l. mg.$^{2/3}$ sec.$^{-1/2}$.

Controlled potential oxidation of ferrocene in the above supporting electrolyte using the potentiostat of Lingane and Jones[5] was carried out at a mercury anode at a potential of +0.40 v. *versus* the S.C.E. The anode compartment was separated from the cathode by a fritted disc and a potassium nitrate–agar plug. The cathode compartment was filled with dilute nitric acid solution, and a platinum cathode was used. Twenty-two and a half milligrams of ferrocene in the supporting electrolyte was oxidized. The initial current of 8.4 ma. decreased to 0.1 ma. in 60 minutes electrolysis, and the original yellow solution changed during the electrolysis to the deep blue color characteristic of ferricinium salt solutions. The quantity of electricity consumed during the electrolysis, 10.6 coulombs, was determined by a silver titration coulometer. The theoretical value for a one-electron oxidation step is 11.6 coulombs.

A polarogram of the ferricinium salt solution resulting from the electrolysis, showed a well defined cathodic wave with a half-wave potential of +0.30 v, *versus* the S.C.E., agreeing, within the limits of experimental error, with the half-wave potential for the oxidation of ferrocene. The ferrocene–ferricinium ion couple is hence a thermodynamically reversible system in the alcoholic supporting electrolyte.

$$(C_5H_5)_2Fe = [(C_5H_5)_2Fe]^+ + e^-; \; E_0 = -0.56 \text{ v. } (\textit{versus} \text{ the normal hydrogen electrode})$$

The polarographic behavior of the ferricinium perchlorate in a neutral aqueous 0.1 *M* sodium perchlorate supporting electrolyte was studied; the perchlorate solution was prepared by dissolving ferricinium picrate in an equivalent amount of perchloric acid solution, and ether extracting the picric acid. A freshly prepared solution, after removal of oxygen with nitrogen, showed a combined anodic–cathodic polarographic wave, with a half-wave potential of +0.16 v. *versus* the S.C.E.; the shift in half-wave potential is due to the change from an

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[1] First reported by T. J. Kealy and P. L. Pauson, *Nature*, **168**, 1039 (1951). See also Miller, Tebboth and Tremaine, *J. Chem. Soc.*, 632 (1952).

[2] G. Wilkinson, M. Rosenblum, M. C. Whiting and R. B. Woodward, THIS JOURNAL, **74**, 2125 (1952).

[3] G. Wilkinson, *ibid.*, **74**, 6146 (1952).

[4] G. Wilkinson, *ibid.*, **74**, 6148 (1952).

[5] J. J. Lingane and S. L. Jones, *Anal. Chem.*, **22**, 1169 (1950).

alcoholic to aqueous supporting electrolyte. The result confirms other chemical evidence that the ferricinium ion in neutral aqueous solution partially decomposes quite rapidly to form some ferrocene.

The Ruthenocene–Ruthenicinium Ion System.—Ruthenocene has similarly been found to give a well defined anodic wave at the dropping mercury electrode; the supporting alcoholic electrolyte used was the same as the one used for ferrocene. The half-wave potential was +0.26 v. *versus* the S.C.E. The value of the polarographic constant, $i_d/Cm^{2/3}t^{1/6}$ was found to be 1.62 μa./mM/l. mg.$^{2/3}$ sec.$^{-1/2}$.

A controlled potential oxidation at a mercury anode of 23.0 mg. of ruthenocene in 50 ml. of the same supporting electrolyte has been made at a potential of 0.40 v. *versus* the S.C.E. The initial current of 6.7 ma. decreased to 0.1 ma. in 60 minutes electrolysis. During the course of the electrolysis an insoluble yellow crystalline solid, ruthenicinium perchlorate, precipitated from the solution. The quantity of electricity measured as before was 8.76 coulombs, agreeing well with the calculated value, 9.57 coulombs, for a one-electron oxidation. The solid was removed leaving a pale yellow solution of ruthenicinium perchlorate in the supporting electrolyte; a polarogram of this solution gave a well defined wave at a potential of +0.22 v. *versus* the S.C.E. The separated perchlorate was dissolved in water and the solution made 0.1 M in sodium perchlorate; after removal of oxygen with nitrogen, a cathodic wave with a half-wave potential of +0.11 v. *versus* the S.C.E. was obtained; ruthenicinium perchlorate slowly separated from this solution in which it is very sparingly soluble.

The Cobalticinium Ion.—Solutions of cobalticinium perchlorate were prepared from cobalticinium picrate solutions by use of an anion exchange resin column. In an oxygen free, 0.1 M sodium perchlorate aqueous supporting electrolyte at pH 6.2, the cobalticinium ion gave a well-defined cathodic wave at the dropping mercury electrode. The half-wave potential was −1.16 v. *versus* the S.C.E. The value of the polarographic constant, $i_d/Cm^{2/3}t^{1/6}$, was found to be 1.77 μa./mM/l. mg.$^{2/3}$ sec.$^{-1/2}$.

Unsuccessful attempts were made to prepare cobaltocene, $(C_5H_5)_2Co$, by controlled potential electrolysis of a neutral one millimolar cobalticinium perchlorate solution. A mercury cathode and divided cell were used, and the potential was −1.5 v. *versus* the S.C.E. The initial current was 7.0 ma. which decreased very slowly being 5 ma. after 60 minutes electrolysis. On continued electrolysis, the polarographic wave for the cobalticinium ion disappeared, indicating that complete destruction of the complex occurs, rather than the simple oxidation of cobaltocene by water.

We are indebted to Professor J. J. Lingane for his helpful advice and suggestions.

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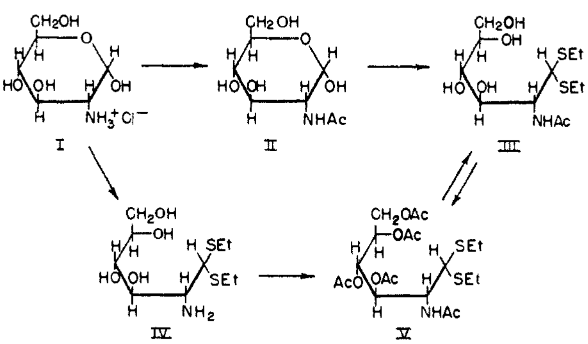
Acetylated Thioacetals of D-Glucosamine

BY M. L. WOLFROM AND KIMIKO ANNO[1]

RECEIVED AUGUST 20, 1952

Wolfrom, Lemieux and Olin[2] reported that the mercaptalation and acetylation of N-acetyl-2-amino-2-deoxy-D-glucose (II, N-acetyl-D-glucosamine)[3,4] produced a crystalline product, m.p. 126–127°, $[\alpha]^{22}\mathrm{D}$ −32° (chloroform), which was described as a pentaacetyl derivative. Further investigation shows that this substance was actually a tetraacetyl derivative obtained in low yield and not again encountered in subsequent preparations. The correct pentaacetyl derivative V is herein described: m.p. 75–77°, $[\alpha]^{28}\mathrm{D}$ +1° (*c* 4, chloroform). Kent[5] has reported, without experimental detail, the same substance with the constants: m.p. 160–161°, $[\alpha]^{23}\mathrm{D}$ +2° (*c* 1, chloroform). It is then apparent that either the melting point of Kent is in error or we have at hand a low melting dimorph. N-Acetyl-2-amino-2-deoxy-D-glucose diethyl thioacetal (III, N-acetyl-D-glucosamine diethyl mercaptal) has been described by Wolfrom, Lemieux and Olin[2]; m.p. 130-131°, $[\alpha]^{23}\mathrm{D}$ − 35° (*c* 4, water). This compound has now been prepared from N-acetyl-2-amino-2-deoxy-D-glucose (II) by an improved method and the above constants verified. For this compound Kent[5] has reported the constants: m.p. 121–122°, $[\alpha]^{23}\mathrm{D}$ −24° (*c* 0.4, water). It is apparent that his preparation was impure. Kent[5] further records that he treated 2-amino-2-deoxy-D-glucose (D-glucosamine) hydrochloride (I) at room temperature with ethanethiol and hydrochloric acid (the recorded[5] density of 1.4 is undoubtedly in error). Treatment of 2-amino-2-deoxy-D-glucose hydrochloride (I) with ethanethiol in the concentrated hydrochloric acid of commerce (*ca.* 12 N) gave a very slow reaction from which we obtained after hydrogen chloride removal, 2-amino-2-deoxy-D-glucose diethyl thioacetal (IV); m.p. 109–110°, $[\alpha]^{23}\mathrm{D}$ −24° (*c* 1, water). Kent[5] records for the hydrochloride: m.p. 75–76°; $[\alpha]^{22}\mathrm{D}$ −18° (*c* 0.16, water). Acetylation of our preparation of 2-amino-2-deoxy-D-glucose diethyl thioacetal (IV) led to the above-mentioned pentaacetyl derivative V while de-O-acetylation of this yielded N-acetyl-2-amino-2-deoxy-D-glucose diethyl thioacetal (III)



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[1] Special Postdoctoral Research Fellow of the National Institutes of Health, United States Public Health Service.

[2] M. L. Wolfrom, R. U. Lemieux and S. M. Olin, *Abstracts Papers Am. Chem. Soc.*, **112**, 12Q (1947); THIS JOURNAL, **71**, 2870 (1949).

[3] R. Breuer, *Ber.*, **31**, 2193 (1898).

[4] T. White, *J. Chem. Soc.*, 428 (1940).

[5] P. W. Kent, *Research* (London), **3**, 427 (1950).

showing the constants reported by us. Oxidation of pentaacetyl-2-amino-2-deoxy-D-glucose diethyl thioacetal (V) to the disulfone derivative has been described by MacDonald and Fischer.[6] These workers employed the thioacetal as an intermediate but did not isolate it in crystalline form.

Experimental

Tetraacetyl-2-amino-2-deoxy-D-glucose Diethyl Thioacetal.—This material was previously described[2] incorrectly as the pentaacetyl derivative. After the authentic pentaacetyl derivative was crystallized in this Laboratory, the tetraacetyl derivative was not again encountered. A file sample, however, was available for examination; m.p. 126–127° (from methanol–water), $[\alpha]^{22}$D −32° (*c* 4, chloroform).

Anal. Calcd. for $C_{18}H_{31}O_8NS_2$: C, 47.66; H, 6.89; N, 3.09; S, 14.14. Found: C, 47.87; H, 6.63; N, 3.01; S, 14.08.

Preparation of N-Acetyl-2-amino-2-deoxy-D-glucose Diethyl Thioacetal (III).—N-Acetyl-2-amino-2-deoxy-D-glucose[4] (30.0 g.) was dissolved in 120 ml. of concentrated hydrochloric acid (*ca.* 12 *N*) and stirred mechanically with 120 ml. of ethanethiol for 24 hr. at 0°. The reaction mixture was then neutralized with an excess (*ca.* 700 g.) of basic lead carbonate. After the addition of 500 ml. of water, the solids were removed by filtration and washed with 1000 ml. of water. The filtrate and washings were dewatered under reduced pressure and the residue was extracted at room temperature with 150 ml. of abs. ethanol. The solvent was removed under reduced pressure from the filtered extract and the residue was crystallized from methanol–ether; yield 36 g. (81%), m.p. 124–127°, $[\alpha]^{30}$D −30° (*c* 4, water). Pure material was obtained on further crystallization from methanol–chloroform–ether as described previously[2]; m.p. 129.5–130.5°, $[\alpha]^{23}$D −35° (*c* 4, water).

Pentaacetyl-2-amino-2-deoxy-D-glucose Diethyl Thioacetal (V).—N-Acetyl-2-amino-2-deoxy-D-glucose diethyl thioacetal (3.0 g.) was acetylated with acetic anhydride (10 ml.) and pyridine (10 ml.) for 24 hr. at room temperature. This solution was then poured into 250 ml. of ice and water and the resultant mixture was extracted with chloroform. The chloroform extract was treated with a saturated aqueous solution of cadmium chloride and the filtered chloroform layers were washed successively with water, saturated aqueous sodium bicarbonate and again with water. The sirup obtained on solvent removal from the dried chloroform solution crystallized on standing for several days in a desiccator over phosphorus pentoxide. Pure material (elongated prisms) was obtained on recrystallization from ligroin (b.p. 65–110°); yield 3.6 g. (79%), m.p. 75–77°, $[\alpha]^{28}$D +1° (*c* 4, chloroform).

Anal. Calcd. for $C_{20}H_{33}O_9NS_2$: C, 48.47; H, 6.71; N, 2.83; S, 12.94. Found: C, 48.69; H, 6.53; N, 2.89; S, 13.07.

This substance was also obtained in high yield on acetylation, effected in the above manner, of the 2-amino-2-deoxy-D-glucose diethyl thioacetal described below.

De-O-acetylation of pentaacetyl-2-amino-2-deoxy-D-glucose diethyl thioacetal (0.50 g.) in abs. methanol (30 ml.) was effected by passing in a stream of anhydrous ammonia for 20 min. at 0° followed by standing of the solution at room temperature for 2 hr. The residue obtained on solvent removal under reduced pressure was crystallized from methanol–chloroform–ether; yield 0.33 g. (100%), m.p. 127–128° unchanged on admixture with the above described N-acetyl-2-amino-2-deoxy-D-glucose diethyl thioacetal.

2-Amino-2-deoxy-D-glucose Diethyl Thioacetal (IV).—2-Amino-2-deoxy-D-glucose hydrochloride (5.00 g.) was shaken mechanically with 20 ml. of concentrated hydrochloric acid (*ca.* 12 *N*) and 20 ml. of ethanethiol in a sealed tube at room temperature for 2 days. The tube was allowed to stand at room temperature with occasional shaking until all of the starting material had dissolved; 2.5 months were required. The tube was opened and the solution was neutralized with an excess of lead carbonate, filtered and the filtrate was treated with an excess of silver carbonate. The filtered solution was treated with an excess of hydrogen sulfide, filtered and dewatered under reduced pressure to a sirup which was crystallized from ethanol–ether; yield 2.65 g. (40%), m.p. 102–107°, $[\alpha]^{27}$D −21° (*c* 1.8, water). Pure crystals (needles) were obtained on further crystallization effected in the same manner; m.p. 109–110°, $[\alpha]^{23}$D −24° (*c* 1, water). The aqueous solution of this substance was basic in reaction and gave a positive ninhydrin test.

Anal. Calcd. for $C_{10}H_{23}O_4NS_2$: C, 42.08; H, 8.12; N, 4.91; S, 22.47. Found: C, 42.22; H, 8.20; N, 4.97; S, 22.37; Cl^-, absent.

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[6] D. L. MacDonald and H. O. L. Fischer, THIS JOURNAL, **74**, 2087 (1952).

The Crystal Structure of Tetrachlorophosphonium Dichloroiodide[1,2]

BY WILLIAM F. ZELEZNY AND NORMAN C. BAENZIGER

RECEIVED JULY 23, 1952

Although tetrachlorophosphonium dichloroiodide[3] (PCl_6I) has been known for almost a century, its crystal structure has not been reported. Accordingly, this structure was made the topic of an investigation.

Experimental

The compound was prepared by the reaction of phosphorus pentachloride and iodine monochloride in solution in carbon disulfide, yielding a finely divided, light yellow precipitate. Contact with the moisture of the air was prevented by keeping the precipitate covered with carbon tetrachloride, this protection being necessary since this compound reacts vigorously with water.

Tetrachlorophosphonium dichloroiodide readily yields crystals by sublimation in a small evacuated container. The handling of these crystals was made difficult by the compound's reactivity with moisture which precluded handling them in the atmosphere, and by its high vapor pressure which prevented manipulation of the crystals within a dry-box. To overcome these difficulties the compound, with its protective covering of carbon tetrachloride, was introduced into a 10-mm. glass tube, one end of which had been drawn to a capillary. The carbon tetrachloride was then removed by evacuation of the 10-mm. tube, care being taken that evacuation was not continued long enough to permit the vaporization of the solid PCl_6I. The 10-mm. tube was sealed off and the section containing the PCl_6I heated to 140°, resulting in rapid sublimation of the compound with deposition of crystals in the capillary section of the tube. The capillary tube was then sealed off and held in a constant temperature oven at 80° until grain growth had taken place and only one crystal remained. Many such trials were necessary in order to obtain crystals of suitable size and orientation.

X-Ray Diffraction Data.—Intensity data and approximate unit cell dimensions were obtained from zero-layer Weissenberg diagrams of single crystals recorded on multiple films with unfiltered Mo radiation. Intensities were estimated by the visual comparison method. Molybdenum radiation was chosen for obtaining the intensity data in preference to Cu Kα radiation since the latter was strongly absorbed by these crystal. However, the final unit cell dimensions were obtained from powder diagrams taken with CuKα radiation.

The unit cell is tetragonal, with the dimensions a = 9.26 Å., c = 5.68 Å., and contains two molecules. From these data the density is calculated to be 2.53 g./cc. Systematic extinction was observed only for the (0k0) reflections when k was odd, indicating space groups $P\bar{4}2_1$ (D_4^2) and $P\bar{4}2_1m$

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[1] From a thesis submitted by Wm. F. Zelezny in partial fulfillment of the requirements for a Ph.D. degree at the State University of Iowa, August, 1951.

[2] For material supplementary to this article order Document 3681 from American Documentation Institute, 1719 N Street, N. W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

[3] E. Baudrimont, *Compt. rend.*, **55**, 362 (1862).

($D_{2}^{3}d$). Space group $P\bar{4}2_1$ does not permit a tetrahedral arrangement of atoms around the phosphorus atom. Since the structure appeared to be isotypic with tetramethylammonium dichloroiodide[4] and since the Patterson projection could be explained on the basis of this structure, the structure based on $P\bar{4}2_1m$ was chosen.

Crystal Structure.—Using ($hk0$) data, a Patterson projection was made on ($00l$) and the approximate x- and y-parameters determined. From these parameters the signs of the $F(hk0)_{\text{obsd}}$ were calculated and used in a Fourier projection on ($00l$). The x- and y-parameters were refined as much as possible by a repetition of this Fourier projection. The z-parameters were obtained from a Patterson projection on (110). In order to obtain better agreement between the calculated and observed F values, an empirical temperature correction factor of the form $e^{-1.51 \sin^2\theta}$ was applied to the calculated F values. It was felt by the authors that the usual scheme of computing R_1 does not make sufficient allowance for reflections, which, while not zero, are not sufficiently strong to record on film with ordinary exposures. Accordingly, a slightly modified method of calculating the R_1 values, consisting of assigning each absent or unobserved reflection an F value which was calculated as follows, was used. The minimum intensity observable was corrected by the angle factors corresponding to each of the unobserved reflections. Taking one-half of the square roots of the quantities thus obtained yielded F values which were arbitrarily assigned to the absent reflections for the purpose of calculating R_1. The R_1 calculated in this manner is defined as R_1^*. Using the parameters chosen an R_1^* value of 0.27 was obtained.

The compound proved to be isostructural with tetramethylammonium dichloroiodide,[4] with the following atoms at the following positions of space group $D_{2}^{3}d$-$P\bar{4}\,2_1m$: 2 P at (b) (0 0 $^1/_2$), ($^1/_2$ $^1/_2$ $^1/_2$); 2 I at (c) (0 $^1/_2$ z), ($^1/_2$ 0 $\bar{z}$) with z = 0.161; 4 Cl at (e) x, $^1/_2 + x$, z; $\bar{x}$, $^1/_2 - x$, z; $^1/_2 + x$, $\bar{x}$, $\bar{z}$; $^1/_2 - x$, x, $\bar{z}$ with $x = 0.18_0$, $z = 0.16_1$; 8 Cl at (f) xyz; $^1/_2 - x$, $^1/_2 + y$, $\bar{z}$; $\bar{x}\bar{y}z$; $^1/_2$. x, $^1/_2 - y$, $\bar{z}$; $\bar{y}x\bar{z}$; $^1/_2 + y$, $^1/_2 + x$, z; $y\bar{x}\bar{z}$; $^1/_2 - y$, $^1/$ · x, z with $x = 0.15_5$, $y = 0.07_9$, $z = 0.29_8$.

This structure consists of regularly tetrahedral PCl_4^+ ions, and linear $ClICl^-$ ions with the interatomic distances in ångström units are

P–8-fold Cl	1.98
I–4-fold Cl	2.36
8-fold Cl–8-fold Cl (within PCl_4^+ tetrahedra)	3.23
8-fold Cl–8-fold Cl (from one PCl_4^+ to the next)	3.50
4-fold Cl–8-fold Cl	3.56

Extensive calculations of intensities based on selected chlorine positions near those given above showed that the positions of chlorine atoms could be changed considerably without affecting the R_1^* value. For example

x for 4 (e)	0.16	0.17	0.18	0.19	0.20
R_1^*	.285	.271	.270	.272	.277

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(4) R. C. L. Mooney, *Z. Krist.*, [A] **100**, 519 (1939).

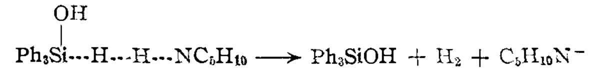
COMMUNICATIONS TO THE EDITOR

HYDROGEN ISOTOPE EFFECT IN THE HYDROLYSIS OF TRIPHENYLSILANE

Sir:

Recently, Gilman, Dunn and Hammond reported[1] that triphenylsilane-*d* was hydrolyzed in moist piperidine "almost six times faster than its protium analog." They attributed this unusual isotope effect to the displacement of a hydride ion in such a manner that a hydrogen–hydrogen bond of considerable strength is present in the transition state of the reaction. This picture of the reaction path might be formulated as

$$OH^- + Ph_3SiH + HNC_5H_{10} \longrightarrow$$



$$\overset{\displaystyle OH}{\overset{|}{Ph_3Si}}\text{---}H\text{---}H\text{---}NC_5H_{10} \longrightarrow Ph_3SiOH + H_2 + C_5H_{10}N^-$$

Because of the unusual effect reported for this reaction, we have examined several similar reactions which involve the formation of hydrogen, presumably by abstraction of a hydride ion. To enhance any isotope effects, tritium, rather than deuterium, was used in competitive measurements of k_T/k_H, the ratio of the isotopic reaction rates.

The alkaline alcoholic hydrolysis[2] of tripropylsilane-*t* was found to be about 0.7 as fast as that of its protium analog. The alcoholysis of lithium aluminum hydride-*t*[3] and of lithium borohydride-*t*[4] did not give consistent values of k_T/k_H, possibly because of changes in the reacting species; the observed values fell between 1.2 and 0.8.

In view of these results we have reinvestigated the hydrolysis of triphenylsilane in moist piperidine. Tritium-labeled triphenylsilane was prepared[5] by the reduction of triphenylchlorosilane with lithium aluminum hydride-*t*.[3] The triphenyl-silane-*t* was dissolved in a 1.0 *M* solution of water in piperidine, in a previously evacuated system, and permitted to react at 25°. At intervals, the reaction was stopped by cooling to −80°, and the evolved hydrogen was collected. The volume of each fraction was measured manometrically and its tritium content was determined in an ion chamber with a vibrating reed electrometer. The total volume and tritium content of the fractions agreed with those expected from analysis[5] of the triphenylsilane-*t* by hydrolysis with moist piperidine and potassium hydroxide. The experimental results are given in Table I. The ratio of the rate constants is calculated for each gas fraction from the expression

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(1) H. Gilman, G. E. Dunn and G. S. Hammond, THIS JOURNAL, **73**, 4499 (1951).

(2) F. P. Price, *ibid.*, **69**, 2600 (1947).

(3) K. E. Wilzbach and L. Kaplan, *ibid.*, **72**, 5795 (1950).

(4) W. G. Brown, L. Kaplan and K. E. Wilzbach, *ibid.*, **74**, 1343 (1952).

(5) H. Gilman and G. E. Dunn, *ibid.*, **73**, 3404 (1951).