acid.[14] The temperature of the resulting exothermic reaction was maintained at about 40°[15] by means of external cooling. After the addition was complete, stirring was continued for one hour and the resulting slurry of product and solvent cooled to 5°. The white crystalline solid was then collected on a suction filter, washed with fresh acetone and dried. In each case the sulfone was obtained in practically pure form directly from the reaction mixture. A mixture melting point determination of the sulfones thus produced indicated that each was identical with a sample of the same sulfone prepared according to the reaction sequence outlined in Chart I.

Racemic α-Dichloroacetamido-β-hydroxy-4-ethylsulfonylpropiophenone (XIII).—Prepared by the oxidation of racemic α-dichloroacetamido-β-hydroxy-4-ethylmercaptopropiophenone[1] according to the above procedure, m.p. 184.0–185.0°.

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_5S$: Cl, 19.26; N, 3.81. Found: Cl, 18.96; N, 3.71.

RENSSELAER, NEW YORK

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[14] Obtained from Buffalo Electro-Chemical Co., Inc.

[15] The temperature, except in the case of VII (see footnote 7), can be varied within fairly wide limits. Thus in some cases the temperature was allowed to rise to 55–60° without detrimental effects.

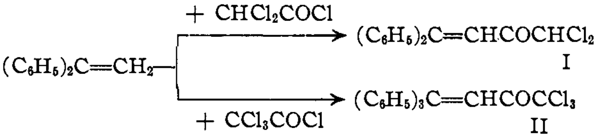
NOTES

The Uncatalyzed Condensation of 1,1-Diphenylethylene with Chlorinated Acetyl Chlorides

BY FELIX BERGMANN AND JOSEPH KLEIN

RECEIVED MARCH 4, 1953

The direct acylation of the β-carbon atom of 1,1-diphenylethylene is dependent on the presence of activating groups attached to the reacting COCl group. It has been shown, *e.g.*, that the –COCl[1] or the –COOR[2] radical, benzyl and aryl residues[3] exert such an activating influence, which decreases in the order given. From a comparison of phosgene[4] with oxalyl chloride it becomes evident that it is the neighboring carbonyl which increases the reactivity of the –COCl group in the substitution under discussion. Therefore it appeared probable that any α-carbonyl would exert such an influence. Since the chlorides of glyoxylic acids and its homologs are unstable compounds–if existing at all–we applied the reaction to acid chlorides, in which the α-carbonyl is replaced by the CCl_2 group. Thus dichloroacetyl chloride, which is derived from glyoxylic acid chloride, was condensed with 1,1-diphenylethylene to form the ketone I. In a similar way, trichloroacetyl chloride, which is related to oxalyl chloride, gave the ketone II, accompanied by large amounts of the open-chain dimer of the hydrocarbon.[5]



$$(C_6H_5)_2C{=}CH_2 \xrightarrow{+\ CHCl_2COCl} (C_6H_5)_2C{=}CHCOCHCl_2 \quad \text{I}$$

$$(C_6H_5)_2C{=}CH_2 \xrightarrow[+\ CCl_3COCl]{} (C_6H_5)_3C{=}CHCOCCl_3 \quad \text{II}$$

The ketone I behaved like a derivative of an α-ketoaldehyde, *e.g.*, with 2,4-dinitrophenylhydrazine two products were formed, a yellow hydrazone and a deep-red osazone. The keto group in the compound II, however, is sterically hindered and thus unreactive.

The absorption spectra of these ketones, when compared with β,β-diphenylacrolein (Table I), reveal that at short wave lengths the chlorinated side chain has practically no influence, whereas for the long wave maximum I shows a shift of 100 Å. and II of 280 Å. toward the red.

TABLE I

ABSORPTION SPECTRA OF β,β-DIPHENYL-α,β-UNSATURATED CARBONYL COMPOUNDS IN 95% ETHANOL

Compound	Maxima at	
1. β,β-Diphenylacrolein	2260 (4.3)	3000 (4.1)
2. Ketone I	2310 (4.1)	3100 (4.1)
3. Ketone II	2250 (4.0)	3280 (4.2)

Experimental

Condensation of 1,1-Diphenylethylene with Dichloroacetyl Chloride.—The ethylene (12 g.) and dichloroacetyl chloride (74 g., 7.5 equiv.) were heated in a current of hydrogen to 112–115° for 60 hours. The excess acid chloride was distilled off, the residue dissolved in benzene, washed with water and sodium carbonate, and then fractionated. The portion distilling at 170–195° (1.5 mm.) was redistilled, yielding a yellow oil of b.p. 178–182° (2 mm.). This fraction (5 g.) proved to be the expected ketone, 1,1-diphenyl-3-keto-4,4-dichlorobutene-1 (I).

Anal. Calcd. for $C_{16}H_{12}OCl_2$: C, 65.9; H, 4.1; Cl, 24.4. Found: C, 65.7; H, 4.1; Cl, 24.5.

The reaction with Brady's reagent at room temperature for 24 hours gave a mixture, from which first yellow crystals separated. The substance crystallized from butanol in yellow plates of m.p. 168°. It gave a positive Beilstein test and, according to analysis, represents a monohydrazone of I.

Anal. Calcd. for $C_{22}H_{16}O_4N_4Cl_2$: C, 56.0; H, 3.4; Cl, 15.0. Found: C, 56.0; H, 3.7; Cl, 14.4.

From the mother liquor a deep red precipitate was obtained on standing, which crystallized from dioxane–butyl acetate in microcrystals of m.p. 248°. This derivative is chlorine-free and corresponds to an osazone of I.

Anal. Calcd. for $C_{28}H_{20}O_8N_8$: C, 56.4; H, 3.35; N, 18.8. Found: C, 56.4; H, 3.8; N, 18.8.

Condensation of 1,1-Diphenylethylene with Trichloroacetyl Chloride.—The ethylene (12.8 g.) and trichloroacetyl chloride (64 g., 5 equiv.) were refluxed for 30 hours at a temperature of 116–118° in a current of hydrogen. The mixture was treated as above and yielded a fraction of boiling point 195–215° (3 mm.), which crystallized upon trituration

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[1] M. S. Kharasch, S. S. Kane and H. C. Brown, THIS JOURNAL, **64**, 333 (1942).

[2] F. Bergmann and A. Kalmus, *J. Chem. Soc.*, 4521 (1952).

[3] F. Bergmann, S. Israelashvili and D. Gottlieb, *ibid.*, 2522 (1952).

[4] F. Bergmann, M. Weizmann, E. Dimant, S. Patai and J. Szmuszkowicz, THIS JOURNAL, **70**, 1612 (1948).

[5] Monochloroacetyl chloride failed to condense with 1,1-diphenylethylene.

with methanol. The m.p. of this material, 16.3 g., was 67–72° (unsharp). Since repeated recrystallizations from methanol did not give a substance with sharp m.p., we dissolved the material in petroleum ether and chromatographed it on alumina, collecting fractions of 50 ml. Fractions 5–8 gave a crystalline residue of m.p. 86–87°, which upon recrystallization from isopropyl alcohol formed yellow cubes of m.p. 87°.

Anal. Calcd. for $C_{16}H_{11}OCl_3$: C, 59.0; H, 3.4. Found: C, 59.1; H, 3.4.

The ketone II did not react with any of the usual carbonyl reagents.

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Reductions with Hydrazine Hydrate Catalyzed by Raney Nickel. I. Aromatic Nitro Compounds to Amines[1,2]

BY D. BALCOM AND ARTHUR FURST

RECEIVED APRIL 13, 1953

Hydrazine, though a powerful reducing agent is not used extensively to reduce aromatic nitro compounds to amines. The rate of reaction is too slow. If employed in a sealed tube[3] or in high boiling solvents[4] almost all functional groups are reduced.

With the addition of a small amount of Raney nickel catalyst, hydrazine hydrate will selectively reduce an aromatic nitro compound to an amine at room or steam-bath temperature. Yields are excellent ranging from 80 to 99%. Under these conditions other functional groups, namely, carbonyls, will not be affected. To eliminate loss due to foaming a large excess of solvent alcohol is necessary. We have confirmed Kuhn's[5] observation that no reduction takes place even after 18 hours if no catalyst is added. The mechanism of the reaction is unknown, but hydrazine when catalytically decomposed liberates only water and gases[6] so that elimination of by-products is not a problem.

Experimental

As all of the aromatic nitro compounds listed here were reduced by the same method, only a general procedure is given. In each case the amino compound listed was also obtained by the reduction of the nitro compound by a procedure obtained from the literature. Mixed melting points as well as fusion analysis[7] helped prove the identity of the amino compound. In some cases the hydrochloride rather than the free amine was isolated.

Generalized Procedure.—To the nitro compound dissolved in alcohol (10 ml./g.) was added 2–3 molar ratios of hydrazine hydrate 100%. The solution was placed on the steam-bath and when just warm a small amount of Raney Ni was added. The solution frothed. As the reaction proceeded (5 to 60 min.) the color changed from yellow to almost colorless. More catalyst was added to decompose the excess hydrazine and the solution was heated to boiling to drive off the dissolved gases. The hot solution was filtered to remove the Ni, boiled with decolorizing carbon and filtered again. The free amine was isolated by cooling the solution to *ca.* 50° and then pouring into a large excess of water; or the hydrochloride salt was obtained by evaporating the solvent to *ca.* 5–10 ml., adding *ca.* of 5 ml. ofconcentrated hydrochloric acid and cooling the mixture. The precipitates were isolated and dried.

Amines.—By this procedure *p*-aminobiphenyl ether[8] was obtained in 96.5% yield. Other amines obtained in yield between 80 and 99% were *p*-aminocinnamic acid,[9] *m*-aminobenzophenone,[10] 2-methyl-4′-aminobiphenyl,[11] 4,4′-diaminodiphenyl ether[12] and aniline.

Biological Testing.—These compounds were tested for their effect on the mouse Sarcoma-37. No inhibitory action was noted.[13]

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[1] Presented before the Division of Organic Chemistry at the 123rd Meeting of the American Chemical Society in Los Angeles, California, March, 1953.

[2] This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service, and from the Catherine Stern Memorial Fund.

[3] (a) T. Curtius, *J. prakt. Chem.*, **76**, 233, 238, 281, 301 (1907); (b) E. Müller and G. Zimmermann, *ibid.*, 111, 272 (1925).

[4] Huang-Minlon, THIS JOURNAL, **70**, 2802 (1948).

[5] L. P. Kuhn, *ibid.*, **73**, 1510 (1951).

[6] L. F. Audrieth and B. A. Ogg, "The Chemistry of Hydrazine," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 145.

[7] N. Goetz-Luthy, *J. Chem. Educ.*, **26**, 159 (1949).

[8] H. I. Jones and A. N. Cook, THIS JOURNAL, **38**, 1534 (1916).

[9] F. Wollring, *Ber.*, **47**, 111 (1914).

[10] R. Geigy and W. Konigs, *ibid.*, **18**, 2400 (1885).

[11] H. France, I. M. Heilbron and D. H. Hay, *J. Chem. Soc.*, 1283 (1939).

[12] G. A. Reynolds, THIS JOURNAL, **73**, 4996 (1951).

[13] A. Furst and B. L. Freedlander, *Stanford Med. Bull.*, **10**, 308 (1952).

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Preparation of 1-Methyl-3-phenyl-3-(γ-dimethylaminopropyl)-piperidine

BY F. F. BLICKE AND EU-PHANG TSAO

RECEIVED APRIL 9, 1953

Phenyldi-(γ-dimethylaminopropyl)-acetonitrile, prepared from phenylacetonitrile, γ-dimethylaminopropyl chloride and sodamide, was hydrolyzed to the corresponding acetic acid. The latter compound was refluxed with thionyl chloride, the excess thionyl chloride removed and the residue heated until the evolution of methyl chloride stopped. The 1-methyl-3-phenyl-3-(γ-dimethylaminopropyl)-2-piperidone was reduced with lithium aluminum hydride to the corresponding piperidine.

Experimental

Phenyldi-(γ-dimethylaminopropyl)-acetonitrile.—Phenylacetonitrile (35.2 g.) in 50 cc. of toluene was added, gradually, to a stirred mixture of 29.3 g. of sodamide in 100 cc. of toluene at 40–50°. The mixture was stirred for 1 hour, then 90 g. of γ-dimethylaminopropyl chloride[1] was added, dropwise, to the stirred mixture at 40–50°. The material was refluxed for 6 hours and treated in the usual manner. After fractionation 70.0 g. (81.3%) of nitrile was obtained, b.p. 155–158° (1 mm.).

The dihydrochloride, prepared from an ethereal solution of the base and hydrogen chloride, melted at 280–282° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{18}H_{31}N_3Cl_2$: N, 11.66; Cl, 19.72. Found: N, 11.55; Cl, 19.71.

Phenyldi-(γ-dimethylaminopropyl)-acetic Acid.—A mixture of 57.4 g. of the nitrile, 94 cc. of concd. sulfuric acid and 63 cc. of water was refluxed for 2 hours. The cold mixture was poured into water and sodium hydroxide was added until the mixture was only slightly acidic. It was then decolorized with Norite. The filtered solution was made alkaline whereupon an oil separated. A further amount of oil was obtained by extraction of the aqueous solution with chloroform and removal of the solvent. When the oil was warmed under 16 mm. pressure for some time, it be-

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[1] A. Marxer, *Helv. Chim. Acta*, **24**, 209 E (1941).

came crystalline; m.p. 116–117° after recrystallization from acetone. This material was found to be the acid amide.

Anal. Calcd. for $C_{18}H_{31}ON_3$: N, 13.77. Found: N, 13.58.

The amide was refluxed with 150 cc. of 70% sulfuric acid for 48 hours. The mixture was poured onto ice, the solution was decolorized with Norite, filtered and the filtrate made alkaline with sodium hydroxide (*p*H 8–9). After the precipitated oil had been warmed under 16 mm. pressure, it became crystalline. The product was dissolved in absolute alcohol, the solution was filtered and the filtrate evaporated to dryness. The acid melted at 197–198° after recrystallization from dioxane.

Anal. Calcd. for $C_{18}H_{30}O_2N_2$: N, 9.15. Found: N, 8.96.

1-Methyl-3-phenyl-3-(γ-dimethylaminopropyl)-2-piperidone.—A mixture of 24.5 g. of the acid and 75 cc. of thionyl chloride was refluxed for 1.5 hours. The excess thionyl chloride was removed and the solid residue was heated in an oil-bath (200–205°) for 40 minutes when the evolution of gas practically stopped. The cold residue was dissolved in water, the solution was made alkaline and extracted with ether. Upon fractionation 12.5 g. (57%) of product was obtained, b.p. 148–150° (0.01 mm.).

The hydrochloride, obtained by the use of hydrogen chloride, melted at 182–183° after recrystallization from methyl ethyl ketone.

Anal. Calcd. for $C_{17}H_{27}ON_2Cl$: N, 9.02; Cl, 11.40. Found: N, 9.06; Cl, 11.61.

1-Methyl-3-phenyl-3-(γ-dimethylaminopropyl)-piperidine.—The piperidone (9.6 g.), dissolved in 30 cc. of ether, was reduced with 1.4 g. of lithium aluminum hydride dissolved in 70 cc. of ether. The mixture was stirred and refluxed for 5 hours, 3 cc. of water was added and the product was isolated in the usual manner; b.p. 122–124° (0.5 mm.), yield 7.8 g. (86%).

Since both the hydrochloride and the methobromide were hygroscopic, the methiodide was prepared. One gram of the base, dissolved in ether was treated with 2 g. of methyl iodide. After 2 hours the precipitated methiodide was recrystallized from methyl ethyl ketone; m.p. 172–173°.

Anal. Calcd. for $C_{18}H_{31}N_2I$: N, 6.97; I, 31.58. Found: N, 6.93; I, 31.50.

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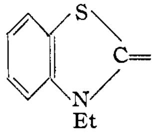
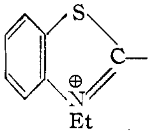
The Significance of Basicity and Acidity of Nuclei in Cyanine Type Condensations

BY L. G. S. BROOKER, S. G. DENT, JR., D. W. HESELTINE AND E. VAN LARE

RECEIVED JUNE 6, 1953

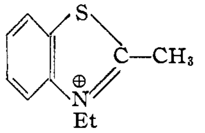
The gain in stabilization in passing from the net-uncharged form to the positively charged form of certain heterocyclic rings (*e.g.*, from I to II) is a quantity (the "basicity") that has considerable

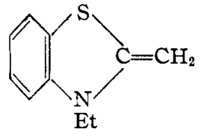

I


II

significance for the absorptions of cyanine and related dyes containing these nuclei.[1] It is now suggested that this "basicity" has an equal significance in reactions leading to these dyes.

These reactions commonly employ quaternary salts of heterocyclic bases containing a reactive methyl group (III is a typical cation), the cations losing a proton to give methylene bases (*e.g.*, IV)


III


IV

which are the reactive intermediates.[2] The formulas show that the formation of methylene base by the process III → IV involves the same loss of ring stabilization as in II → I, and, as a general proposition, a methylene base will be liberated from the corresponding cation the more readily, the lower the basicity of the nucleus in the sequence established by the "deviation" and similar procedures.[1] The *availability* of methylene base in a given reaction (which will in large measure determine whether that reaction will take place or not) therefore depends partly on the basicity of the particular nucleus and partly on the basic nature of the reaction medium.

By this reasoning it becomes possible to correlate a great many hitherto unrelated empirical observations and to account for many seeming anomalies, of which the following examples are illustrative.

Salts of a number of the less basic cations in the sequence[1] referred to react directly with *p*-dimethylaminobenzaldehyde in ethanol solution to give high yields of styryl dyes, whereas salts of more basic cations require piperidine as catalyst. For the first group, the aldehyde is itself sufficiently basic to liberate methylene base, but not for the second group. Again, salts of highly basic nuclei, such as α-picoline ethiodide, fail completely to give carbocyanine by the pyridine–ethyl orthoformate method. Here the nucleus is so basic that an insufficient concentration of methylene base is reached under the conditions of the experiment. Similarly, the low yields of carbocyanines given by salts of certain thiazoles (*e.g.*, 2,4-dimethylthiazole ethiodide)[3] are a consequence of the high basicity of these nuclei.[1] Introduction of a negative substituent (as in 5-ethoxycarbonyl-2,4-dimethylthiazole ethiodide) increases the apparent reactivity of the 2-methyl group[4] (*i.e.*, the yields of certain dyes are higher) by lowering the basicity of the nucleus and increasing the availability of the methylene base.

Less is known about the actual reactivity of a methylene base, as distinct from its availability. It is possible that the reactivity increases with increasing basicity of the ring, though this is still uncertain.

By somewhat similar reasoning, the yields of dyes of the merocyanine and oxonol types may be correlated with the "acidity" of the ketomethylene compounds that give them.[5] Such condensations also take place under basic conditions, and it is reasonable to suppose that the first step is the loss

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(1) L. G. S. Brooker, A. L. Sklar, H. W. J. Cressman, G. H. Keyes, L. A. Smith, R. H. Sprague, E. Van Lare, G. VanZandt, F. L. White, and W. W. Williams, THIS JOURNAL, **67**, 1875 (1945), and other papers of the series.

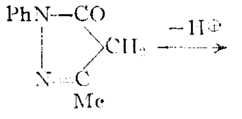
(2) W. H. Mills and R. Raper, *J. Chem. Soc.*, **127**, 2466 (1925).

(3) N. I. Fisher and F. M. Hamer, *J. Chem. Soc.*, 2502 (1930).

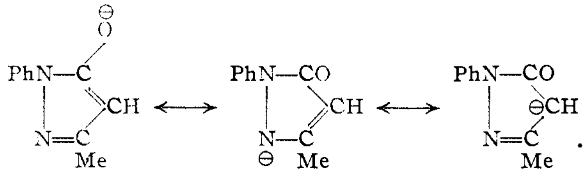
(4) J. Götze and H. Socher, *Beihefte Z. ver. deut. Chem.*, No. 40, 1 (1940).

(5) L. G. S. Brooker, G. H. Keyes, R. H. Sprague, R. H. VanDyke, E. Van Lare, G. VanZandt, F. L. White, H. W. J. Cressman, and S. G. Dent, Jr., THIS JOURNAL, **73**, 5332 (1951), especially page 5348.

of a proton from the ketomethylene compound (*e.g.*, V) to give an enolate anion (*e.g.*, VI) which is the reactive intermediate. Ions such as VI are



V



(a) VI (b) (c)

the more stabilized by resonance, the higher the electron-attracting power (or "acidity") of the nucleus in the sequence recently established.[5] Under given basic conditions, the availability of an enolate anion is therefore greater, the higher the "acidity" of the nucleus, and on the assumption that the presence of enolate ion is necessary for the ensuing reaction, the, in general, greater ease of reaction of ketomethylene compounds derived from the more highly acidic nuclei[5] can readily be understood.

The actual reactivity of an enolate ion is clearly distinct from its availability. This reactivity is very possibly dependent upon high electron density at the methylene carbon, as shown in VI(c). But the contribution of this structure will be relatively less, the greater the attraction for the electron shown by oxygen and nitrogen in the competing structures VI(a) and VI(b). By this argument the actual reactivity of an enolate ion would be expected to be reduced by the attraction of the electron to atoms in the nucleus other than the methylene carbon, but this again is uncertain.

RESEARCH LABORATORIES
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Synthesis of Tertiary Carbon^{14}-Labeled DDT[1,2]

BY D. R. BUHLER, C. H. WANG AND B. E. CHRISTENSEN

RECEIVED APRIL 22, 1953

Although 1-C^{14} ring labeled 2,2-bis-(*p*-chlorophenyl)-1,1,1-trichloroethane has been synthesized by Fields,[3] *et al.*, with a specific activity of 54 μc./mM., recent studies on the mode of action and detoxification mechanism of DDT have made it imperative to synthesize uniquely labeled DDT with a higher specific activity on the millimole scale.

Several proposed schemes[4,5] based on known reactions which could be used for the preparation of chain labeled DDT have appeared in the literature; however, none are supported by experimental procedures which would give the necessary information regarding the feasibility on a millimole scale such as demanded for isotopic preparations.

One of the most ingenious of these is that of Fry[4] for labeling DDT in the tertiary position; unfortunately Fry discontinued his work. The method which was devised in this Laboratory is a microscale adaptation of Fry's original suggestion. The over-all yield for this procedure was found to be 10%.

Experimental

C^{14}-Carbonyl Labeled *p*,α-Dichloroacetophenone.—Prepared according to the method of Van Bruggen,[6] *et al.*, and then diluted with ordinary *p*-chlorobenzoic acid and converted to the acid chloride. The acid chloride was converted to crude dichloroacetophenone with diazomethane and dry hydrogen chloride; yield 44.5%, m.p. 99.0–99.5°.

Tertiary Carbon^{14}-labeled *p*-Chloro-α-trichlorobenzyl Alcohol.—The *p*,α-dichloroacetophenone was chlorinated in a trichloroacetic acid solvent using chlorine gas. This product was reduced to the alcohol with aluminum isopropoxide; yield 70.0%, m.p. of the acetate 123–124°.

Tertiary Carbon^{14}-labeled 2,2-Bis-*p*-(chlorophenyl)-1,1,1-trichloroethane.—The crude carbinol was condensed with dry chlorobenzene in a sulfuric acid medium. The isolated product DDT gave m.p. 104–104.5° (lit. 108–108.5°) with a specific activity of 1.49×10^8 c.p.m./mM. The over-all chemical and radioactivity yield of purified *p*,*p*′-DDT based on the original $BaCO_3$ was approximately 10%.

The radioactivity of the various compounds was determined as barium carbonate in the conventional manner; counting data were corrected for background and self-absorption.

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[1] Published with the approval of the Monograph Publication Committee as Research Paper No. 228, School of Science, Department of Chemistry.

[2] A more detailed form of this paper has been deposited as Document 3990 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting $1.25 for photoprints, or $1.25 for 35 mm. microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

[3] M. Fields, J. Gibbs and D. E. Walz, *Science*, **112**, 591 (1950).

[4] E. M. Fry, THIS JOURNAL, **71**, 3238 (1949).

[5] F. A. Gunther and R. C. Blinn, *J. Chem. Ed.*, **27**, 654 (1950).

[6] J. T. Van Bruggen, C. K. Claycomb and T. T. Hutchens, *Nucleonics*, **7**, 45 (1950).

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The Conversion of Veratraldehyde to Vanillin by Nitrobenzene and Alkali

BY W. J. BRICKMAN[1] AND C. B. PURVES

RECEIVED APRIL 11, 1953

One method of studying the structure of wood lignins and lignosulfonic acids is to determine the amounts of vanillin they yield when oxidized with nitrobenzene and aqueous caustic soda under pressure. Parallel experiments are also carried out with samples previously methylated by various reagents, and also with methylated and non-methylated "model" substances of the guaiacyl propyl type.[2,3] Veratraldehyde has been obtained by heating methylated lignosulfonic acids with aqueous alkali,[4,5] but apparently not when nitrobenzene is also present. The following experiments

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[1] Holder of an Allied Chemical and Dye Corporation Fellowship, 1952–1953.

[2] F. E. Brauns, "The Chemistry of Lignin," Academic Press, Inc., New York, N. Y., 1952, Chapter XIX, pp. 552–562.

[3] B. Leopold, *Acta Chem. Scand.*, **6**, 38, 49, 55, 63, 1294 (1952); *Svensk Papperstidn.*, **55**, 816 (1952). These articles include many recent references.

[4] G. H. Tomlinson and H. Hibbert, THIS JOURNAL, **58**, 348 (1946).

[5] K. Kratzl and I. Keller, *Monatsh.*, **83**, 197, 205 (1952). Earlier references to the supposed "aldol" cleavage are given.

show that veratraldehyde is converted to vanillin in at least 30% yield by nitrobenzene and 2 N alkali at 160°, and this reaction therefore competes with the Cannizzaro oxidation–reduction change known to be produced by alkali alone.[6] This observation is not inconsistent with the view that the p-hydroxyl group in vanillin may be present as an ether in the lignin precursor, and that cleavage of a 3-carbon side chain in the precursor may produce a para-substituted vanillin by the reverse of an aldol condensation.[5]

Experimental

The directions of Stone and Blundell[7] were followed. Pure veratraldehyde, 10.0 mg., nitrobenzene, 0.06 cc., and 1.0 cc. of 2 N aqueous sodium hydroxide were heated together in a stainless steel micro-bomb for three hours at 160°. This bomb had a metal to metal seal with no gasket. After isolation, 0.01-cc. aliquots of the centrifuged liquor were spotted on filter paper for chromatography, the spots were made acidic with the vapor of glacial acetic acid and were then dried in the air. n-Butyl ether saturated with water was the developing agent, and the ascending chromatographic technique was used for 11 to 12 hr., since the descending method was inconveniently rapid. After having been located with a 2,4-dinitrophenylhydrazine spray, aldehydes were extracted with ethanol from the proper parts of the chromatogram.

The content of vanillin in the ethanol extract, 25 cc., was determined according to Lemon[8] by adding 4 cc. of 0.2% ethanolic potassium hydroxide, diluting to 50 cc. with absolute ethanol, and examining the absorption of the solution at wave length 354 mμ. A Beckman Model DU spectrophotometer with a tungsten tube light source was used; plots were made at 5 mμ intervals over the range 320 to 400 mμ against the logarithm of the % transmission, and were assessed against calibration plots for pure vanillin at three different, known concentrations. Other control experiments showed that the recovery of vanillin by the chromatographic technique used was about 87%. Duplicate experiments gave 29.7 and 34.2% recoveries (uncorrected for the chromatographic loss) of vanillin from veratraldehyde.

The above oxidation of veratraldehyde with alkaline nitrobenzene was repeated on a 100-fold scale in another bomb. After being centrifuged, the alkaline liquors were extracted with ether to remove impurities, were acidified, and again extracted with ether to remove phenolic and acidic substances. Phenolic aldehydes were recovered from this extract in a saturated solution of sodium bisulfite, which was then acidified and extracted with ether. The residue left on evaporation of the ether was dissolved in ethanol and was used to prepare a crystalline 2,4-dinitrophenylhydrazone.[9] After recrystallization (yield 0.276 g. or 14%), the product had the correct m.p. 270–271°, not depressed by admixture with a sample of the same m.p. made from pure vanillin.

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[6] H. Decker and R. Pschorr, *Ber.*, **37**, 3403 (1904).

[7] J. E. Stone and M. J. Blundell, *Anal. Chem.*, **23**, 771 (1951).

[8] H. W. Lemon, *ibid.*, **19**, 846 (1947).

[9] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY
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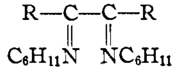
Reaction of Acetoin and Hydroxyacetaldehyde with Cyclohexylamine[1]

BY J. F. CARSON

RECEIVED APRIL 14, 1953

The non-enzymatic browning of vegetables which is generally attributed to reaction of amino groups of amino acids or proteins with reducing sugars is being investigated by the use of simple α-hydroxycarbonyl compounds and aliphatic amines as models for sugars and amino acids. In particular the reactions of acetoin and hydroxyacetaldehyde with primary aliphatic amines have been studied with the idea that α-hydroxyimino compounds might be isolated which would be analogous to the open chain formulas of the 1-amino-1-desoxy sugars.[2]

When acetoin is dissolved in anhydrous primary aliphatic amines at room temperature in the absence of air and allowed to stand several days, removal of excess amine by distillation yields colorless oils generally soluble in hydrocarbons. Short exposure to dry air produces darkening and precipitation of resin. With cyclohexylamine, however, two oxidative products could be isolated, crystalline cyclohexylamine salt of acetic acid and the new crystalline diimine, diacetyldicyclohexylimine I (R = CH_3). The mechanism whereby the primary condensation product of acetoin and amine is split to acetic acid and also oxidized to a derivative of diacetyl has not been investigated. Hydroxyacetaldehyde and cyclohexylamine in a similar way yield small quantities of the crystalline glyoxaldicyclohexylimine II (R = H). No acid has been isolated from this reaction.


$$R-\underset{\underset{C_6H_{11}N}{\|}}{C}-\underset{\underset{NC_6H_{11}}{\|}}{C}-R$$

I, R = CH_3 II, R = H

The structures of the two diimines were established by ultimate analysis and by acid hydrolysis to yield diacetyl or glyoxal and cyclohexylamine. The diimines, on catalytic hydrogenation with platinum oxide, each absorb two moles of hydrogen to yield oily diamines. In the ultraviolet in methanol solution, diacetyldicyclohexylimine shows a strong absorption maximum at 213 mμ and a weak, broad inflection in the range 245–260 mμ. Glyoxaldicyclohexylimine has a maximum at 218 mμ and a second weak maximum at 267 mμ. The principal maxima are near the range where conjugated dienes absorb.

Reaction of diacetyl with cyclohexylamine yields only small quantities of the diimine, the bulk of product being of a different nature.[3] Glyoxaldicyclohexylimine, however, could be prepared in good yield by reaction of 30% aqueous glyoxal solution with cyclohexylamine in alcoholic or aqueous solution.[4] Simple crystalline aliphatic 1,2-diimines have not heretofore been described.

Acknowledgment.—The author gratefully acknowledges the assistance of L. M. White and G. E. Secor for analyses and G. Bailey for ultraviolet absorption spectra.

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[1] Presented at 123rd National Meeting of American Chemical Society, Los Angeles, March, 1953.

[2] The importance of 1-amino-1-desoxy sugars as possible intermediates in Maillard browning reactions has been emphasized by J. Hodge and C. Rist (THIS JOURNAL, **74**, 1494 (1952); **7** , 316 (1952)) and A. Gottschalk and S. M. Partridge (*Nature*, **165**, 684 (1950)).

[3] J. F. Carson, THIS JOURNAL, **75**, 4300 (1953).

[4] K. Maurer and E. H. Woltersdorf (*Z. physiol. Chem.*, **254**, 18 (1938)) have shown that the reaction of glyoxal bisulfite with aliphatic amines in alcohol yields the corresponding N-alkyl-α-amino acid-N-alkylamide. In our experience, the diimine is obtained in quantity only with free glyoxal. Reaction of glyoxal bisulfite with cyclohexylamine in refluxing ethanol yielded only traces of the diimine and resinous material; no amide was isolated.

Experimental

Reaction of Acetoin and Cyclohexylamine.—Ten grams of crystalline dimer[5] and 30 g. of anhydrous cyclohexylamine were shaken together in a flask, from which the air was displaced by nitrogen, until the acetoin had dissolved (one hour) and then allowed to stand protected from oxygen for three days. Removal of excess cyclohexylamine *in vacuo* < 30° yielded an almost colorless viscous oil. A solution of the oil in 100 ml. of benzene was exposed to dry oxygen for several minutes and allowed to stand three days during which time 1.5 g. of cyclohexylamine acetate crystallized out. The mother liquor upon dilution with 100 ml. of hexane followed by standing a week deposited an additional 2 g. of faintly colored salt. The salt was recrystallized by solution in 150 parts of boiling benzene followed by slow cooling to yield cyclohexylamine acetate as large colorless needles, m.p. 143.5–145° (dec.).

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.86. Found: C, 60.5; H, 10.7; N, 8.75.

The identity of the compound as cyclohexylamine acetate was confirmed by microscopic comparison with an authentic sample.

The amber mother liquor was concentrated *in vacuo* to a deeply colored oil, dissolved in 30 ml. of methanol and kept at −20° overnight. Filtration in the cold yielded 9.7 g. (32%) of pink platy crystals. Recrystallization from 30 ml. of methanol at −20° yielded 7 g. (23%) of pure diacetyldicyclohexylimine as large, lustrous, colorless micaceous plates, m.p. 81.5–82.5; ultraviolet absorption in methanol, λ_{max} 213 mμ, log ε 4.075.

Anal. Calcd. for $C_{16}H_{28}N_2$: C, 77.36; H, 11.36; N, 11.28. Found: C, 77.1; H, 11.3; N, 11.2.

Attempts to improve the yields of oxidation products by bubbling air through hydrocarbon or alcohol solutions of the initial oily condensation product yielded only dark resinous products. On the other hand, neither the cyclohexylamine acetate nor the diimine could be obtained until the oil was exposed to air. Similarly, the reaction of acetoin with aniline under the same conditions yielded the diacetyldianil in small quantities only on exposure to air.

Acid Hydrolysis of Diacetyldicyclohexylimine.—A solution of 710 mg. of diacetyldicyclohexylimine in 100 ml. of 95% ethanol and 15 ml. of 6 *N* hydrochloric acid was distilled until 100 ml. of distillate was collected. From the distillate, diacetyl bis-2,4-dinitrophenylhydrazone was prepared in the usual manner and recrystallized from nitrobenzene in an 86% yield, identified by microscopic crystallographic comparison with an authentic sample. The distillation residue was converted to the *p*-toluenesulfonamide of cyclohexylamine[6] in a 78% yield.

The derivative was recrystallized from 20 parts of methanol-water (1:1) as colorless, fibrous needles, m.p. 85.7–86.4°.

Anal. Calcd. for $C_{13}H_{19}NSO_2$: C, 61.62; H, 7.56; N, 5.53. Found: C, 61.8; H, 7.57; N, 5.54.

Reaction of Glycolaldehyde and Cyclohexylamine.—Crystalline glycolaldehyde dimer (1.4 g.) was shaken with 10 g. of anhydrous cyclohexylamine in the absence of air for eight hours and allowed to stand overnight. Removal of excess amine by vacuum distillation yielded a pasty white solid which was dissolved in hexane and filtered from resinous material. The hexane solution at −20° yielded 1.6 g. (31%) of glyoxaldicyclohexylimine. No crystalline product could be obtained if air was rigidly excluded. Recrystallization from 25 parts of methanol or 15 parts of ethyl acetate yielded the pure glyoxaldicyclohexylimine as colorless lustrous micaceous plates, similar in appearance to the corresponding diacetyl compound, m.p. 149–150° (sl. dec.); ultraviolet absorption in methanol: λ_{max} 217 mμ, log ε 4.340; λ_{max} 267 mμ, log ε 2.532. Hydrolysis of the compound to glyoxal and cyclohexylamine was performed as with the diacetyl derivative.

Anal. Calcd. for $C_{14}H_{24}N_2$: C, 76.36; H, 10.98; N, 12.71. Found: C, 76.4; H, 11.0; N, 12.7.

Reaction of Glyoxal with Cyclohexylamine.—Twelve grams of a 33% aqueous solution of glyoxal was added to a precooled (0°) solution of 20 g. of cyclohexylamine in 200 ml. of ethanol. After standing overnight, the amber solution, containing crystalline material, was cooled to −20° and filtered to yield 10 g. of product. An additional 1.9 g. was obtained from the mother liquor (77% yield). Recrystallization from methanol yielded the pure colorless compound identical with the product obtained with glycolaldehyde. Reaction of glyoxal with *n*-butylamine or isopropylamine yielded only dark oils from which no pure product could be isolated by crystallization or distillation.

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(5) Low melting crystalline dimer was obtained by inoculation of a commercial sample of liquid monomeric acetoin with a granule of zinc according to the procedure of W. Dirscherl and E. Braun, *Ber.*, **63**, 417 (1930). Similar results were obtained when the higher melting dimeric modification was used.

(6) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., Second Ed., 1940, p. 48.

Dichlorofumaric Acid

BY NELSON R. ELDRED AND DONALD M. YOUNG

RECEIVED FEBRUARY 21, 1953

The preparation and properties of dichlorofumaric acid have apparently never been reported. (Reaction of chlorine with acetylenedicarboxylic acid or its sodium salt has been reported to result in splitting of the acid with formation of hydrogen chloride, carbon dioxide and unidentified products.[1]) Since no clear-cut results were obtained by the authors in attempts to prepare dichlorofumaric acid or its ester by isomerization of dimethyl dichloromaleate (readily obtained from dichloromaleic anhydride) with mineral acids or amines, a less direct method of synthesis was used.

Chlorination of succinonitrile to yield a mixture of dichloromaleonitrile and dichlorofumaronitrile,[2] followed by separation of the isomers and acid hydrolysis of the dichlorofumaronitrile, gave the desired dichlorofumaric acid.

The structures of dichlorofumaronitrile, dichlorofumaric acid, dichloromaleic anhydride, and both related dimethyl esters were confirmed by their infrared spectra. The melting point of dichlorofumaric acid (180–182°) is much higher than that of dichloromaleic acid (118–120°) or of dichloromaleic anhydride which is also reported to melt at 118–119°.[3]

Experimental

Dichlorofumaronitrile.—Succinonitrile (145 g., 1.81 moles) was heated at 130–140° under illumination of a sun lamp, and chlorine was introduced until, after 18 hours, absorption stopped. The product was flash distilled and then fractionated using a 30-plate column. The first 30% of the distillate (b.p. 159° at 745 mm.) was a white solid which, after recrystallization from petroleum ether, weighed 53 g. (20% yield) and melted at 54–55°. (Its infrared absorption spectrum showed peaks at 4.5 μ corresponding to the nitrile group and at 11.9 μ corresponding to the *trans* configuration.)

Anal. Calcd. for $C_4Cl_2N_2$: C, 32.68; H, 0.00; N, 19.05. Found: C, 32.80; H, 0.02; N, 19.01.

The higher boiling material, which contained the dichloromaleonitrile, was not purified. Both dichloronitriles are powerful lachrymators and are very volatile.

Dichlorofumaric Acid.—Dichlorofumaronitrile (56 g., 0.38 mole) and 750 g. of 60% sulfuric acid were heated under reflux for 14 hours. The solution was then cooled and filtered. The white, crystalline product was combined with additional material obtained by extracting the filtrate with ether and recrystallized from a mixture of xylene and ace-

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(1) W. Lossen and W. Bergau, *Ann.*, **348**, 341 (1906).

(2) O. W. Cass, U. S. Patent 2,443,494.

(3) P. Karrer and E. Testa, *Helv. Chim. Acta*, **32**, 1025 (1949).

tone. The purified product weighed 59 g. (84% yield) and melted at 180–182°. (The spectrum showed absorption peaks at 5.79 μ (carbonyl group), and 11.62 μ associated with the *trans* configuration.)

Anal. Calcd. for $C_4H_2Cl_2O_4$: C, 25.97; H, 1.09; Cl, 38.33; neut. equiv., 92.5. Found: C, 26.06; H, 1.16; Cl, 38.79; neut. equiv., 91.6.

Dimethyl Dichlorofumarate.—The dimethyl ester of dichlorofumaric acid was prepared by treating the acid with methanol and sulfuric acid. It boiled at 125° at 20 mm., $n^{20}D$ 1.4820. (The spectrum had absorption peaks at 6.13 μ (conjugated double bond), 7.9 μ (C–O–C), 5.75 μ (carbonyl group), and 11.1 and 11.75 μ (*trans* configuration).)

Anal. Calcd. for $C_6H_6O_4Cl_2$: C, 33.83; H, 2.84; Cl, 33.29. Found: C, 34.28; H, 2.93; Cl, 33.31.

Dimethyl Dichloromaleate.—Dichloromaleic anhydride was prepared in 7.5% yield by chlorinating maleic anhydride at 180° using $FeCl_3$–$CaCl_2$ catalyst.[4] The yield can be increased by further chlorination of the recovered intermediate chloromaleic anhydride. The dichloromaleic anhydride, after recrystallization from isopropyl ether and from carbon tetrachloride, was treated with methanolic hydrogen chloride. The dimethyl dichloromaleate obtained boiled at 121° at 20 mm., $n^{20}D$ 1.4830, d^{20}_4 1.3993, d^{25}_4 1.3943. (The spectrum of this ester, like that of the dimethyl dichlorofumarate, showed absorption peaks at 6.13, 7.9 and 5.75 μ. The bands at 11.1 and 11.75 μ were replaced, however, by a strong band at 14.6 μ, associated with the *cis* configuration. Both esters, dichlorofumaronitrile, and dichloromaleic anhydride (but not dichlorofumaric acid) had an unassigned absorption peak varying between 9.8–9.9 μ.)

Anal. Calcd. for $C_6H_6O_4Cl_2$: C, 33.83; H, 2.84; Cl, 33.29. Found: C, 33.94; H, 2.88; Cl, 33.42.

Acknowledgments.—The authors wish to thank Mr. Harry Vineyard for technical assistance, Mr. C. M. Lovell for determination and interpretation of the infrared spectra, and Mr. Quentin Quick and his staff for the microanalyses.

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[4] C. R. Milone, U. S. Patent 2,391,261; F. Johnston and L. W. Newton, private communication.

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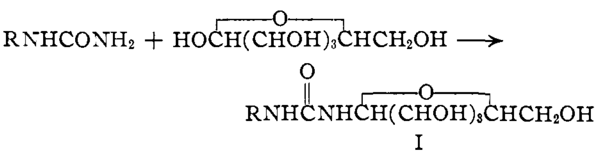
Long-Chain Alkylurea N-Glycosides[1]

BY JOHN G. ERICKSON AND JOAN S. KEPS

RECEIVED APRIL 22, 1953

Schoorl[2] found that aldose sugars react with urea, methylurea, dimethylurea, phenylurea, benzylurea, thiourea, biuret and urethan. Dilute aqueous sulfuric acid was used to catalyze the reaction. Helferich and Kosche[3] did closely similar work. No one seems to have used any alkylureas higher than methylurea.

We have found that the long-chain alkylureas react with aldohexoses in warm dilute alcoholic hydrochloric acid. The products presumably have structure I. The reactions fail in the absence of acid.



$$\mathrm{RNHCONH_2 + HO\overbrace{CH(CHOH)_3C}^{O}HCH_2OH \longrightarrow RNH\overset{\overset{O}{\|}}{C}NH\overbrace{CH(CHOH)_3C}^{O}HCH_2OH}$$

I

Ketohexoses do not react, even in the presence of acid. Neither the alkylureas nor the sugars used are very soluble in alcohol and rather long reaction times are therefore necessary.

Experimental

Dodecylurea N-Galactoside.—A mixture of dodecylurea (22.8 g., 0.10 mole), galactose (19.8 g., 0.11 mole), concd. hydrochloric acid (2.5 g.), and 95% ethanol (200 ml.) was stirred and heated at 50° for 100 hours, then cooled and filtered. Washing with water and hot benzene gave 15.6 g. (40%) of white solid, m.p. 165–188° (dec.).

Anal. Calcd. for $C_{19}H_{38}N_2O_6$: C, 58.44; H, 9.81; N, 7.18. Found: C, 58.31; H, 9.64; N, 7.05.

Octadecylurea N-Glucoside.—A mixture of octadecylurea (6.2 g., 0.02 mole), glucose (4.0 g., 0.022 mole), concd. hydrochloric acid (0.5 g.) and 95% ethanol (100 ml.) was stirred and heated at 50° for 147.5 hours, cooled and filtered. Washing with hot benzene left 1.5 g. (27%), m.p. 175–188° (dec.); m.p., after further washing with water and hot benzene, 181–189° (dec.).

Anal. Calcd. for $C_{25}H_{50}N_2O_6$: C, 63.26; H, 10.62; N, 5.90. Found: C, 63.20; H, 10.42; N, 6.16.

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[1] Paper No. 147, Journal Series, General Mills, Inc., Research Dept.

[2] M. N. Schoorl, *Rec. trav. chim.*, **22**, 31 (1903).

[3] S. B. Helferich and W. Kosche, *Ber.*, **59**, 69 (1926).

A Note on the Heat of Vaporization of Chlorotrifluoroethylene (C_2F_3Cl)[1]

BY GEORGE T. FURUKAWA, ROBERT E. MCCOSKEY AND MARTIN L. REILLY

RECEIVED MARCH 4, 1953

Oliver, *et al.*,[2] recently reported the entropy of chlorotrifluoroethylene in the ideal gaseous state at 244.80°K. (normal boiling point) and 1 atm. as 73.18 cal. deg.$^{-1}$ mole^{-1} from the results of their low temperature calorimetric measurements. These workers computed the entropy of vaporization from their vapor pressure data and the Clapeyron equation. In many calculations of this sort large uncertainties arise on account of the inaccuracies in the density data and the derivative of the vapor pressure. In connection with the program at the National Bureau of Standards involving the spectral assignments for a series of compounds related to chlorotrifluoroethylene, it was felt desirable to determine the heat of vaporization of chlorotrifluoroethylene directly to eliminate any uncertainty that may exist in this quantity. As this molecule is considered to be a "key" member of the series, an accurate value for the entropy was especially desirable to verify the spectral assignment.[3] This note deals with the measurement of the heat of vaporization of chlorotrifluoroethylene.

Experimental

Apparatus.—The vaporization experiments were made in an adiabatic calorimeter similar in design to that described by Osborne and Ginnings[4a] and by Aston, *et al.*,[4b] in which a throttle valve is contained within the space enclosed by the adiabatic shield. Briefly, as electrical energy was sup-

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[1] This investigation was conducted under research sponsored by the Ordnance Corps, Department of the Army.

[2] G. D. Oliver, J. W. Grisard and C. W. Cunningham, THIS JOURNAL, **73**, 5719 (1951).

[3] D. E. Mann, N. Acquista and E. K. Plyler, *J. Chem. Phys.*, submitted for publication.

[4] (a) N. S. Osborne and D. C. Ginnings, *J. Research Natl. Bur. Standards*, **39**, 453 (1947); (b) J. G. Aston, H. L. Fink, G. J. Janz and K. E. Russell, THIS JOURNAL, **73**, 1939 (1951).

plied to evaporate the liquid, the throttle valve was controlled to remove the vapor isothermally. A nickel resistance thermometer, wound on the tube between the calorimeter and the valve, served to sense the temperature of the vapor as it was removed. The shield temperature was controlled manually.

The International Temperature Scale[5] was used. The temperature in degrees Kelvin was obtained from the relation °K. = 273.16° + °C.

Material.—The highly purified chlorotrifluoroethylene sample, inhibited with terpene-B hydrocarbon, was received from E. I. du Pont de Nemours and Company. The material was degassed by slow freezing and pumping, and about 90% was distilled into the calorimeter. Most of the inhibitor remained behind. The liquid-soluble solid-insoluble impurities in the sample transferred into the calorimeter were found from the equilibrium melting curve[6] to be 0.08 mole per cent.

Results.—The heat of vaporization measurements were made at the normal boiling point, 244.80°K., reported by Oliver, *et al.*[2] The experimentally observed quantity, γ, the energy input per unit mass of sample collected,[7] is related to the heat of vaporization l by the expression

$$l = \gamma - \beta$$

where

$$\beta = Tv(\mathrm{d}p/\mathrm{d}T)$$

In the quantity β, v is the specific volume of the liquid, T the absolute temperature and p the vapor pressure. The results of the measurements and the subsequent computations are summarized in Table I.

TABLE I

HEAT OF VAPORIZATION OF CHLOROTRIFLUOROETHYLENE AT 244.80°K.

C_2F_3Cl mol. wt. = 116.477; 1 cal. = 4.1840 abs. j.

γ, abs. j. g.$^{-1}$	β, abs. j. g.$^{-1}$	l, abs. j. g.$^{-1}$	L, abs.j.mole^{-1}
180.16	0.74	179.42	20898
179.89	.74	179.15	20867
179.96	.74	179.22	20875
179.97	.74	179.23	20876
		Mean	20879
		Standard deviation of the mean	±6

The quantity β was evaluated using the density of chlorotrifluoroethylene as given by E. I. du Pont de Nemours and Company[8] and the vapor pressure reported by Oliver, *et al.*[2] In terms of the thermochemical calorie (1 cal. = 4.1840 abs. j.), the heat of vaporization becomes 4990 cal. mole^{-1}. Considering the precision (Table I) and the various possible sources of error, the total uncertainty in the value given is believed to be ±4 cal. mole^{-1}. The value (4965 cal. mole^{-1}) calculated by Oliver, *et al.*,[2] is in fairly good agreement with the experimental value obtained.

Combining this experimental value for the heat of vaporization with the low temperature heat capacity work of Oliver, *et al.*,[2] the entropy of chlorotrifluoroethylene in the ideal gaseous state at 244.80°K. and 1 atm. becomes 73.28 ± 0.10 cal. deg.$^{-1}$ mole^{-1}. The uncertainty of the entropy was obtained by statistically combining the uncertainty (±0.10 cal. deg.$^{-1}$ mole^{-1}) assigned by Oliver, *et al.*,[2] to their value of entropy (52.74 cal. deg.$^{-1}$ mole^{-1}) for the liquid chlorotrifluoroethylene at 244.80°K., and the uncertainty (±0.02 cal. deg.$^{-1}$ mole^{-1}) assigned for the entropy of vaporization (20.38 cal. deg.$^{-1}$ mole^{-1}) in this work. The correction (+0.16 cal. deg.$^{-1}$ mole^{-1}) for gas imperfection was computed on assumption that the gas can be represented by a Berthelot equation of state, and the uncertainty of this correction is considered to be negligible.

Acknowledgment.—The authors are indebted to R. C. Downing and D. E. Kvalnes of E. I. du Pont de Nemours and Company for the highly purified sample.

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[5] H. F. Stimson, *J. Research Natl. Bur. Standards*, **42**, 209 (1949).

[6] G. T. Furukawa, D. C. Ginnings, R. E. McCoskey and R. A. Nelson, *ibid.*, **46**, 195 (1951).

[7] N. S. Osborne, *ibid.*, **4**, 609 (1930).

[8] "Kinetic" Technical Bulletin B-6, E. I. du Pont de Nemours and Company, 1952.

The Conversion of Codeinone to Codeine

BY MARSHALL GATES

RECEIVED APRIL 3, 1953

No satisfactory method for the potentially important reduction of codeinone to codeine has yet been described,[1] primarily because of the ease with which the oxide ring is opened by the usual methods, both chemical and catalytic. We have found that this reduction can be effected easily and nearly quantitatively by means of sodium borohydride.[2]

We are indebted to Merck and Co., Inc., for generous gifts of thebaine and codeine.

Experimental[3]

Codeine from Codeinone.—A solution of 194 mg. of codeinone, m.p. 185–187°, in 10 cc. of methanol was treated with 0.5 g. of sodium borohydride which had just been suspended in 12 cc. of methanol. The mixture was allowed to stand for 1.5 hours, concentrated to about half the original volume and diluted with 10 cc. of 10% sodium hydroxide. The clear colorless solution was heated momentarily to boiling, diluted with water and extracted four times with chloroform. The washed, dried and filtered chloroform extract on concentration left 196 mg. of codeine as a colorless glass which crystallized readily on scratching, m.p. 153–157°. Recrystallization from quite dilute methanol gave 173 mg. (83.4%) of pure codeine hydrate, m.p. 157–158.5°, $[\alpha]^{26}\mathrm{D}$ −136° (*c* 2.80, alc.), whose mixed m.p. with authentic codeine hydrate was undepressed.

Its **hydrobromide**, colorless needles from water, melted at 151–160° with effervescence, resolidified and remelted with extensive decomposition at 273–278°,[4] as did both the hydrobromide of authentic codeine and a mixture of the two.

Anal. Calcd. for $C_{18}H_{21}NO_3 \cdot HBr \cdot 2H_2O$: C, 51.93; H,

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[1] C. Schöpf and H. Hirsch, *Ann.*, **489**, 242 (1931), have reported this transformation in poor yield by the action of stannous chloride and hydrochloric acid. For further comments on this reduction see S. P. Findlay and L. F. Small, THIS JOURNAL, **72**, 3247 (1950).

[2] The stereospecificity of this reduction seems worthy of comment. In the two cases described in the experimental section, this stereospecificity was complete. However, with both *cis*- and *trans*-dihydrothebainone (oxide ring open) both sodium borohydride and lithium aluminum hydride give mixtures of the epimeric C_6 alcohols.

[3] All melting points are corrected.

[4] Dott, *Pharm. J. Trans.*, [3] **14**, 917, 973 (1884), has reported the m.p. of codeine hydrobromide dihydrate as 190–192°. It has been prepared by us a number of times from several different samples of codeine and has always exhibited the behavior described above.

6.30; Br, 19.20; H_2O, 8.65. Found: C, 52.07; H, 6.24; Br, 18.82, 19.64; H_2O, 8.83.

1-Bromocodeine from 1-Bromocodeinone.—Under similar conditions, 101 mg. of 1-bromocodeinone[5] yielded 101 mg. of crude 1-bromocodeine, m.p. 158–160.5°, which on crystallization from ethyl acetate gave 72 mg. (71%) of pure 1-bromocodeine, m.p. 161–163°, whose mixed m.p. with authentic 1-bromocodeine[6] was undepressed.

Its methiodide melted at 262.5–264°[7] with decomposition, and did not depress the melting point of the methiodide obtained from authentic 1-bromocodeine.

Anal. Calcd. for $C_{19}H_{23}NO_3BrI$: C, 43.86; H, 4.46. Found: C, 43.89; H, 4.43.

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[5] M. Gates and G. Tschudi, THIS JOURNAL, **74**, 1109 (1952).

[6] E. Speyer and H. Rosenfeld, *Ber.*, **58**, 1110 (1925).

[7] E. Vongerichten, *Ann.*, **297**, 204 (1897), has reported the melting point of this methiodide to be 242–244°.

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4-Alkyldiphenylketimine Hydrochlorides and Related Ketones

BY I. R. KAPLAN, H. N. PARTON AND J. VAUGHAN

RECEIVED MAY 19, 1953

In connection with another investigation which has since been discontinued, the ultraviolet absorption spectra of a series of 4-alkyldiphenylketimine hydrochlorides and the related ketones were determined. Of the compounds examined, four appear to be new. Ketimines were prepared by the method adopted by Pickard and Vaughan.[1] The hydrochlorides were precipitated from ethereal solution with dry hydrogen chloride, repeatedly recrystallized from chloroform solution and washed well with ether. Of the alkyl-substituted benzophenones, the methyl compound was prepared by the Friedel–Crafts reaction and the others were obtained by hydrolysis of the ketime hydrochlorides with 6 *N* hydrochloric acid. Spectral data were obtained with a Hilger "Uvispek" spectrophotometer and the range covered was 2100–3200 Å. Approximately 1 × 10^{-4} *M* solutions in methanol were used for all compounds. Absorption curves of the alkylated compounds have the simple shape shown by the parent bodies (*e.g.*, see Culbertson[2]).

TABLE I

	Ketone			Ketimine hydrochloride		
4-Substituent	M.p. or b.p., °C.	$\lambda_{max.}$ (Å.)	$\epsilon_{max.} \times 10^{-4}$	M.p.,[a] °C.	$\lambda_{max.}$ (Å.)	$\epsilon_{max.} \times 10^{-4}$
H	M. 48	2520	1.750	310	2755	1.665
Methyl	M. 58	2590	1.745	244	2855	1.570
Ethyl	B. 318–320	2535	1.555	264[b]	2820	1.660
Isopropyl	B. 338–340 (774 mm.)	2570	1.660	260[c]	2875	1.715
t-Butyl[d]	B. 198 (13 mm.)	2585	1.755	280-282[e]	2875	1.680

[a] Visible sublimation occurred to a greater or less extent with each salt, beginning 20–30° below recorded m.p. [b] *Anal.* Calcd. for $C_{15}H_{16}NCl$: N, 5.71; Cl, 14.47. Found: N, 5.58; Cl, 14.30. [c] Calcd. for $C_{16}H_{18}NCl$: N, 5.40; Cl, 13.66. Found: N, 5.44; Cl, 13.55. [d] Calcd. for $C_{17}H_{18}O$: C, 85.70; H, 7.56. Found: C, 85.86; H, 7.86; n^{19} 1.5762. [e] Calcd. for $C_{17}H_{20}NCl$: N, 5.13; Cl, 12.96. Found: N, 5.15; Cl, 12.88.

Analysis of the 4-*t*-butylbenzophenone was carried out by Dr. A. D. Campbell of Otago University.

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[1] P. L. Pickard and D. J. Vaughan, THIS JOURNAL, **72**, 876 (1950).

[2] J. B. Culbertson, *ibid.*, **73**, 4818 (1951).

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Pipecolic Acid in *Phaseolus vulgaris:* Evidence on its Derivation from Lysine

BY N. GROBBELAAR[1] AND F. C. STEWARD

RECEIVED JULY 7, 1953

After the discovery of pipecolic acid as a prominent constituent of the green bean (*Phaseolus vulgaris*) and of other plants, the question of its origin and metabolic relationships arises. Advantage has been taken of the availability of lysine containing radioactive carbon to test the possibility that it may arise from, or be interconvertible with, lysine by a process of ring closure and loss of ammonia. The lysine used in this experiment was prepared synthetically by Dr. R. W. Helmkamp of the University of Rochester and was made available to us through the courtesy of Dr. Leon Miller, also of the University of Rochester.

The lysine was labelled in the ε-position and was made available to us dissolved in dilute salt solution. The specific activity of the lysine was 0.85 microcurie per milligram and 10 mg. of L-lysine was dissolved in 0.65 ml. of 0.9% sodium chloride solution.

The plants selected for the experiments were grown in pots and had fruits approximately 10 cm. in length. The morphology of the specimen selected for the first experiment is shown in Fig. 1. It will be noted that there were two developing fruits in the axil of the same leaf which was removed (X in Fig. 1). The main branch bearing the fruits was also decapitated (Y in Fig. 1). The method was to inject with a hypodermic needle, 0.25 ml. of the autoclaved lysine solution into the cavities surrounding the two lower ovules of fruit A (Fig. 1).

After the elapse of an appropriate period (55 hours) the tissue of the injected fruit was dissected and sampled and also the tissue of the adjacent fruit in the same leaf axil (B in Fig. 1).

In sampling the material for analysis, the ovules and carpel walls were treated separately and all the rest of the tissue of the plant examined as a whole. The weights of the organs analyzed are given in Table I.

TABLE I

FRESH WEIGHTS OF TISSUES EXTRACTED

Material	Weight, g.
First Experiment	
Injected fruit	2.468
carpel wall	2.229
ovules	0.239
Uninjected fruit	4.501
carpel wall	3.530
ovules	0.971
Rest of shoot	15.521
Second Experiment	
Stem tissue (F–F)	0.446
Fruit	8.098
carpel wall	5.395
ovules	2.703
Rest of shoot	37.600

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[1] Predoctoral Rockefeller Foundation Fellow at Cornell University.

At the time of harvesting the material all of the injected solution had been absorbed from the carpel cavities. It was found that the ovules of the two fruits had sizes as indicated in Fig. 1.

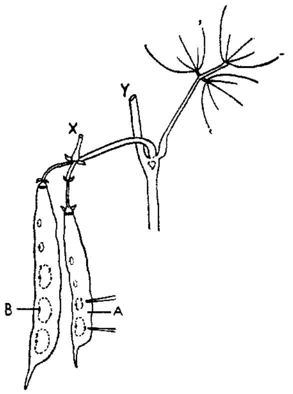

Fig. 1.

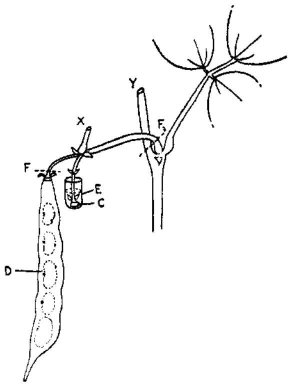

Fig. 2.

The sampled plant material was treated as follows: (1) The carpel walls and ovules were treated with 5 times their weight of 70% ethanol in a Potter glass homogenizer. (2) The rest of the shoot was also treated with 5 times its weight of 70% ethanol in a Waring Blendor. The material so treated was centrifuged to separate the ethanol extract and the insoluble material re-extracted with a similar volume of alcohol. The combined alcoholic extracts were evaporated to dryness at room temperature in a stream of air and used for two-directional paper chromatographic analysis. The insoluble residues were hydrolyzed with 6 *N* HCl for 18 hours at 120° in sealed ampules, evaporated to dryness, re-dissolved in water and this solution also used for chromatographic examination.

The paper chromatographic procedure adopted was as follows: Recognizing that the amounts in question might be small, the papers used were restricted to 5 inches by 5 inches of Whatman #1. Chromatographic cabinets (American Museum jars) of the dimensions 4.5 × 6 × 6 inches were used. These were already fitted with heavy ground glass covers. The papers were suspended vertically and the solvent allowed to ascend. The solvents were firstly aqueous phenol and secondly collidine–lutidine (3:1) saturated with water. The approximate distance of travel of the solvent was about 5 inches and these procedures required approximately 2.5 hours in each direction.

Because of the danger of losing the labelled carbon as carbon dioxide during ninhydrin treatment, in case it had been converted to a carboxyl group in the plant, radioautographs of the chromatograms were first prepared. The procedure here was as follows: Before exposing the film to the chromatogram, the time period necessary was estimated by scanning the chromatogram with a Geiger–Müller counter and measuring the activity of the radioactive spots. A piece of X-ray No-Screen Film, 5 × 5 inches, was then placed immediately behind the chromatogram. The chromatogram and the film were held in place by two sheets of stout cardboard and rubber bands. A needle was pierced through the cardboard, film and chromatogram at two places in order to permit the chromatogram and developed radioautograph to be exactly superimposed. Exposure times of the order of one week were found adequate to produce strong spots on the radioautographs.

The chromatograms were then sprayed with ninhydrin and the color developed in air at 60° for about ten minutes. Clear separation of the principal free amino acids in the plant material was obtained as shown in Fig. 3.

On these chromatograms lysine and pipecolic acid could be readily recognized when present, the latter by its distinctive color, position and crimson fluorescence in ultraviolet light.

The first results observed were as follows: The injected lysine was absorbed by the carpel wall of the injected fruit (A in Fig. 1). The activity passed however via the vascular system predominantly to the ovules contained in the carpel B (Fig. 1).

TABLE II

TOTAL RADIOACTIVITY OF PLANT FRACTIONS

Material	Radioactivity in counts/second Alcohol soluble	Alcohol insoluble
First Experiment		
Injected fruit	947[a]	452[a]
carpel wall	806	339
ovules	141	113
Uninjected fruit	240[a]	167[a]
carpel wall	33	0
ovules	207	167
Rest of shoot	30	. . .
Second Experiment		
Stem tissue (F–F)	2008	477
Fruit	1525[a]	1063[a]
carpel wall	271	392
ovules	1254	671
Rest of shoot	0	. . .

[a] Summation of radioactivity of carpel wall and ovule fractions.

As shown in Table II the activity of these ovules was much greater than the activity of the ovules of the injected fruit. The carpel wall of fruit B had a negligible amount of activity whereas both the alcohol-soluble and alcohol-insoluble extracts of the carpel wall of fruit A showed strong activity. The activity present in the ovules of the fruit B was found to be present in both the alcohol-soluble fraction and also in the alcohol-insoluble fraction.

Examination of the paper chromatograms and the radioautographs immediately showed the following results. The carpel wall that had initially absorbed the lysine (fruit A) contained a rather small amount of pipecolic acid in the alcohol-soluble extract. This, however, was labelled with C^{14} in quite high specific activity. Some (lysine and a spot in the position of glutamic acid) of the remaining amino acids of this same extract also contained radioactivity but in very much smaller specific activity. In the alcohol-soluble extract of the seeds of fruit A, pipecolic acid was weakly labelled. The remaining radioactivity of this extract was contained in material (probably alcohol-soluble proteins) that remained at the origin of the chromatogram.

However, in the alcohol-soluble extract of the ovules from the adjacent fruit B, which had received their lysine via the vascular system, the activity occurred *exclusively* in the pipecolic acid. As mentioned above, a negligible amount of radioactivity was present in the carpel wall of this fruit. The exact superposition of the ninhydrin-reactive spot of pipecolic acid and the spot corresponding to radioactivity for these samples is indicated in Fig. 3.

These results clearly demonstrate the transformation of lysine to pipecolic acid in the developing carpel wall and ovules of the bean. Since the entry of lysine into the developing fruit is at a distance from the point of application and since the material inevitably enters the fruit via the vascular system, it seems quite clear that pipecolic acid represents one of the first conversion products of the lysine.

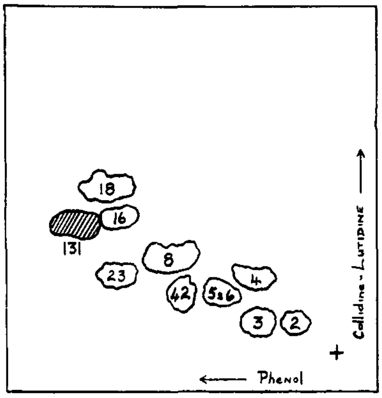

Fig. 3.—Two-directional chromatogram of the alcohol-soluble extract of the ovules of fruit B (Fig. 1). Spots are labelled: aspartic acid, 2; glutamic acid, 3; serine, 4; asparagine, 5; glycine, 6; alanine, 8; valine, 16; leucine, 18; γ-aminobutyric acid, 23; peptide, 42; pipecolic acid, 131. The shaded spots were radioactive.

A further experiment was performed with the following modifications. Recognizing that the most useful information had been obtained from the developing fruit and ovules which had received pipecolic acid via the vascular system, the following procedure was adopted.

A plant very similar to the one used in the previous experiment was again selected and trimmed as before. It also bore two fruits in the same leaf axil. One of the fruits (C in Fig. 2) was severed and the pedicel immersed in 0.4 ml. of aqueous solution containing the lysine (E in Fig. 2). The plant was allowed to absorb this solution directly. The total amount of this solution was absorbed over a period of approximately 72 hours. After 96 hours the plant was sampled in the manner already described and similar extracts and determinations were made. In this case, the piece of stem tissue indicated between letters F and F on Fig. 2 was separately extracted.

The sizes of the seeds of fruit D were found to be as indicated in Fig. 2. The weights of the tissues extracted are given in Table I while the total activities of the final extracts and hydrolysates are given in Table II.

In principle the results were the same as in the earlier experiment. The alcohol-soluble fraction of the ovules of fruit D in Fig. 2 was labelled exclusively and strongly in pipecolic acid. The alcohol-soluble fraction of the carpel wall of fruit D contained very little radioactivity but again it all occurred in the small amount of pipecolic acid present.

In the absorbing peduncle C (Fig. 2) and the adjacent stem tissue (F–F in Fig. 2) the alcohol-soluble fraction was strongly radioactive and all its radioactivity occurred in two compounds. The one compound appeared on the chromatograms in the position occupied by glutamic acid while the other superimposed with a purple ninhydrin spot below alanine (X in Fig. 4). These tissues contained no detectable pipecolic acid.

The hydrolysates of the alcohol-insoluble fractions of the ovules, carpel wall and tissue F–F all yielded the same results. All the radioactivity was always found in two spots on the radioautographs. The one spot superimposed with a purple spot in the position normally occupied by glutamic acid. The second spot superimposed with the purple spot (Y in Fig. 5) on the chromatogram. The position of this latter spot is very close to that of ε-aminohexanoic acid[2] or δ-aminovaleric acid.[2,3] The behavior of this compound on $CuCO_3$-treated paper also seems to indicate that it is not an α-amino acid.[4]

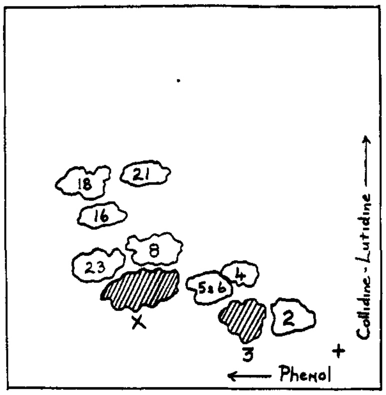

Fig. 4.—Two-directional chromatogram of the alcohol-soluble extract of stem tissue F–F (Fig. 2). Spots are labelled as in Fig. 3. Additional spots are: tyrosine, 21 unidentified spot, X. The shaded spots were radioactive.

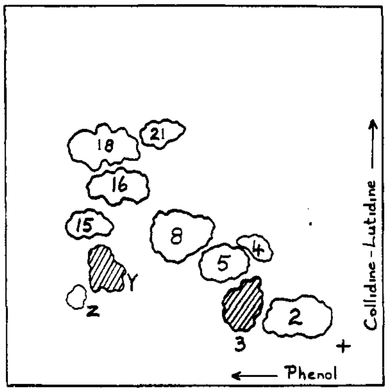

Fig. 5.—Two-directional chromatogram of the acid hydrolysate of the alcohol-insoluble fraction of the stem tissue F–F (Fig. 2). Spots are labelled as in Figs. 3 and 4. Additional spots are: proline, 15; unidentified spots, Y and Z. The shaded spots were radioactive.

These experiments establish the transformation of lysine to pipecolic acid in the developing green bean. Further work will be necessary to determine completely the intermediate steps. The radioactive compounds X, Y and "glutamic acid" might act as intermediates in this transformation. It would, however, seem more probable that they act as intermediates during the incorporation of the carbon of lysine into the markedly lysine-deficient protein moiety. Inasmuch as radioactivity also appears in the alcohol-insoluble fractions, use can be made of this technique to investigate protein synthesis.

Acknowledgment is made of the fact that this work forms part of a program of investigation directed by F. C. S., supported by the Grasselli Grant to the New York State College of Agriculture at Cornell University.

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(2) C. E. Dent, *Biochem. J.*, **43**, 169 (1948).

(3) R. M. Zacharius, Ph.D. Thesis, University of Rochester, 1953.

(4) H. R. Crumpler and C. E. Dent, *Nature*, **164**, 441 (1949).

Oxidation of Aryl Trityl Sulfides with Hydrogen Peroxide

By D. C. Gregg, C. A. Blood, Jr., and D. E. Weiman

Received April 28, 1953

Recent attempts to characterize aryl trityl sulfides by preparation of sulfoxides and sulfones by means of oxidations in acidic media have been unsuccessful.[1,2] Apparently the sulfides were cleaved in the acidic media because partial oxidations produced significant amounts of the diaryl disulfides and triphenylcarbinol. Complete oxidations produced the arylsulfonic acids, or derivatives of these, and triphenylcarbinol.

Knoll[3] observed no reaction during an unsuccessful attempt to prepare phenyl trityl sulfone by oxidation of phenyl trityl sulfide with hydrogen peroxide in glacial acetic acid at room temperature for 12 hours.

During the present work, phenyl trityl sulfide (I) in glacial acetic acid was kept at 21–22° for 12 hours with the same mole ratio of hydrogen peroxide as was used by Knoll. There was isolated a 44% yield of benzophenone (II), and small amounts of phenol (III), diphenyl disulfide and trityl peroxide. The rate of oxidation of I was markedly increased by the addition of an equimolar quantity of sulfuric acid, and after ten minutes at 26–28° a 65% yield of II was obtained.

o-Tolyl trityl sulfide in acetone was oxidized very slightly, if at all, by an excess of hydrogen peroxide during six hours at room temperature. In the presence of mercuric chloride and much less peroxide, a 41% yield of II was obtained in ten minutes.

By using four moles of hydrogen peroxide per mole of I in acetic acid at an initial temperature of 80°, oxidation was complete within ten minutes. Good yields of II, III and benzenesulfonic acid (as its sodium salt) were obtained. At an initial temperature of 60° and the same reaction period, an 81% yield of II was obtained, and at 40°, not over 50% of I had reacted.

The experimental evidence appeared to indicate that the main reactions during the oxidation of an aryl trityl sulfide by hydrogen peroxide in acidic media were, (a) the oxidation of either free or incipient aryl thiol through the disulfide stage to arylsulfonic acid, and (b) the oxidation of either free or incipient trityl cation to II and III.

Acknowledgment.—This work was supported by a Frederick Gardner Cottrell grant from the Research Corporation, New York, N. Y.

Experimental[4]

Preparation of Aryl Trityl Sulfides.—The sulfides were prepared by using the procedures previously reported.[5]

Oxidation of I at Room Temperature.—To 200 ml. of glacial acetic acid were added 4.2 g. (0.012 mole) of I and 0.024 mole of hydrogen peroxide, as Superoxol. The reaction mixture was kept at 21–22° for 12 hours and then poured into water. This mixture was extracted with ether, and the ethereal solution then extracted with 20% sodium hydroxide. A small amount of III was obtained from the alkaline extract. From the ethereal solution was obtained 0.15 g. (5%) of trityl peroxide, a 44% yield of II (1.9 g. of its 2,4-dinitrophenylhydrazone), and 0.1 g. (8%) of diphenyl disulfide.

Oxidation of I in Presence of Sulfuric Acid.—To 200 ml. of glacial acetic acid were added 9.6 g. (0.027 mole) of I and 1.52 ml. (0.027 mole) of concentrated sulfuric acid. To this solution was added 0.054 mole of hydrogen peroxide. By cooling, the solution was kept at 26–28° for ten minutes. The yields were: II (65%, 6.4 g. of the 2,4-dinitrophenylhydrazone); III, 0.9 g. (35%); 0.3 g. (4.5%) of trityl peroxide; and 0.6 g. (30%) of diphenyl disulfide.

Oxidation of *o*-Tolyl Trityl Sulfide in Presence of Mercuric Chloride.—To 100 ml. of acetone at 28° were added 5.15 g. (0.014 mole) of *o*-tolyl trityl sulfide and 0.028 mole of hydrogen peroxide. A solution containing 4.5 g. (0.016 mole) of mercuric chloride in 35 ml. of acetone was added dropwise for 12 minutes. After two minutes the mixture was cooled, and 0.8 g. of *o*-tolylmercaptomercuric chloride was obtained by filtration. After evaporation of the filtrate, the residue was found to contain 0.3 g. of the mercaptomercuric chloride, 14% of III, 41% of II and 10% of *o*-tolyl disulfide.

Oxidation of Sulfides at 80°.—To 120 ml. of glacial acetic acid was added 9.6 g. (0.027 mole) of I. The solution was heated to 80°, and 0.108 mole of hydrogen peroxide added dropwise within three minutes. The reaction was strongly exothermic, and after a total of ten minutes the solution was poured into 300 ml. of cold water. The aqueous suspension was extracted with ether, and 1.3 g. (50%) of III was obtained from the ethereal solution by alkaline extraction. From the ethereal solution was obtained 4.5 g. (91%) of II. The aqueous acetic acid was evaporated to dryness, and after addition of sodium hydroxide 3.3 g. (62%) of sodium benzenesulfonate was obtained. By using identical conditions, 10 g. of *p*-tolyl trityl sulfide was oxidized. The yields were: II, 4.5 g. (91%); III, 1.7 g. (68%); sodium *p*-toluenesulfonate, 2.6 g. (45%). A similar oxidation of *o*-tolyl trityl sulfide produced II (79%) and III (45%). An oxidation of *m*-tolyl trityl sulfide produced II (80%) and III (50%).

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[1] D. C. Gregg and C. A. Blood, Jr., *J. Org. Chem.*, **16**, 1255 (1951).

[2] D. C. Gregg, K. Hazleton and T. F. McKeon, Jr., *ibid.*, **18**, 36 (1953).

[3] R. Knoll, *J. prakt. Chem.*, **113**, 40 (1926).

[4] The Superoxol was Merck's 30% hydrogen peroxide. The identity of each oxidation product and each derivative was established, where possible, by mixed melting points with an authentic sample. The sodium arylsulfonates were characterized by preparing the corresponding arylsulfonamides and S-benzylthiuronium salts. All yields are based on complete cleavage of the sulfides. Temperatures are uncorrected.

[5] D. C. Gregg, H. A. Iddles and P. W. Stearns, Jr., *J. Org. Chem.*, **16**, 246 (1951).

Existence of Two Solid Forms of 2-Methylfuran

By James B. Hickman

Received April 1, 1953

In the course of continuation of earlier work[1] on the f.p.-composition behavior of the system, 2-methylfuran-methanol, it was found that 2-methylfuran upon cooling gives two distinct halts in the time–temperature curve, presumably corresponding to two different solid modifications. The higher-melting solid (I), f.p. −90.19°, obtained by rapid cooling, is evidently the one concerned in the f.p. data previously reported.[1,2] The lower-melting solid (II), f.p. −101.92°, can be obtained by slower cooling, ordinarily resulting in inception of freezing from a less highly supercooled liquid. (The f.p. values stated represent results reproduced three or more times within ±0.01°; however, if the shortness of equilibrium time, and the extent of extrapolation of the equilibrium curve involved are

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[1] J. B. Hickman and J. L. Hall, *Proc. W. Va. Acad. Sci.*, **22**, 72 (1950).

[2] E. I. du Pont de Nemours Corp., "New Products Bulletin," No. 24, May 4, 1948.

considered, ±0.1° should be regarded as the uncertainty of the absolute value of the f.p. data).

Although the time–resistance cooling curve for solid II shows the usual portions representing recovery from supercooling, equilibrium, and cooling of the solid, it has been found impossible to freeze the entire contents of the f.p. tube to solid II, since at a temperature 2–7° below the f.p., a sudden rise in temperature occurs, and the tube is shattered. Since the form of the curve strongly indicates complete solidification to solid II in the immediate vicinity of the temperature-sensitive portion of the resistance thermometer, the temperature rise presumably is occasioned by the freezing to solid I of pockets of liquid contained in portions of the tube not adjacent to the temperature-sensitive element.

If a glass or metal rod cooled in liquid nitrogen is touched to the surface of the liquid from which solid II is separating, solid I at once begins to form, and the temperature rises correspondingly. If only a small amount of solid II has separated when this change is caused to take place, the f.p. tube remains intact. In Fig. 1, the time marked A corresponds to initial separation of solid II, induced by causing the mechanical stirrer to scratch the wall of the f.p. tube, while the time marked B corresponds to touching the surface with the cooled rod.

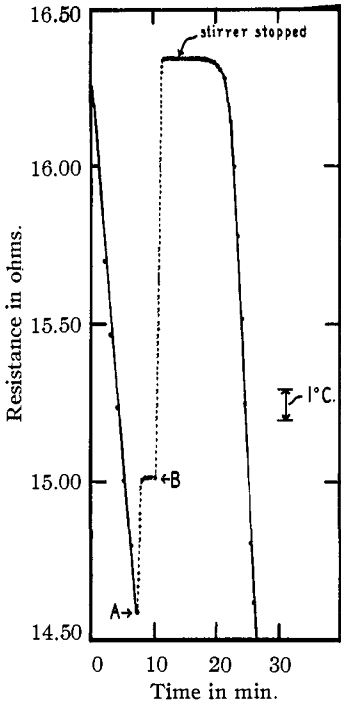

Fig. 1.—Time–resistance cooling curve, 2-methylfuran.

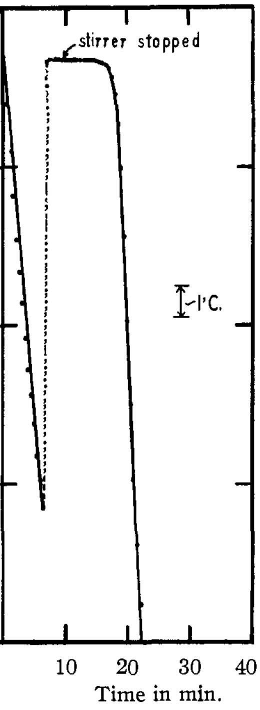

Fig. 2.—Time–resistance cooling curve, solid I.

Figure 2 represents data obtained by measurements on a sample from which no solid II separated, while Fig. 3 represents similar data for a sample allowed to solidify as solid II. Two minutes after the time corresponding to the last point in Fig. 3, the temperature sharply increased, and the f.p. tube was shattered.

In all experiments here reported, liquid nitrogen was used as a coolant.

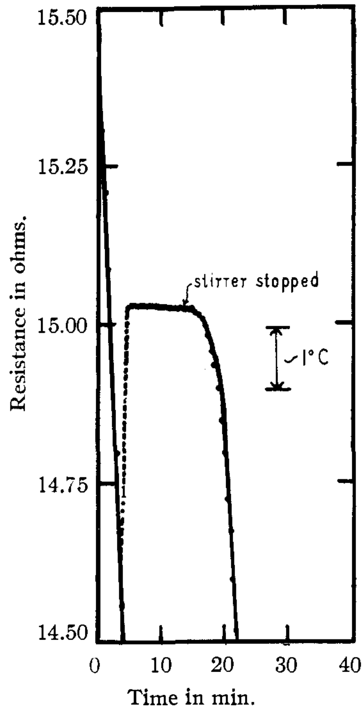

Fig. 3.—Time–resistance cooling curve, solid II.

Large-scale plots of the data of Figs. 2 and 3 were analyzed by the methods of Rossini and co-workers[3–5] to obtain f.p. and estimated purity values. In applying these methods, a much shorter equilibrium time than recommended had to be used, with corresponding decrease in certainty of results.

Purity in excess of 99.5% for the liquid regardless of which solid was separating was estimated, eliminating the possibility that the phenomenon here dealt with is the separation of two different materials from a highly impure solution.

Experimental

2-Methylfuran.—Du Pont Electrochemicals 2-methylfuran was washed with an acidified saturated solution of iron(II) sulfate to remove peroxides, separated, dried over calcium chloride and distilled through a six-plate column. The 2-methylfuran was diluted before distillation with about one third its own volume of heavy mineral oil to reduce the possibility of spontaneous polymerization. A typical 100 ml. sample taken for use distilled in the range 62.7–62.8° (cor.) at a pressure (cor.) of 730.9 mm. Sealed bottles of 2-methylfuran became slightly yellow within a few hours. This was found to have no measurable effect on the f.p. or on the conditions concerned with formation of the two solids; nevertheless, only freshly distilled material was used.

Determination of Cooling Curves.—Time–resistance cooling curves were determined for 20-ml. samples, using conventional f.p. tube, mechanical reciprocating stirring, and liquid nitrogen as a coolant. Temperatures were measured by means of a platinum resistance thermometer calibrated by the U. S. National Bureau of Standards, the resistance values being determined by means of a calibrated Leeds and Northrup type G-2 Mueller Bridge. Curves of resistance *vs.* time were plotted and analyzed. Only the resistance values corresponding to the f.p. were converted to temperature by means of the Callendar equation.

In carrying out a determination, the sample was placed in the f.p. tube, the stirrer started and the temperature

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(3) W. J. Taylor and F. D. Rossini, *J. Research Natl. Bur. Standards*, **32**, 197 (1944).

(4) B. J. Mair, A. R. Glasgow, Jr., and F. D. Rossini, *ibid.*, **26**, 591 (1941).

(5) A. R. Glasgow, Jr., A. J. Streiff and F. D. Rossini, *ibid.*, **35**, 355 (1945).

allowed to fall to −80° with the jacket at atmospheric pressure. At this temperature, evacuation of the jacket space to 0.1 mm. gave slow cooling, with probable formation of solid II, while evacuation to 100 mm. gave faster cooling, usually resulting in separation of solid I without detectable formation of solid II. If the sample was allowed to supercool more than about 15°, the halt corresponding to solid II was very brief, with a spontaneous rise in temperature and separation of solid I after a period of one-half to 3 minutes. Such supercooling could be prevented by momentarily tilting the f.p. tube, causing the stirrer to rub against the side of the tube inducing initial formation of solid II crystals.

From the available evidence, the change involved appears to be monotropic, solid II being the metastable form. The fact that no conclusive evidence for complete solidification of the sample to solid II has been obtained, and that no definite temperature is associated with the inception of change from solid II to solid I seems to indicate that solid II is continuously changing to solid I at a finite rate. It is not to be inferred that the rather sudden increase in temperature 2–7° below the f.p. of solid II necessarily corresponds to conversion of the solid II to solid I, but more probably that liquid remaining unfrozen in the necessarily unstirred sample is in contact with sufficient solid I to freeze directly to this form.

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N-Fluoroacetyl Derivatives of Carcinogenic Amines[1]

BY EUGENE SAWICKI AND F. E. RAY

RECEIVED MAY 4, 1953

In a previous paper[2] trifluoroacetyl derivatives of carcinogenic amines were described. The fluoroacetyl analogs were prepared for a comparative study of their carcinogenic and cancer therapeutic activity. It is probable that in animal metabolism these compounds would be hydrolyzed to the carcinogenic amine and fluoroacetic acid. Fluoroacetic acid and its derivatives are known convulsant poisons.[3] Essentially, fluoroacetic acid is a Krebs cycle poison.[4] It has been postulated[5–7] that activated fluoroacetic acid and oxalacetic acid molecules react to form a fluorocitric acid which blocks the conversion of citric acid to α-ketoglutaric acid in the body. On this basis the N-fluoroacetyl derivatives have been prepared to test their effect on living cells and malignant tumors. Table I lists these new fluoroacetyl derivatives.

TABLE I

Compound	M.p.,[a] °C.	Yield, %	Nitrogen, % Calcd.	Nitrogen, % Found
2-FA[b]-biphenyl	93–94	92	6.11	6.00
4-FA-biphenyl	179–180	95	6.11	6.06
4,4′-diFA-biphenyl	316–318 dec.	85	9.21	9.10
2-FA-naphthalene	106–107	90	7.82	7.60
2-FA-fluorene	168–169	97	5.81	5.99[c]
2,7-DiFA-fluorene	253–255	88	8.86	8.70
4-FA-2′,3-dimethyl-azobenzene	155–157	96	14.7	14.5

[a] All melting points are uncorrected. [b] FA = Fluoroacetylamino. [c] Calcd.: C, 74.69; H, 4.98. Found: C, 74.97; H, 5.11.

Experimental

General Procedure. (**a**).—Nine and seven-tenths g. (0.01 mole) of fluoroacetyl chloride[8] was added dropwise to an ice-cold stirred solution of 0.01 mole of the monoamine in 5 ml. of benzene and 2 ml. of pyridine. The stirred mixture was warmed for 5 minutes and then 20 ml. of water was added. The benzene was evaporated at room temperature under a vacuum and the crude crystals were crystallized from heptane.

(**b**).—Nineteen and four-tenths g. (0.02 mole) of fluoroacetyl chloride was added dropwise to a stirred ice-cold solution of 0.01 mole of the diamine in 20 ml. of pyridine. The mixture was stirred an additional half hour at 0–10° and then poured into 100 ml. of ice-cold 25% sulfuric acid. The precipitate was crystallized from methyl cellosolve.

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[1] The work described in this paper was supported by a grant from the Sloan–Kettering Institute for Cancer Research.

[2] E. Sawicki and F. E. Ray, THIS JOURNAL, **75**, 2519 (1953).

[3] H. McCombie and B. C. Saunders, *Nature*, **158**, 382 (1946).

[4] C. Liebecq and R. Peters, *Biochim. Biophys. Acta*, **3**, 215 (1949).

[5] P. Buffa and R. A. Peters, *J. Physiol.* (*London*), **110**, 488 (1950).

[6] P. Buffa, R. A. Peters and R. W. Wakelin, *Biochem. J.*, **48**, 467 (1951).

[7] C. Martius, *Ann.*, **561**, 227 (1949).

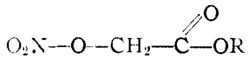
[8] E. Sawicki and F. E. Ray, *J. Org. Chem.*, in press (1953).

The Infrared Spectrum and Structure of Glycolate Nitrate Esters

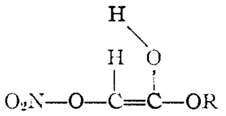
BY W. D. KUMLER[1]

RECEIVED MARCH 6, 1953

The structure of glycolate nitrate esters is expected to be mainly



but the possibility exists that some enol may be present.



If this is the case the infrared spectrum should have a frequency in the 3 μ region corresponding to the O–H vibration.

The esters[2] used in this study were: isopropylglycolate nitrate, $n^{25}\text{D}$ 1.4163; *n*-butylglycolate nitrate, $n^{25}\text{D}$ 1.4235; *s*-butylglycolate nitrate, $n^{25}\text{D}$ 1.4270; isoamylglycolate nitrate, $n^{25}\text{D}$ 1.4250. The spectra were determined on the pure liquids with a Perkin–Elmer Model 21 Infrared Spectrograph with a sodium chloride prism, using a sodium chloride cell without a spacer.

In Fig. 1 is the spectrum of *s*-butylglycolate nitrate. It is to be observed, that there is a strong band at 3.43 μ due to C–H but also a weaker but rather broad band with a peak at 2.93 μ which is evidence of the presence of O–H. It would appear that there is some enol present in this molecule. The spectra of the other three esters all show this band near 2.93 μ. For comparison the spectrum of ethyl acetoacetate which is known to have about 7.7% enol in the liquid is shown in Fig. 2. It is to be noted that it has a similar band with a peak

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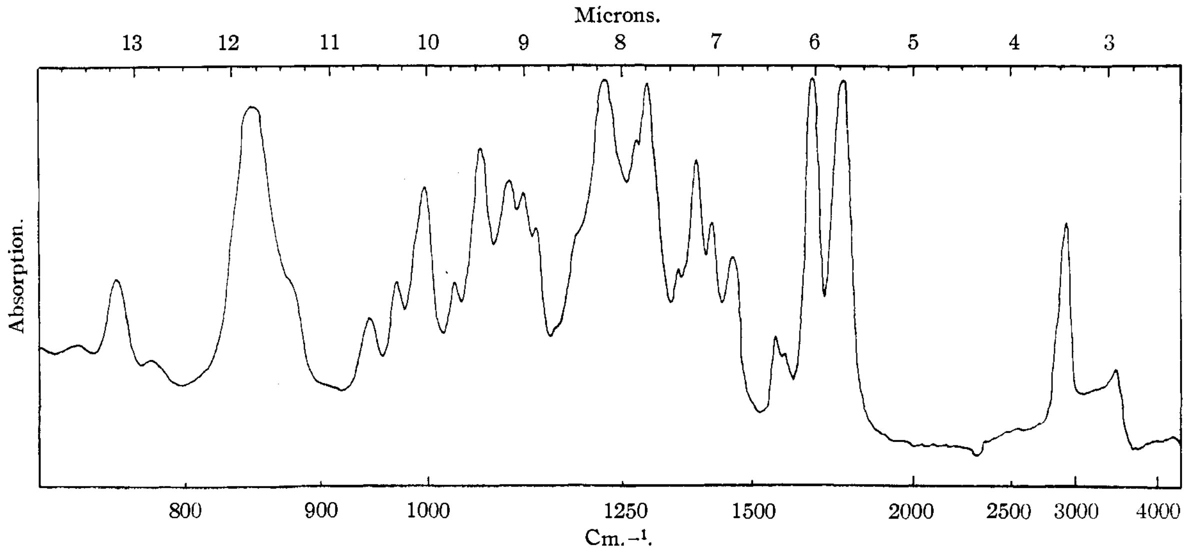
[1] Requests for reprints should be sent to W. D. Kumler at the College of Pharmacy, University of California, San Francisco 22, California.

[2] J. G. Bird, H. K. Iwamoto, C. J. Carr and J. C. Krantz, Jr., *J. Pharmacol. Expt. Therap.*, **97**, 475 (1949).



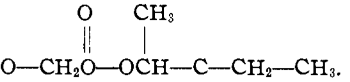


Fig. 1.—*s*-Butylglycolate nitrate, $O_2NO—CH_2\overset{\overset{O}{\|}}{O}—O\overset{\overset{CH_3}{|}}{C}H—C—CH_2—CH_3$.

at 2.96 μ. The height and breadth of this band are neither as great with respect to the C–H band as they are in the case of *s*-butylglycolate nitrate. Since the number of C–H bonds differ only by one in the two compounds the relative height and breadth of the bands near 3 μ should give an indication of the amount of enol in the compounds. On this basis one would conclude that there is somewhat more enol in liquid *s*-butylglycolate nitrate than in liquid ethylacetoacetate.

If this 3 μ band is due to enol then it should change on being measured in dilute solution in a solvent such as carbon tetrachloride. The broad character of the band in the liquid is attributed to hydrogen bonding, and mainly intermolecular hydrogen bonding because the ring formed by intramolecular hydrogen bonding would be seven membered and therefore relatively unstable. In Fig. 3 the plot of the spectrum for this region for a 0.42% solution of the compound in carbon tetrachloride in a 2-mm. cell shows all of these predictions are fulfilled. The band is considerably narrower and is of lower extinction, the total amount of absorption having been reduced to about one-fourth of that shown by the pure liquid in this region. The maximum has shifted from 2.93 to 2.88 μ, close to the wave length characteristic of a free OH. All of these changes are the expected result of the suppression of intermolecular hydrogen bonding in dilute solution.

The strong band at 5.73 μ or 1745 cm.⁻¹ is attributed to the carboxylic ester C=O and the one at 6.04 μ or 1656 cm.⁻¹ to the nitrate group. Ethyl nitrate for example has a strong band at 6.10 μ or 1639 cm.⁻¹. Any absorption in the range 1600–1660 cm.⁻¹ expected from C=C present in the enol, would thus be obscured by this nitrate band.

I wish to thank Dr. Harry K. Iwamoto for supplying the glycolate nitrate esters and Dr. Louis A. Strait and Mr. M. K. Hrenoff for measuring ethyl nitrate. I am especially indebted to Professor Richard M. Badger for his expert advice and counsel during the investigation.

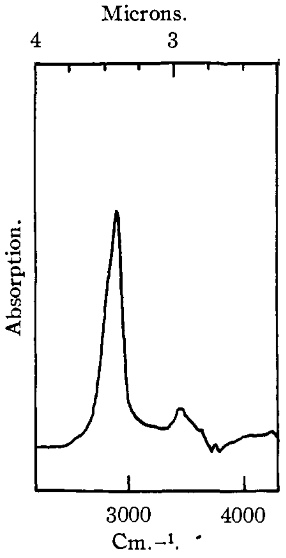


Fig. 2.—Ethyl acetoacetate.

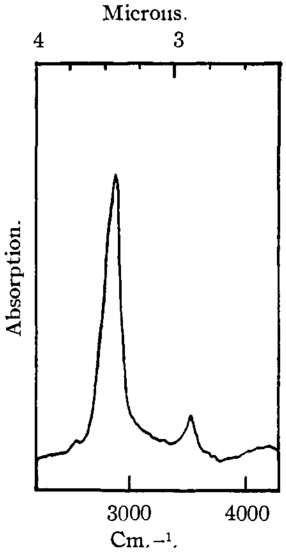


Fig. 3.—*s*-Butylglycolate nitrate, 0.210 g. in 50 ml. of CCl_4, 20-mm. cell.

CONTRIBUTION NO. 1785 FROM THE
GATES AND CRELLIN CHEMICAL LABORATORIES OF THE
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Vapor Phase Depolymerization of Trioxane

BY ARTHUR W. SCHNIZER, GENE J. FISHER AND ALEXANDER F. MACLEAN

RECEIVED APRIL 14, 1953

Liquid phase homogeneous acid-catalyzed depolymerization of trioxane has been described as an *in situ* source for formaldehyde.[1] Using hetero-

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[1] J. F. Walker and A. F. Chadwick, *Ind. Eng. Chem.*, **39**, 974 (1947).

geneous, fixed-bed acid catalysis, it is possible to convert trioxane vapors conveniently to anhydrous, gaseous formaldehyde in good yield. Conversions as high as 89% were obtained in the equipment shown in Fig. 1 at 220–230° and at mass velocities of 0.3 to 0.4 g. trioxane/g. catalyst-hr. Since no by-products (such as carbon monoxide, carbon dioxide, hydrogen, other water insoluble gases, or methyl formate) and no unreacted trioxane were found in the product stream, it is possible that quantitative conversions were actually approached. Mechanical losses from paraformaldehyde formation in the water absorber used for calibration were noted but not corrected for.

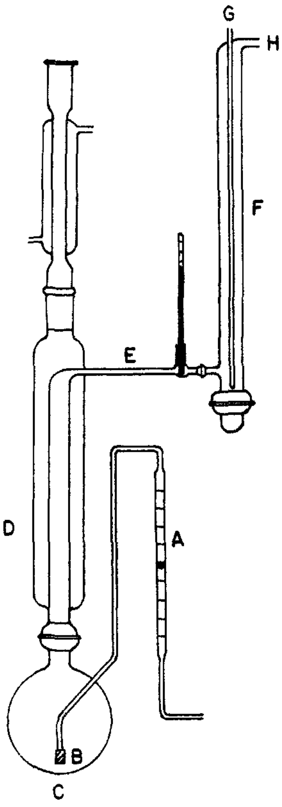

Fig. 1.

Catalysts used included Amberlite IR-120 ion-exchange resin, potassium acid sulfate-on-activated charcoal, potassium acid sulfate-on-silicon carbide, and phosphoric acid-on-silicon carbide. Of these, the last was the most satisfactory, since the others either gave undesirable by-products (methyl formate or sulfur compounds) or had a short life. A 32% phosphoric acid-on-silicon carbide catalyst was used intermittently for 50 hours with no detectable decrease in activity.

Experimental

Flow of trioxane vapors was regulated by controlled vaporization with an inert carrier gas. Nitrogen was metered (A) through a fritted glass gas dispersion tube (B) into boiling trioxane (C). Trioxane saturated nitrogen at 99.5° was obtained by cooling the vapors in a thermostatic condenser (D) containing refluxing *s*-butyl alcohol in the jacket. The vapors were preheated (E) to 200° and passed into the electrically-heated depolymerizer (F) containing 106 g. (135 cc.) of 32% phosphoric acid-on-carborundum maintained at 220–230° as indicated by thermocouple (G). Formaldehyde evolved (H) should be kept at temperatures of 160° or above, or polymerization to paraformaldehyde catalyzed by traces of water may occur. The nitrogen flowmeter was calibrated in terms of the rate of trioxane delivered to the depolymerizer.

The catalyst was prepared by absorbing 185 g. of a 77% phosphoric acid solution on 297 g. of porous silicon carbide granules (4–8 mesh) and drying at 110° for 16 hours.

In a typical run 15.5 g. (0.172 mole) of trioxane was vaporized in 30 minutes, and the product gases were absorbed in water. Titration of the base liberated on the addition of sodium sulfite to a neutralized aliquot showed that 13.8 g. (0.469 mole, 89%) of formaldehyde had been formed. No water insoluble gases were formed, and analyses of the absorbate for trioxane and ester were negative.

CELANESE CORPORATION OF AMERICA
PETROLEUM CHEMICALS RESEARCH &
DEVELOPMENT DEPARTMENT
CLARKWOOD, TEXAS

The Ignition Limits of 1-3 Mixtures of Carbon Disulfide and Oxygen[1,2]

BY ALBERT L. MYERSON AND FRANCIS R. TAYLOR

RECEIVED JANUARY 12, 1953

In 1935, Semenoff[3] summarized the status of the study of CS_2 oxidation by pointing out that "the experimental results are hardly reproducible, and the difficulties immense." The first extensive work[4] had consisted of the determination of the boundaries in cylindrical flasks. Only a general picture resulted, owing to the great difficulties encountered in reproducing boundary points. A paper by Sagulin[5] on this explosion system and one by Prettre and Lafitte,[6] who studied CS_2–air mixtures, had presented rather limited observations of ignition limits.

It could be concluded from the published results cited that the greatest deterrent to reproducibility is the sensitivity of the reaction to surface conditions. To overcome this difficulty, a procedure was developed whereby each flask was cleansed without washing, using the heating process described in the experimental section. It was thus possible to reproduce most explosions within a few degrees centigrade and a few mm. pressure. Ignition limits were obtained for several sizes of Pyrex and quartz flasks, and include a third limit hitherto not reported. These data also resulted in orderly relationships between induction time, τ (period between mixing of gases and explosion) and temperature at constant pressure, and between τ and pressure at constant temperature. In past studies of CS_2–O_2 systems, induction times varied at random with pressure and temperature.

Experimental

To determine whether or not a given mixture of CS_2 and O_2 would explode, the ignition flask was first brought to the desired temperature in an air-stirred thermostat (±0.2°). Carbon disulfide was then admitted to the evacuated (0.1 μ) ignition flask through a stopcock connected to the vessel by 2-mm. bore capillary. The system back of the stopcock was evacuated and filled with oxygen to a calculated pressure. When the stopcock was opened, the mixture in the flask quickly attained the desired equilibration value.

Explosion, if it took place, could be observed visually by a brilliant violet flash, and was also detected and timed by a photomultiplier and associated circuit. A fairly heavy yellow deposit, probably of $(CS)_n$ and S, was left on the flask by the explosion; a very light deposit could usually be found even when ignition did not occur. After observation, the flask was removed from the thermostat and cleaned of all surface impurities by repeatedly evacuating, filling with oxygen, and flaming to a red heat with a gas–oxygen flame. This treatment, which removed all products as SO_2 and CO_2, caused some distortion of Pyrex flasks but had very little effect upon quartz in which most of the explosions were carried out. After flaming, the flask was returned to the thermostat and maintained at 300° and a few tenths of a micron of pressure for three hours. The vessel was then

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[1] This research was performed under Contract No. AF33(038)-20863 with Wright Air Development Center, Dayton, Ohio.

[2] Presented at the 123rd Meeting of the American Chemical Society at Los Angeles, California, March, 1953, and the Meeting-in-Miniature of the Philadelphia Section of the American Chemical Society, January, 1953.

[3] N. Semenoff, "Chemical Kinetics and Chain Reactions," Clarendon Press, Oxford, 1935, p. 280.

[4] H. W. Thompson, *Z. physik. Chem.*, **10B**, 273 (1930); H. W. Thompson and C. F. Kearton, *ibid.*, **14B**, 359 (1931).

[5] A. B. Sagulin, *ibid.*, **1B**, 275 (1928).

[6] M. Prettre and P. Lafitte, *Compt. rend.*, **190**, 796 (1930).

ready for another explosion, which occurred under almost identical conditions.

Long induction periods were usually observed, and were quite frequently of at least 15 seconds duration and as long as several minutes. Since even the longest induction times correlate so well with other ignition data, it can be concluded that the results are relatively free of pre-ignition and other effects of incomplete mixing.

A check was made on the temperature of the gases after admission of the cold O_2 to the CS_2 and flask at thermostat temperature. A very fine thermocouple was placed inside the ignition vessel and the temperature change was followed with a suspension galvanometer. Results indicated that upon addition of the oxygen the temperature dropped to a minimum of only a few tenths of a degree below the thermostat temperature in a very short time, and recovered slowly, in a matter of seconds (5–10). Thus as far as cooling effects are concerned, the boundary temperatures found can be considered to be high by not more than a few tenths of a degree centigrade.

The CS_2 used was purified by fractionating a C.P. grade of analyzed material in an 18-in. silvered Stedman column. A constant boiling (±0.1°) fraction was obtained using a reflux ratio of 15:1 and a reflux rate of 5 ml./min. The purified liquid was dried over $CaSO_4$ and kept in a tube ending in a packless valve to obviate air leakage. Pure oxygen was prepared by the thermal decomposition of $KClO_3$ using Fe_2O_3 as a catalyst. Airco spectrometrically pure O_2 was also used with no difference in results.

Results

The ignition limits obtained are shown in Fig. 1, and are characteristic of a branched chain explosion. In the pressure range of the first limit it is generally accepted that the probability of an active center diffusing to and being destroyed at the wall is inversely proportional to the pressure. This leads to a first boundary relationship between total initial pressure p and flask diameter d, such that pd^2 is a constant. For the two smaller flasks, $d_1^2/d_2^2 = 0.71$, while $p_2/p_1 = 0.72 \pm 2\%$ over the range 115 to 140° to satisfactorily confirm this relationship. The data for the two large flasks, relative to the data for the smaller, are qualitatively but not quantitatively, in accord with this relationship.

The second limits of the two smaller flasks show the convergence expected for a homogeneous gas phase process. This would correspond to chain breaking in three-body collisions, as postulated by Lewis and von Elbe for the H_2–O_2 explosion. However, it can be noted that the second limits of the two larger flasks of essentially equal size do not converge with the limits of the smaller flasks. If the lack of convergence were due to surface effects, the coincidence of the second boundaries of the two smaller flasks of unequal size would be rather improbable. This low probability is especially likely for smaller flasks with their greater surface-to-volume ratio. The explanation for the lower second limits of the larger flasks thus would seem to involve the increasing importance of thermal explosion. Further experiments with vessels coated with inorganic materials should help to elucidate this phase, since the surface will be identical for all vessel sizes.

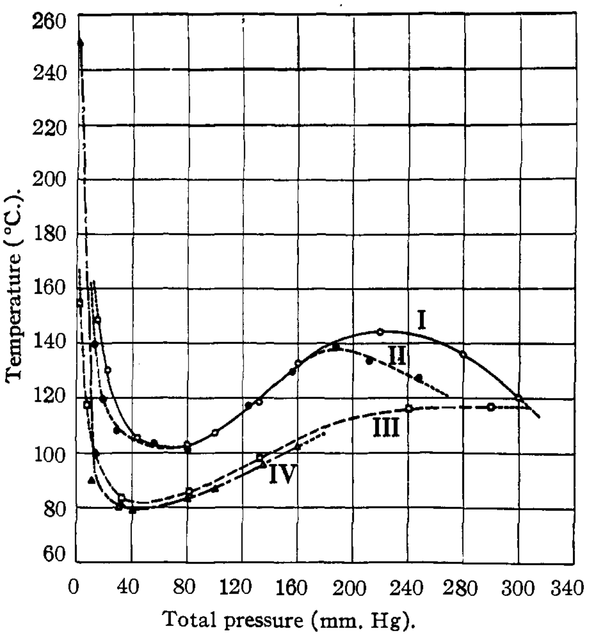

Fig. 1.—Ignition limits of $CS_2 + 3O_2$ as a function of total pressure and temperature. Curve I of flask I, 4.15 cm. diam., quartz; II, 5.05 cm. diam., quartz; III, 6.05 cm. diam., quartz; IV, 5.85 cm. diam., Pyrex.

The definite existence of a third limit can be noted on Fig. 1. That this was not reported by Thompson and Kearton[3] can be ascribed to the inhibition caused by reaction products. The latter could easily accumulate under the conditions used for determinations at the higher pressures of the third limit. In this method, a cold vessel containing the mixture was plunged into the heated thermostat, allowing ample time for slow reaction before thermostat temperature was attained. In the present experiments, it has been shown that a non-explosive mixture formed at the higher pressures of the 3rd limit will not explode at the boundary when heated thereafter; in fact, not until a much higher (by 50° or more) temperature is reached. A relatively dark coating, probably of S and $(CS)_n$, on the vessel surface gives evidence that a considerable reaction is present.

As previously mentioned, it was possible to observe logical variations in induction time as a function of temperature and pressure. Thus in a series of observations at constant pressure at varying temperatures, in the vicinity of a boundary, the curves shown on Fig. 2 were obtained. The induction time (τ) can be considered to be the time interval of the approximately linear or zero-order section of the curve describing the increase in chain carriers from the time of mixing to explosion. One would therefore expect a relationship such as

$$\tau e^{-E^{\ddagger}/RT} = \text{constant}$$

such as is given by Semenoff.[7] Thus a plot of log τ as a function of $1/T$ (°K.) should result in a straight line. Such a graph for the data of Fig. 2 follows such a formula, and exhibits deviations from a straight line which seem to be random in nature. In view of the difficulties entailed in reproducing an induction time in some boundary regions, these deviations are within the limit of experimental error.

In the region of the first limit, data showing the variation in induction time as a function of pressure (at constant temperature) are even more

(7) See ref. 3, pp. 85–87.

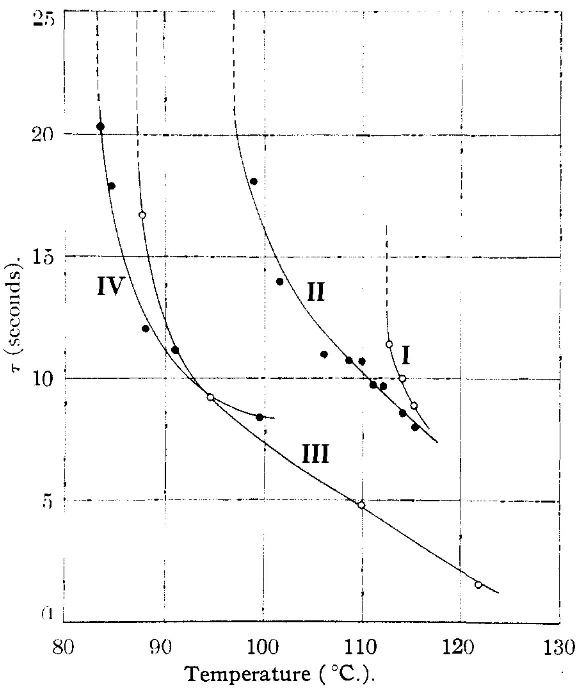

Fig. 2.—Variation of induction time with temperature: curve I, flask I, p = 32 mm.; II, flask II, 32 mm.; III, flask IV, 101 mm.; IV, flask IV, 80 mm.

satisfactory. We believe that these data can be satisfactorily interpreted through consideration of the basic processes of chain propagation. This will be considered in future publications when more data are available.

The present work represents the initial efforts of a more extensive study of the CS_2–O_2 system, which will include spectroscopic as well as ignition data.

Acknowledgment.—The authors would like to express their appreciation for the coöperation and encouragement of Mr. W. E. Scott.

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The Irradiation of Crystalline Vitamin B_{12} with Neutrons

BY PAUL NUMEROF AND JOHN KOWALD

RECEIVED MARCH 20, 1953

The widespread interest in the biological role of vitamin B_{12} makes its availability in radioactive form for tracer studies highly desirable. Microbiological synthesis of vitamin B_{12} labeled with Co-60[1-3] and P-32[3] has been described. However, isolation of substantial quantities of crystalline vitamin B_{12} from fermentation broths is a fairly tedious operation, and an easier route to the labeled vitamin would be desirable.

A recent communication[4] has claimed the formation of vitamin B_{12} labeled with Co-60 by the irradiation of vitamin B_{12} with thermal neutrons. Since the completion of our work another report[5] has appeared, describing the results of experiments similar to those of Anderson and Delabarre.[4] Such a procedure, if successful, would offer an attractive alternate route to the preparation of the labeled vitamin even if the specific activities obtained were not as high as those obtainable by microbiological synthesis.

In an effort to duplicate this method of preparation of Co-60 labeled vitamin B_{12} we have had a sample of the crystalline vitamin irradiated with neutrons. Our results, which differ from those published,[4,5] are based on the use of countercurrent distribution for the establishment of the identity of the Co-60 labeled material.

Experimental

Fifty milligrams of anhydrous crystalline vitamin B_{12}, sealed in an evacuated quartz vial, was irradiated for 19 days in the Brookhaven National Laboratory reactor through the courtesy of Dr. R. C. Anderson, Chemistry Department, Brookhaven National Laboratory, Upton, Long Island, New York. The irradiation was carried out at a temperature of 30–35° in a special "cold-hole" in the Brookhaven pile at a flux density of 2.7×10^{12} neutrons/cm.^{2}/sec. The exact energy spectrum of the irradiation flux was not known; besides the predominantly thermal neutron flux there were present also undetermined epithermal neutron and gamma radiation fluxes.

After irradiation the quartz vial was allowed to stand for two months to allow the decay of short-lived isotopes. The vial was then opened and the contents dissolved in water. Bioassays of an aliquot of this solution indicated that about one-third of the original biological activity remained. Another portion of the solution, when tested for Co^{++} ions using dithizone in chloroform, and α-nitroso-β-naphthol, gave negative results.

The irradiated material was purified by extraction into benzyl alcohol, after formation of the dicyanide complex, according to the procedure of Rudkin and Taylor.[6] Water was added to the benzyl alcohol extract and the vitamin B_{12} then transferred to the aqueous phase by the addition of chloroform. After decomposition of the dicyanide complex, the aqueous layer was then evaporated to a small volume and vitamin B_{12} crystallized by the addition of acetone.[5] Recrystallization was also carried out from aqueous acetone. Twenty-one milligrams of crystalline material was obtained representing 42% of the weight of the starting material. Five milligrams of this material was used in a countercurrent distribution with the system benzyl alcohol–water.[1] Each tube of the distribution was assayed for biological activity and for radioactivity.

Beta radioactivity was determined with a flow counter operating in the Geiger region; gamma radioactivity was determined with a scintillation counter.

All paper chromatograms were carried out on Whatman #1 paper. The two-dimensional chromatogram of the crystals isolated after irradiation is shown in Fig. 1. The vitamin B_{12} spot, though devoid of radioactivity, is still close to the point of application of the sample at the origin of the chromatogram. In the hope that a longer development time would result in a greater separation of the vitamin B_{12} from the other materials, a unidimensional chromatogram was carried out in which development was continued until the vitamin B_{12} spot had moved 14 cm. from the origin. An autoradiograph of this paper was made, with the results shown in Fig. 2. There are dense areas of radioactivity at the origin and at distances of 1.5, 5 and 6.7 cm. from the origin.

Countercurrent distribution of the purified crystallized sample of vitamin B_{12} was also employed to characterize the material isolated from the irradiated crystals. If Co-60 labeled vitamin B_{12} were present, the distribution of radioactivity/tube should parallel the distribution of bioactivity/

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(1) L. Chaiet, C. Rosenblum and D. T. Woodbury, *Science*, **111**, 601 (1950).

(2) C. Rosenblum and D. T. Woodbury, *ibid.*, **113**, 215 (1951).

(3) E. L. Smith, D. J. D. Hackenshull and A. R. J. Quilter, *Biochem. J.*, **52**, 387 (1952).

(4) R. C. Anderson and Y. Delabarre, THIS JOURNAL, **73**, 4051 (1951).

(5) E. L. Smith, *Biochem. J.*, **52**, 384 (1952).

(6) G. O. Rudkin and R. J. Taylor, *Anal. Chem.*, **24**, 1155 (1952).

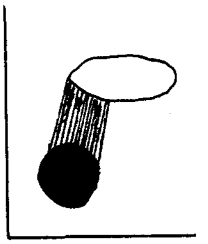

Fig. 1.—Drawing of autoradiograph from two-dimensional paper chromatogram of crystalline vitamin B_{12} isolated from irradiated material. Most of the radioactivity is at the origin with some activity extending to B_{12} area. Elliptical area, which held red color of vitamin B_{12}, was devoid of radioactivity. Horizontal development was with *s*-butanol–water, vertical development, benzyl alcohol–water.

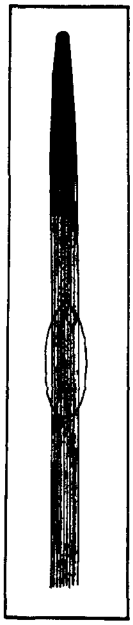

Fig. 2.—Drawing of autoradiograph of unidimensional descending paper chromatogram of crystalline vitamin B_{12} isolated from irradiated material. Four separate radioactive components are evident, as well as radioactivity extending to the solvent front. Red color of B_{12} is enclosed within elliptical area. Developing agent was *s*-butanol–water.

tube. The result of a countercurrent distribution using the benzyl alcohol–water system, is shown in Fig. 3. The distribution also demonstrates the presence of hydrophilic materials of relatively high specific radioactivity. Such high specific activity materials, present in low concentration,[7] could be "carried" by vitamin B_{12} upon repeated crystallization. The ready separation in the distribution of such materials from vitamin B_{12} is not unexpected, since compounds as closely related as vitamin B_{12} and vitamin B_{12a} can easily be resolved with this technique. Vitamin B_{12a}, in which the cyano group of vitamin B_{12} has been replaced by hydroxyl, has a distribution coefficient in the benzyl alcohol–water system of 8, while the distribution coefficient of vitamin B_{12} in the same system is 1.2.[8]

During the isolation and purification of the irradiated material, numerous small fractions were obtained that possessed both biological activity and radioactivity. Table I shows the distribution of radioactivity and biological activity among the major fractions during the isolation of the irradiated crystals.

TABLE I

DISTRIBUTION OF RADIOACTIVITY AND BIOACTIVITY AMONG MAJOR FRACTIONS DURING ISOLATION OF IRRADIATED CRYSTALS

Fraction	Radioactivity Total c./min.	%	Bioactivity Total	%
Original aqueous	1.2×10^8	100	18,000	100
Aqueous (after extraction of original aqueous with benzyl alcohol)	7.4×10^7	62	40	0.2
Benzyl alcohol (after addition of chloroform and extraction with water)	7.3×10^5	0.6	300	1.6
Vitamin B_{12} crystals	3.5×10^6	2.9	12,000	65

Discussion

Irradiation of vitamin B_{12} with thermal neutrons should give atoms of Co-60, resulting from an n,γ-reaction, with recoil energies as high as several hundred electron volts.[9] Such energies are far in excess of that required for the breaking of ordinary chemical bonds, and it would be expected that cobalt atoms, so activated, would be split from the vitamin B_{12} molecule. If some of the gamma quanta emitted during the n,γ-process were of low enough energy, some of the cobalt-60 might conceivably be retained intact within the vitamin B_{12} molecule. However, our results indicate that no detectable amounts of Co-60 labeled vitamin B_{12} were produced under our irradiation conditions.

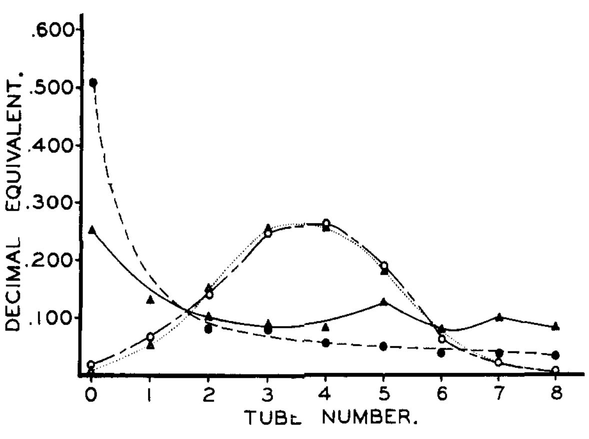

Fig. 3.—Craig countercurrent distribution on 5-mg. sample of irradiated vitamin B_{12} crystals, using the benzyl alcohol–water system: theoretical curve for K = 1.2, ...; biological activity curve, — — — — —; gamma radioactivity, ——; beta radioactivity, - - - -.

These findings, which differ so markedly from those reported by others,[4,5] suggest that experimental conditions in studies on retention of radioactivity in complex molecules, especially those possessing specific biological activity, may require more precise definition than has been the case heretofore. The irradiation of vitamin B_{12} performed by Smith was described as being carried out with thermal neutrons in a nuclear reactor; no specification was made concerning whether or not the irradiation done by Anderson and Delabarre was carried out in a thermal column or in a nuclear reactor. It may well be that the energy spectrum of the irradiating particles was different in each case.

Although epithermal neutrons and gamma radiation were present under our experimental conditions, it would not appear likely that these contributed greatly to the destruction of the vitamin B_{12} during irradiation. Anderson and Delabarre[4] reported about 15–20% of their material had been destroyed after an irradiation cycle of seven days. Assuming a uniform rate of destruction, about 55% of their material would remain after an irradiation cycle of 19 days. Our material, irradiated for 19 days, gave a recovery of about 40% which, in view of the errors in biological assay, does not appear to be significantly different.

The two earlier reports on the irradiation of vitamin B_{12} with neutrons described the use of chromatographic techniques,[4] and the preparation of derivatives without change in specific activity,[5]

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(7) The contents of tube 0 of the distribution were subjected to ultraviolet absorption analysis. No spectrum characteristic of vitamin B_{12}, or any strongly absorbing material, could be found.

(8) C. Rosenblum and D. T. Woodbury, *J. Am. Pharm. Assoc. Sci. Ed.*, **41**, 368 (1952).

(9) R. R. Edwards and T. H. Davies, *Nucleonics*, **2**, 44 (No. 6) (1948).

for the identification of the irradiated material. While in most cases these criteria may be taken as highly indicative of the identity of two materials, the irradiation of a substance such as vitamin B_{12} warrants the application of as many criteria of identity as possible. It is conceivable that complex cobalt compounds, very closely related to vitamin B_{12}, would exhibit similar behavior on chromatography. Furthermore, the possibility must not be overlooked that these compounds might also be capable of undergoing the same exchange of anions as vitamin B_{12} when different cobalamins are made from the parent compounds. Even constant specific activity might, in this case, be misleading, especially since the desired product is present in a very small amount.

Countercurrent distribution, which can so easily effect a separation of two cobalamins as closely related as vitamin B_{12} and vitamin B_{12a}, provides an excellent additional criterion for the identity of the irradiated material. Cobalt-60 labeled vitamin B_{12}, whether prepared by neutron bombardment or by microbiological synthesis, should exhibit the same ratio of radioactivity to biological activity for each tube of a countercurrent distribution. This criterion has so far been met only in the case of microbiological synthesis.[1]

In our work the results of paper chromatography were in themselves enough to question the presence of appreciable amounts of the Co-60 labeled vitamin. The countercurrent distribution merely provided additional support for that conclusion. The results of Anderson and Delabarre[4] and Smith[5] do suggest the possibility that the Co-60 labeled vitamin had actually been prepared by neutron bombardment. However, the lack of information of the behavior of their material in a countercurrent distribution must, in view of the specificity of this technique, still leave open the claim for the preparation of Co-60 labeled vitamin B_{12} by direct neutron bombardment.

The paucity of information on the retention of induced radioactivity as a function of the energy spectrum of the neutrons used for irradiation, makes difficult an exact interpretation of the reasons for the differences between our results and those reported by others.[4,5] It is hoped that further study of these variables will lead to a better understanding of the changes resulting in complex compounds under neutron irradiation.

NEW BRUNSWICK, N. J.

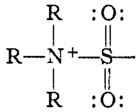
Rotations within Crystalline Trimethylamine Sulfur Trioxide

BY HEROSHI SHIMIZU AND DAN MCLACHLAN, JR.

RECEIVED APRIL 27, 1953

Although compounds of the tertiary amines with sulfur trioxide were prepared[1] in 1883 and have since been put to use in the dye industry,[2] there is still some doubt about their structure in the crystalline state.

This paper is concerned with the structure of the single compound, trimethylamine sulfur trioxide. A selection of the proper chemical structure from the four possible postulated structures of Burg[3] has been made possible by the careful work of Lecher and Hardy[4] on the basis of their own experiments, the work of other investigators,[5] the "Adjacent charge rule" of Pauling,[6,7] and spectroscopic and X-ray data of Gare and McLachlan (unpublished). Lecher and Hardy have chosen the chemical form



$$\begin{array}{ccccc} & \mathrm{R} & & :\mathrm{O}: & \\ & | & & \| & \\ \mathrm{R}- & \mathrm{N}^+ & - & \mathrm{S} & -\ddot{\underset{..}{\mathrm{O}}}:^- \\ & | & & \| & \\ & \mathrm{R} & & :\mathrm{O}: & \end{array}$$

The present investigation needs then only to cover the possible configurations of this type of molecule in the crystal. The four possibilities were considered: 1, the R groups and O groups stationary; 2, the R groups and O groups rotating; 3, the R groups stationary and the O groups rotating; 4, the R groups rotating and the O groups stationary.

Experimental

The samples of the trimethylamine sulfur trioxide were furnished by the American Cyanamid Company through the courtesy of Dr. H. Z. Lecher. The crystals were colorless, acicular, about 5 mm. long and less than 1 sq. mm. in cross section.

Rotation pictures were taken with the crystal rotating about the longest growth axis (which proved to be the hexagonal c-axis) using molybdenum and also copper radiation. Then using copper radiation, Weissenberg X-ray pictures were taken to get the zero, first, second and third layer line pictures from which the unit cell dimensions and systematic extinctions could be determined. Using hexagonal indices, it was found that the non-extinctions were restricted to those indices which satisfy the relationship $(-h + k + l) = 3n$ indicating a rhombohedral cell. The unit cell dimensions are: on the hexagonal lattice, a = 9.22 Å., c = 6.2 Å.; or on the rhombohedral lattice, a = 5.71 Å. and α = 107° 40'. The number of molecules per unit cell is three for the hexagonal cell which is equivalent to one in the rhombohedral cell. The calculated density is 1.52 g./cm.^{3} and the molecular volume is 152 Å.^{3}. The space group is $C_{3v}^5 = R3m$.

The intensities of the zero layer line X-ray diffraction maxima were obtained from the X-ray films using multiple film technique (three films) and visual comparison.

Calculation of the Structure.—The intensities were corrected by the Lorentz and polarization factors[8] to get the "observed" structure factors, $|F_{hk0}|$. Since the phases associated with F_{hkl} values cannot be determined from X-ray data, a Fourier computation of the electronic densities, ρ(xyz), could not be made immediately. To gain some knowledge of the structure, the trial method was used wherein the F_{hkl} values are calculated from various postulated structures and compared with the measured $|F_{hkl}|$ values. The phases are ob-

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(1) F. Beilstein and E. Weigand, *Ber.*, **16**, 1967 (1883).

(2) H. Z. Lecher, M. Scalera and C. T. Lester, U. S. Patent 2,403,226 (1946). See also U. S. Patents 2,402,647 (1946) and 2,396,582 (1946).

(3) A. B. Burg, THIS JOURNAL, **65**, 1629 (1943).

(4) H. Z. Lecher and W. B. Hardy, *ibid.*, **70**, 3789 (1948).

(5) For earlier controversial work see M. Delepine and R. Demars, *Bull. Sci. Pharmacol.*, **30**, 577 (1923); M. Auerbach and R. Wolffenstein, *Ber.*, **32**, 2507 (1899); and L. Mamlock and R. Wolffenstein, *Ber.*, **34**, 2499 (1901).

(6) L. Pauling and L. O. Brockway, THIS JOURNAL, **59**, 13, 17 (1937).

(7) L. Pauling, *J. Phys. Chem.*, **56**, 361 (1952).

(8) M. J. Buerger and G. E. Klein, *J. Applied Phys.*, **17**, 285 (1946)

tained as a by-product of these trials, and the $\rho(xyz)$ maps may be computed.

Since we were able to prove early in the investigation that the rotation of the groups would be about an axis parallel to the z-axis, then only the zero layer line values F_{hk0} were considered in the trials and only the $\rho(xy)$ plot was made in electron densities. The equation used in the F_{hk0} computation is

$$F_{hk0} = e^{-B\left(\frac{\sin\,\theta}{\lambda}\right)^2} \left[\sum_{j} f_j e^{2\pi i\,(hx_j\,+\,ky_j)} + \sum_{j'} f_{j'} J_0 \frac{(4\pi r_{j'}\,\sin\,\theta)}{\lambda}\right]$$

where j refers to the atoms in fixed positions and j′ to the atoms involved in free rotation. The values x_j and y_j are the postulated positions of atom j along the coördinates x and y; $r_{j'}$ is the perpendicular distance from the axis of rotation to atom j′ (or radius of rotation); exp $[-B(\sin\,\theta/\lambda)^2]$ is the temperature factor of Debye–Waller[9,10]; and J_0 $(4\pi r_{j'}\,\sin\,\theta/\lambda)$ is the zero order Bessel function which applies to free circular rotation as discussed by Zachariasen.[11] Table I gives the calculated F_{hk0} values for the four possible rotations referred to earlier for the particular projected distances (N–C) = 1.39 Å. and (S–O) = 1.50 Å. The values are normalized to F_{110} = 100 for comparison purposes. Other combinations of distances were tried but were less favorable. The Debye–Waller temperature factors have been applied to the calculated structure factors with 3 × 10^{-16} cm.^{2} as the most satisfactory value of B. It is interesting that the phases of all the structure factors turned out to be the same, *i.e.*, zero (a result which makes all structure factors positive). This result, however, is not surprising in view of the heavy concentration of atoms at the origin of the projection.

TABLE I

STRUCTURE FACTORS (NORMALIZED TO F_{110})

		Calculated, $(N-C)_\perp$ = 1.39 Å., $(S-O)_\perp$ = 1.50 Å.			
hk0	Observed	C fixed O fixed	C rotating O rotating	C fixed O rotating	C rotating O fixed
110	100	100	100	100	100
300	18.6	11.7	19.9	18.6	16.4
220	18.6	23.5	16.5	18.5	21.4
410	30.3	23.8	31.8	29.4	2.2
330	52.5	62.2	36.9	46.2	54.8
600	28.1	12.3	37.3	28.5	21.3
520	37.6	38.5	27.1	36.2	37.5
440	36.1	45.9	20.1	34.6	37.5
710	11.3	8.4	15.9	13.1	13.4
630	15.0	16.4	14.0	15.7	14.6
550	6.2	11.8	9.3	11.6	9.5
900	4.7	10.9	8.2	8.9	12.5
820	4.4	7.5	8.1	7.6	9.5
730	2.2	3.9	7.7	6.4	5.2

After discovering that the calculated structure factors were positive with all reasonably chosen atomic coördinates, it was possible to make a Fourier density summation using the observed F_{hk0} values. This is shown in Fig. 1 with arbitrary contour intervals. The high peak at the center of each group is due to superimposed nitrogen and sulfur atoms, and the six surrounding low peaks are presumed to be due to the carbon atoms. The oxygen atoms at a greater distance from the center and distributed uniformly about a circle (free rotation) contribute so little to the electron density at any particular area that its effect is hidden.

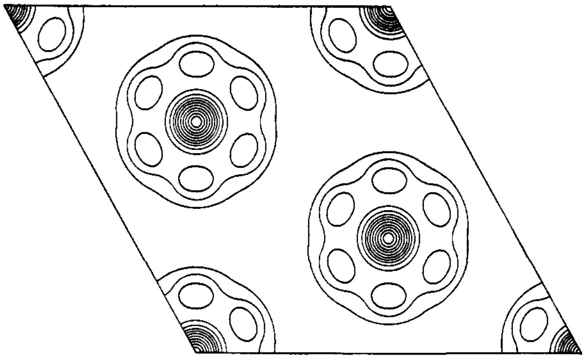

Fig. 1.—The c-axis projection of trimethylamine sulfur trioxide.

A sixfold symmetry in the zero layer of the reciprocal lattice is reflected in the sixfold symmetry of the density projection. Specific gravity considerations require that there be only one molecule per unit rhombohedral cell. For a single molecule of threefold symmetry to display sixfold symmetry, it is a further requirement that, on the average, only one-half of a carbon atom occupy each of the six positions. This condition is fulfilled by two sets of equilibrium positions being occupied by the three atoms either randomly or by highly hindered rotations.

The calculated structure factors were obtained on the basis of the one-half carbon per position. The closest fit was obtained for the conditions given in the fifth column of Table I. These values are plotted in Fig. 2 together with the observed values as a function of sin θ/λ.

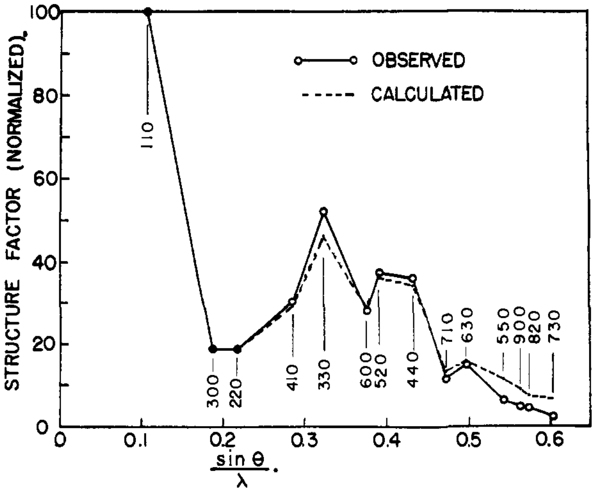

Fig. 2.—Structure factors.

The limitation of this investigation to the c-

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(9) P. Debye, *Ann. Physik*, **43**, 49 (1914).

(10) I. Waller, *Z. Physik*, **17**, 398 (1923).

(11) W. H. Zachariasen, "The Theory of X-Ray Diffraction in Crystals," John Wiley and Sons, New York, N. Y., 1945.

axis projection does not permit the determination of interatomic distances since none of the bonds is believed to be directed exactly perpendicular to the c-axis. However, the sulfur–oxygen projection distance is equal to the reported value of 1.50 Å. for the sulfates.

Summary.—The primary result of this investigation of the crystal structure of trimethylamine sulfur trioxide using X-ray diffraction is that, in the crystalline state, the SO_3 groups rotate about the molecular axes while the $N(CH_3)_3$ groups rotate very little, if at all. The basic unit cell was found to be a rhombohedron with $a = 5.71$ Å. and $\alpha = 107°40'$ and containing one molecule. The space group is $C_{3v}^5 = R3m$ and the calculated density is 1.52 g./cm.^{3}.

Acknowledgments.—The authors are grateful for a grant from the University of Utah Research Fund for the support of this work and to the American Cyanamid Company for furnishing the samples.

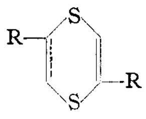
SALT LAKE CITY, UTAH

The Oxidation Products of 2,5-Diphenyl-1,4-dithiadiene

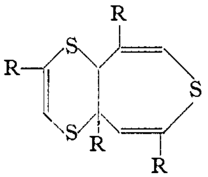
BY H. HARRY SZMANT AND JAMES DIXON

RECEIVED JUNE 1, 1953

The recent publication concerning the chemistry of the 1,4-dithiadiene system[1] and the reports of the Diels–Alder type condensation reactions in the course of the oxidation of thiophene[2] and benzothiophene[3,4] prompts us to report the results obtained in the study of the oxidation of 2,5-diphenyl-1,4-dithiadiene (I).



I



II

($R = C_6H_5$)

When I was treated with an equimolar amount of hydrogen peroxide, there was obtained a compound $C_{32}H_{24}S_3$. Analogy with reactions previously studied[2,3,4] leads to the tentative assignment of structure II to this compound.

Further study is planned, but the behavior of II on vigorous oxidation is in agreement with the structure assigned. With excess hydrogen peroxide acting for a long time, 0.11 g. of II gave 0.025 of the disulfone of I, 0.093 g. of benzoic acid and 0.051 g. of barium sulfate. These amounts are 34, 174 and 169% of the expected ones, if one molecule of the disulfone were formed from each molecule of II. The deficiency in the yield of the disulfone and the excess of benzoic acid and sulfate ion indicates that the disulfone itself is not completely stable.

The disulfone was obtained directly from I, with excess hydrogen peroxide, but in only 50% yield, and accompanied by benzoic and sulfuric acids. This may indicate that even under these conditions II is an intermediate in the oxidation of I to its disulfone.

Experimental[5]

2,5-Diphenyl-1,4-dithiadiene-1,4-tetroxide.—I, 5.55 g., was heated with an excess of hydrogen peroxide in glacial acetic acid until the yellow color of the starting material faded. On cooling there was isolated 50.5% of desired disulfone of I, m.p. 232°.

Anal. Calcd. for $C_{16}H_{12}O_4S_2$: C, 57.82; H, 3.61. Found: C, 57.63; H, 3.78.

The filtrates from the oxidation reaction were concentrated and finally diluted with water in order to isolate additional material. There was obtained only benzoic acid and sulfate ion (precipitated as barium sulfate).

Oxidation of I with Equimolar Hydrogen Peroxide.—Equimolar amounts of I and hydrogen peroxide were heated in glacial acetic acid for one hour and the reaction mixture was poured on ice. The precipitate was crystallized repeatedly from isopropyl alcohol to give yellow crystals, m.p. 128° (II).

Anal. Found: C, 76.12; H, 4.64; S, 19.20; mol. wt. (Rast), 510–560. The repetition of this experiment gave the same results. Found: C, 76.28; H, 4.90. Calcd. for $C_{32}H_{24}S_3$: C, 76.16; H, 4.79; S, 19.09; mol. wt., 502.7.

Quantitative Oxidation of II with Hydrogen Peroxide.—II, 0.1094 g., was heated with an excess of hydrogen peroxide in glacial acetic acid, and nitrogen was used to sweep any carbon dioxide produced in the reaction into a solution of barium hydroxide. The reaction mixture gave on cooling 0.0247 g. (34%) of the disulfone of I, m.p. 232°. The filtrate on concentration gave no additional disulfone and was diluted with water. The aqueous solution was extracted with ether and the ether layer was dried and concentrated. The residual liquid was placed in a desiccator containing sodium hydroxide pellets, and after several days *in vacuo* the residue became solid and there was isolated 0.0928 g. of benzoic acid. The aqueous portion from the extraction was boiled to expel carbon dioxide and then was treated with barium hydroxide to give 0.0507 g. of barium sulfate.

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[1] W. E. Parham, T. M. Roder and W. R. Hasek, THIS JOURNAL, **75**, 1647 (1953).

[2] W. Davies, N. W. Gamble, F. C. James and W. E. Savige, *Chem. Ind.*, 804 (1952).

[3] W. Davies, *et al.*, *J. Chem. Soc.*, 4678 (1952).

[4] F. G. Bordwell, W. H. McKellin and D. Babcock, THIS JOURNAL, **73**, 5566 (1951).

[5] All melting points are uncorrected. Microanalyses by Mr. George Stragand, University of Pittsburgh.

DEPARTMENT OF CHEMISTRY
DUQUESNE UNIVERSITY
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Studies in Low Concentration Chemistry. IV. The Radiocolloidal Properties of Beryllium

BY GEORGE K. SCHWEITZER AND JAMES W. NEHLS

RECEIVED MAY 13, 1953

In 1950, Haymond, Garrison and Hamilton[1] noted the radiocolloidal behavior of beryllium when they found that they could separate carrier-free[2] beryllium-7 from lithium solutions by making such solutions basic and then filtering them through a glass frit. This paper constitutes a further investigation of the radiocolloidal properties of beryllium, using beryllium-7 as a tracer nuclide.

Experimental

Materials.—All inactive chemicals were of analytical reagent quality. All water was triply distilled and was pre-

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[1] H. R. Haymond, W. M. Garrison and J. G. Hamilton, *J. Chem. Phys.*, **18**, 1685 (1950).

[2] The term carrier-free is used to indicate that no inert beryllium has been intentionally added.

served in carbon dioxide-free air. About 0.5 ml. of dilute hydrochloric acid containing 2.0 mc. of beryllium-7 was obtained from Oak Ridge National Laboratory. Using 0.2 ml. of this solution, no indication of the presence of beryllium could be obtained by the method of Klemperer and Martin,[3] which will detect 0.05 microgram with ease. The remainder of the beryllium solution was diluted to one liter, setting a maximum concentration of about 10^{-9} *M*. As needed portions of this solution were treated with sodium hydroxide solution until the *p*H value was approximately 11.0, then filtered through a fine glass frit with the aid of suction, most of the activity being retained on the frit. After washing the filter with distilled water to remove the excess base, dilute nitric acid of the concentration desired for the particular experiment was slowly pulled through the frit, eluting the activity. Half-life and absorption determinations on samples of these solutions showed them to contain beryllium-7 as the only radioactive nuclide.

Radioactivity Measurements.—All determinations of radioactivity were made using a Tracerlab TGC-3A end-window tube attached to a conventional scaler. All activities were counted for a sufficiently long time to give a maximum standard deviation of 1%.

Preparation of Samples.—A small amount of the active beryllium solution was placed in a beaker, dilute nitric acid was added to increase the volume, other substances which were called for in the specific experiment were added and the *p*H was adjusted with dilute sodium hydroxide solution. After standing for 60 min., the solution was centrifuged in a Misco Electric Microcentrifuge for 30 min., filtered through Whatman No. 50 filter paper, or filtered through a fine glass frit. From the radioactivities of 0.100-ml. samples, which were taken before and after filtration or centrifugation, the amount removed could be calculated. The 0.100-ml. samples were measured with a 0.100-ml. micropipet, placed on metal planchets, evaporated to dryness and then counted.

Results

Coagulation Time.—Samples (originally 0.01 *N* in acid) at *p*H values of 8.0, 9.0 and 10.0 were prepared and were allowed to stand for lengths of time from one min. to 60 min. before being filtered. Quadruplicate experiments showed that beyond 5 min. standing time, the percentage of beryllium removed was constant within the standard deviation of 2.4 percentage points. Somewhat similar results have been reported for the radiocolloids of silver, yttrium and zirconium.[4]

***p*H Studies.**—Figure 1 illustrates the results obtained as the *p*H values of various beryllium solutions are varied. Each point on the graph represents at least three determinations, the standard deviation in no case exceeding 3.0 percentage points. Results similar to the filter paper ones were obtained when a fine glass frit was used in filtration studies. These studies are in accord with previous observations on other radiocolloidal elements.[5]

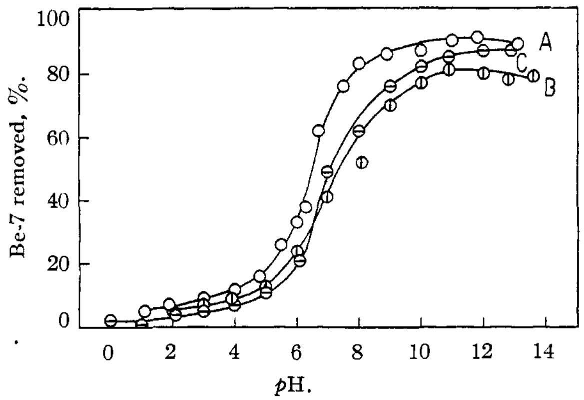

Fig. 1.—The effect of *p*H upon the removal of Be-7 from solutions neutralized with sodium hydroxide: A, samples originally 0.01 *N* in nitric acid, centrifuged; B, samples originally 0.01 *N* in nitric acid, filtered; C, samples originally 1 *N* in nitric acid, centrifuged.

Electrolyte Effects.—Solutions of beryllium 0.001 *N* in nitric acid were made up to various concentrations with different electrolytes, the *p*H was adjusted, and then they were centrifuged. All experiments were done in triplicate and the standard deviations did not exceed 2.8 percentage points. At a *p*H value of 5.0, the addition of sodium nitrate, sodium chloride, sodium bromide or sodium sulfate caused the percentage removal to decrease from 19 to about 1 as the electrolyte concentration increased from 0.001 *N* to over 1.0 *N*. At a *p*H value of 7.0, the addition of these same electrolytes resulted in a decrease in percentage removed from 63 to about 50 as the salt concentration increased from 0.001 *N* to over 1.0 *N*. The addition of sodium hydrogen carbonate at a *p*H of 7.0 caused a much more marked decrease in percentage removed, only 11% being removable from a 1.0 *N* solution. At a *p*H value of 9.0, the addition of sodium nitrate, sodium chloride, sodium bromide, or sodium nitrate again decreased the percentage removed from 85 to 0.001 *N* to less than 80 at concentrations above 1.0 *N*. Sodium hydrogen carbonate caused a marked decrease in removal, only 51% being centrifuged at a concentration of 1.0 *N*. Similar trends were observed when the activity was removed by filtration, either through filter paper or a glass frit. The effects of added electrolytes on other radiocolloids agree with these observations.[5]

Solvent Effects.—Figure 2 indicates the effects of the composition of the solvent upon the per cent. radiocolloid centrifuged. Each point on the graph represents at least three determinations, the standard deviation never exceeding 2.9 percentage points. Similar results were obtained when removal of the radiocolloid was effected by filtration.

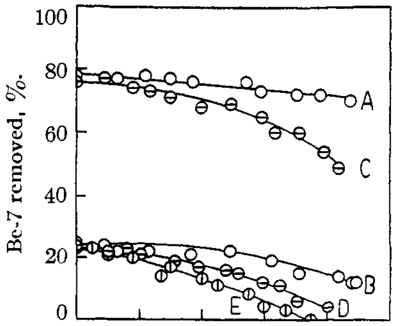

Fig. 2.—The effect of the presence of a non-aqueous solvent upon the removal of Be-7: A, ethanol at *p*H 10; B, ethanol at *p*H 6; C, 2-methylpropanol-2 at *p*H 10; D, 2-methylpropanol-2 at *p*H 6; E, 1,4-dioxane at *p*H 6.

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[3] F. W. Klemperer and A. P. Martin, *Anal. Chem.*, **22**, 828 (1950).

[4] G. K. Schweitzer and J. W. Nehls, This Journal, **74**, 6186 (1952); J. D. Kurbatov and M. H. Kurbatov, *J. Phys. Chem.*, **46**, 441 (1942); M. H. Kurbatov and J. D. Kurbatov, *J. Chem. Phys.*, **13**, 208 (1945).

[5] G. K. Schweitzer and W. M. Jackson, *J. Chem. Education*, **29**, 513 (1952).

These results compare favorably with those previously reported on silver[4] and polonium.[6]

Filtration Efficiency.—Filter papers of various relative retentivities and glass frits of various degrees of porosity were used to separate the radiocolloids at *p*H values of 7.0 and 10.0. As the relative retentivities of Schleicher and Schnell filter papers decreased and as the porosity of the frits increased, the per cent. radiocolloid removed decreased.

Effect of Stirring.—To test the effect of previous agitation upon the extent of radiocolloid removal, a series of samples originally 0.01 *N* in nitric acid was rapidly stirred for 60 min. after adjustment of the *p*H, and the removable activity was compared to that for similar samples which were not stirred. At a *p*H value of 7.0, 27% of the activity could be removed from the stirred samples by filtration through filter paper as compared to 38% for those not stirred. These values are the averages for four determinations, the standard deviations being 2.1 and 2.6 percentage points, respectively. Similar results were obtained for filtration through a glass frit and for centrifugation. Results showing a decrease in removal for stirred samples were also obtained at a *p*H value of 10.01. These results might be interpreted as the breaking up of the radiocolloidal aggregates into smaller groups which were not removed with as great an efficiency.

Diffusion.—The diffusion coefficients of the beryllium were determined at several *p*H values using the method of Anderson and Saddington.[7] At a *p*H at 2.0 the diffusion coefficient was 0.34 cm.^{2}/day; at *p*H 6.0 it was 0.29 cm.^{2}/day; the value was 0.13 cm.^{2}/day at a *p*H of 8.0 and 0.11 cm.^{2}/day at *p*H 10.0. Each determination was made in triplicate and no standard deviation exceeded 0.02 cm.^{2}/day. Assuming the validity of the Einstein–Stokes equation, the average radii of the aggregates were calculated to be 7 Å. at *p*H 2.0 increasing to 22 Å. at *p*H 10.0. Similar results are reported by Hevesy and Paneth for polonium,[8] and Schubert and Conn for zirconium and barium.[9]

Acknowledgment.—The authors wish to express their gratitude to the U. S. Atomic Energy Commission for the grant of funds which made this work possible.

(6) G. Bouissieres, R. Chastel and L. Vigneron, *Comp. rend.*, **224**, 43 (1947).

(7) J. S. Anderson and K. Saddington, *J. Chem. Soc.*, S 381 (1949).

(8) G. Hevesy, *Phil. Mag.*, **25**, 390 (1913); **27**, 586 (1914); F. Paneth, *Kolloid Z.*, **13**, 1 (1913).

(9) J. Schubert and E. E. Conn, *Nucleonics*, **4**, No. 6, 2 (1949).

DEPARTMENT OF CHEMISTRY
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KNOXVILLE 16, TENNESSEE

3-Methyl-5-anisyl-4-carbethoxy-2-cyclohexene-1-one

BY WALTER T. SMITH, JR., AND DANIEL S. P. EFTAX

RECEIVED APRIL 9, 1953

The preparation of 3-methyl-5-substituted-4-carbethoxy-2-cyclohexene-1-ones by the acid-catalyzed monodecarbethoxylation of 3-methyl-5-substituted-4,6-dicarbethoxy-2-cyclohexene-1-ones has been reported only in those cases in which the 5-substituent is alkyl.[1] Various earlier attempts to accomplish the monodecarbethoxylation have been unsuccessful in those cases in which the 5-substituent is aryl.[2,3]

Horning and Field[4] devised an alternate method for the preparation of 3-methyl-4-carbethoxy-5-anisyl-2-cyclohexene-1-one. The final step in their method was the cyclization of ethyl α,γ-diacetyl-β-anisylbutyrate with phosphoric acid in acetic acid. On this final step the yield of crude product was 22%.

A reinvestigation of the action of sodium ethoxide on ethyl anisal-bis-acetoacetate has shown that the product of this reaction is not 3-methyl-5-anisyl-2-cyclohexen-1-one as previously reported,[5] but that this reaction provides a new and improved method for the synthesis of 3-methyl-5-anisyl-4-carbethoxy-2-cyclohexene-1-one. The yield in the last step is 47%. The method has the further advantage that the starting material can be prepared in good yield in only one step from anisaldehyde.[5]

The identity of the product is established by comparison with the melting points previously reported[4] for the compound itself and for its dinitrophenylhydrazone. The *p*-nitrophenylhydrazone was also prepared. In addition, the monoester was converted to the known 3-methyl-5-anisyl-2-cyclohexene-1-one by alkaline saponification, followed by decarboxylation.

By the procedures described here, together with methods previously reported,[6] it is possible to use ethyl anisal-bis-acetoacetate as the common starting material for the preparation not only of 3-methyl-5-anisyl-2-cyclohexen-1-one, but also for the 4-carbethoxy derivative and the 4,6-dicarbethoxy derivative.

Experimental

3-Methyl-4-carbethoxy-5-anisyl-2-cyclohexene-1-one.—Ethyl anisal-bis-acetoacetate (60 g., 0.16 mole) was dissolved in 240 ml. of absolute ethanol containing 1.9 g. (0.082 mole) of sodium and refluxed for five hours. At the end of this period a small amount of sodium carbonate (4.8 g.) precipitated on cooling and was separated by filtration. The remaining orange solution was poured into 250 ml. of water containing chipped ice and 15 ml. of concd. hydrochloric acid; 40 g. (87%) of pale yellow solid separated. Subsequent recrystallizations from 95% ethanol yielded 21.5 g. (47%) of colorless crystals, m.p. 71–73°. The 2,4-dinitrophenylhydrazone melted at 182.5–183.5°.[4]

The yellow *p*-nitrophenylhydrazone[7] was recrystallized from 95% ethanol and melted at 195–196°.

Anal. Calcd. for $C_{23}H_{25}O_5N_3$: C, 65.25; H, 5.96; N, 9.92. Found: C, 65.16; H, 5.98; N, 10.06.

3-Methyl-5-anisyl-2-cyclohexene-1-one.—3-Methyl-4-carbethoxy-5-anisyl-2-cyclohexene-1-one (13 g., 0.043 mole) was dissolved in 100 ml. of 95% ethanol and the solution was added to 60 ml. of water containing 8 g. of sodium hydroxide; the mixture was refluxed for one-half hour, cooled to room temperature, acidified with 40 ml. of 1:1 hydro-

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(1) E. C. Horning, M. O. Denekas and R. E. Field, *J. Org. Chem.*, **9**, 547 (1944).

(2) E. Knoevenagel, *Ann.*, **303**, 223 (1898).

(3) E. C. Horning and R. E. Field, THIS JOURNAL, **68**, 384 (1946).

(4) E. C. Horning and R. E. Field, *ibid.*, **68**, 387 (1946).

(5) W. T. Smith, Jr., and P. G. Kort, *ibid.*, **72**, 1877 (1950).

(6) E. C. Horning and R. E. Field, *ibid.*, **68**, 384 (1946).

(7) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," Third Ed., John Wiley and Sons, Inc., 1948, p. 171.

chloric acid and refluxed for 15 minutes. At the end of this period the light brown mixture was poured into 500 ml. of water whereupon 10 g. of brown solid separated. The melting point was 60–61.5°. Recrystallization from 50 ml. of 95% ethanol gave 7.5 g. (77%) of pale yellow crystals, m.p. 62.5–63.5°. A mixed melting point with an authentic sample prepared according to the procedure of Horning and Field[4] showed no depression.

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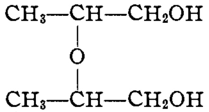
Synthesis and Identification of Dipropylene Glycol Isomers

BY A. R. SEXTON AND E. C. BRITTON

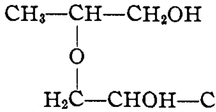
RECEIVED JANUARY 31, 1953

When one mole of propylene oxide is treated with propylene glycol, three isomers of dipropylene glycol may theoretically result.



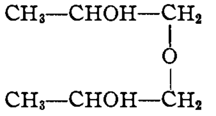
$$\begin{array}{l}\mathrm{CH_3{-}CH{-}CH_2OH}\\ \quad\;\; |\\ \quad\;\; \mathrm{O}\\ \quad\;\; |\\ \mathrm{CH_3{-}CH{-}CH_2OH}\end{array}$$

I, 2,2'-oxydi-1-propanol (diprimary alcohol)



$$\begin{array}{l}\mathrm{CH_3{-}CH{-}CH_2OH}\\ \quad\;\; |\\ \quad\;\; \mathrm{O}\\ \quad\;\; |\\ \mathrm{H_2C{-}CHOH{-}CH_3}\end{array}$$

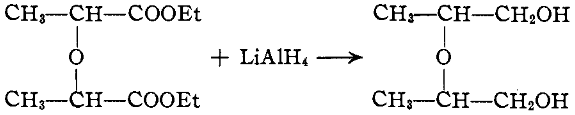
II, 2-(2-hydroxypropoxy)-1-propanol (primary-secondary alcohol)



$$\begin{array}{l}\mathrm{CH_3{-}CHOH{-}CH_2}\\ \qquad\qquad\;\; |\\ \qquad\qquad\;\; \mathrm{O}\\ \qquad\qquad\;\; |\\ \mathrm{CH_3{-}CHOH{-}CH_2}\end{array}$$

III, 1,1'-oxydi-2-propanol (disecondary alcohol)

The three isomers have been prepared and their physical properties determined. The diprimary alcohol I was prepared in 91% yield by the reduction of diethyl dilactate with lithium aluminum hydride.



$$\begin{array}{l}\mathrm{CH_3{-}CH{-}COOEt}\\ \quad\;\; |\\ \quad\;\; \mathrm{O}\\ \quad\;\; |\\ \mathrm{CH_3{-}CH{-}COOEt}\end{array} + \mathrm{LiAlH_4} \longrightarrow \begin{array}{l}\mathrm{CH_3{-}CH{-}CH_2OH}\\ \quad\;\; |\\ \quad\;\; \mathrm{O}\\ \quad\;\; |\\ \mathrm{CH_3{-}CH{-}CH_2OH}\end{array}$$

The synthesis of the primary-secondary isomer (II) was based on the work of earlier investigators[1-4] which showed that addition of propylene oxide to an alcohol with alkaline catalyst yields largely a secondary alcohol. On this basis 1-methoxy-2-propanol[1] was treated with propylene oxide using sodium catalyst to give 1-(2-methoxyisopropoxy)-2-propanol, b.p. 76–78° (10 mm.). This was heated with 48% hydrobromic acid to give methyl bromide and 2-(2-hydroxypropoxy)-1-propanol in 52% yield.

The disecondary isomer (III) was prepared by treating propylene oxide with propylene glycol using sodium as the catalyst. This gave largely the disecondary isomer since propylene oxide reacts much faster with a primary alcohol than with a secondary alcohol. The product was distilled and on recrystallization from diethyl ether melted at 45–46.5°.

A study of infrared absorption curves (Fig. 1) in the region of 8 to 10 μ showed the three isomers to be distinctively different. The compounds were studied in 1% solution of carbon disulfide in 1-mm. cells.

The absorption curve for the ether linkage is designated by E, the primary OH curve by P and the secondary OH curve by S.

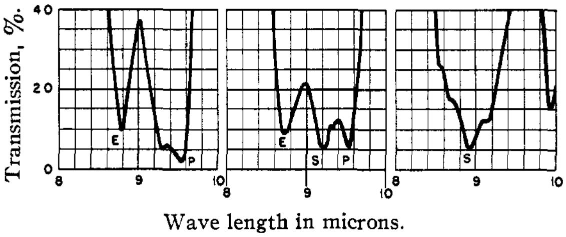


Fig. 1.—Left curve, 2,2'-oxydi-1-propanol; middle curve, 2-(2-hydroxypropoxy)-1-propanol; right curve, 1,1'-oxydi-2-propanol.

Experimental

I. **Preparation of 2,2'-Oxydi-1-propanol.**—The apparatus consisted of a 5-l., 5-neck flask equipped with a stirrer, thermometer, dropping funnel, nitrogen inlet and reflux condenser. The condenser was vented through a Dry Ice trap and calcium chloride drying tube.

After sweeping the flask with nitrogen, 45 g. (1.15 moles) of finely powdered lithium aluminum hydride was added. The flask was cooled in an ice–water-bath. With stirrer going and nitrogen bubbling through, 1500 g. of dry diethyl ether was added slowly. The ice-bath was removed and the mixture refluxed on a water-bath 3 hours to dissolve the lithium aluminum hydride. To this mixture 218 g. (1.08 mole) of dilactic acid diethyl ester[5] in 286 g. of dry diethyl ether was added dropwise over a period of two hours at 15–18°. The temperature was controlled by adding ice to the water-bath. The mixture was then slowly warmed to reflux and held at this temperature for 4 hours.

Fifty grams of ethyl acetate was added dropwise to destroy any unreacted lithium aluminum hydride, followed by slow addition of 250 cc. of water and finally 4–6 moles of 35% hydrochloric acid. The nitrogen was then shut off and the ether distilled off on a steam-bath. The still residue (966 g.) was passed through Dowex-50 cation exchange resin to remove the lithium and aluminum. The filtrate was distilled under vacuum to remove water and hydrochloric acid, and gave 122 g. (0.91 mole) of 2,2'-oxydi-1-propanol boiling at 102° at 5 mm. and at 225.7° at 760 mm. It did not solidify at −40° and had specific gravity 1.0316 (25/25), 1.0018 (60/4); $n^{25}\mathrm{D}$ 1.4410, $n^{60}\mathrm{D}$ 1.4296.

Anal. Calcd. for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.63; H, 10.53.

Its **bis-*p*-nitrobenzoate**, prepared in 86.5% yield, melted at 142–143°.

Anal. Calcd. for $C_{20}H_{20}N_2O_9$: N, 6.48. Found: N, 6.54.

Its **bis-triphenylmethyl ether**, prepared in 70% yield,[6] melted at 131–132°.

Anal. Calcd. for $C_{44}H_{42}O_3$: C, 85.40; H, 6.84. Found: C, 85.2; H, 7.0.

II. **Synthesis of 2-(2-Hydroxypropoxy)-1-propanol.**—The apparatus was the same as described under I. Nine hundred grams (10 moles) of 1-methoxy-2-propanol[1] and 4 g. of metallic sodium were added to the flask. The mixture was heated to 80° and 406 g. (7 moles) of propylene oxide was added dropwise at 80–100° over a period of 4 hours. The mixture was distilled on a 1¼" × 4' column packed with 3/16" KA2S stainless steel saddles at a 10/1 reflux ratio to give 430 g. (2.9 moles) of 1-(2-methoxyisopropoxy)-2-propanol, b.p. 76–78° (10 mm.). Two moles of this was mixed with 3 moles of 48% hydrogen bromide and refluxed at 80–108° until no more methyl bromide was liberated. The methyl bromide (88.5% of theory) was collected in a Dry Ice trap. The residue was passed through a bed of Amber-

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[1] H. C. Chitwood and B. T. Freure, THIS JOURNAL, **68**, 680 (1946).

[2] R. G. Kadesch, *ibid.*, **68**, 41 (1946).

[3] P. D. Bartlett, *ibid.*, **70**, 926 (1948).

[4] A. A. Petrov, *J. Gen. Chem.* (*U.S.S.R*), **14**, 1038 (1944).

[5] Pierre Vieles, *Ann. chim.*, [11] **3**, 143 (1935).

[6] Prepared according to M. K. Seikel and E. H. Huntress, THIS JOURNAL, **63**, 593 (1941).

lite IR4B anion exchange resin to remove the excess hydrogen bromide. The filtrate was distilled under vacuum to remove the water, and 139 g. (1.04 mole) of 2-(2-hydroxypropoxy)-1-propanol, b.p. 96–96.5° (4 mm.), 224° (760 mm.), were obtained. This is a 52% yield based on alcohol taken. The substance did not solidify at −40°. It possessed the following properties: sp. gr. 1.0229 (25/25), 0.9925 (60/4); n^{25}D 1.4391, n^{60}D 1.4283.

Anal. Calcd. for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.68; H, 10.45.

Its bis-*p*-nitrobenzoate, prepared in 85% yield, melted at 83–84°.

Anal. Calcd. for $C_{20}H_{20}N_2O_9$: N, 6.48. Found: N, 6.40.

III. **Preparation** of 1,1′-Oxydi-2-propanol.—The apparatus was the same as used in I above. Twenty moles (1520 g.) of propylene glycol and 16 g. of sodium metal were added to the flask under a nitrogen blanket and the mixture was heated to 105°. Twenty moles (1160 g.) of propylene oxide was added dropwise at 105–144° over a period of 3.5 hours. The mixture was distilled as in II above and 1092 g. (8.15 moles) of 1,1′-oxydi-2-propanol; b.p. 113–114° (10 mm.), 222.2° (760 mm.), yield 47.5%, was obtained. On recrystallizing from ether this material melted at 45–46.5°. It had the following properties: sp. gr. 0.9878 (60/4), n^{60}D 1.4284.

Anal. Calcd. for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.70; H, 10.50.

Its bis-*p*-nitrobenzoate, prepared in 96% yield, melted at 150–151°.

Anal. Calcd. for $C_{20}H_{20}N_2O_9$: N, 6.48. Found: N, 6.42.

Its **bis-triphenylmethyl** ether, prepared[6] in 75% yield, had m.p. 145–146°.

Anal. Calcd. for $C_{44}H_{42}O_3$: C, 85.40; H, 6.84. Found: C, 85.07; H, 6.84.

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The Iodine Complexes of Polyalkylbenzenes[1]

BY M. TAMRES, D. R. VIRZI AND S. SEARLES

RECEIVED JANUARY 31, 1953

In recent papers, Mulliken has proposed structures for the benzene complexes with silver ion[2] and with iodine.[2,3] His structure for the Ar·Ag$^+$ complex with the silver ion in the region between and somewhat above two carbon atoms in the aromatic ring, makes plausible the observation that continued methyl substitution in the ring eventually leads to a decrease in stability of the complex. (The association constant of silver ion with mesitylene is smaller than that with the xylenes or with toluene,[4] a result which is opposite to the normal inductive effect.) This decrease in stability may occur when there are no longer available two adjacent unsubstituted carbon atoms to serve as a site for the silver ion.[2] The fact that the complex with durene is more stable than that with mesitylene[5] is still in accord with this hypothesis.

Mulliken considered several structural possibilities for the Ar·I$_2$ complex. These are as follows (where the roman numerals and the capital letters in parentheses designate the models in references 2 and 3, respectively): the iodine molecule located along an edge or corner of the benzene ring with the iodine axis either in the plane of the ring (II or T and L), or perpendicular to the plane of the ring (III or E), or inclined to the plane of the ring (O); the iodine axis coinciding with the sixfold symmetry axis of benzene with the two iodine atoms on the same side of the benzene plane (IV or A), or on opposite sides of the benzene plane (V); the iodine molecule located with its center on the sixfold axis of symmetry of the aromatic ring, with the iodine axis being parallel and slightly above the plane of the aromatic ring (I or R). Of these possibilities, the one favored most strongly by Mulliken on the basis of spectroscopic and electrostatic principles is model R (or I). With this model it would be difficult to imagine that the methyl groups in polymethylbenzenes could interact sterically with the iodine molecule, as they apparently do with the silver ion, and one would expect hexamethylbenzene to be a stronger base toward iodine than any of the other methylbenzenes.[6] The results published recently by Andrews and Keefer[5] on the interaction of of polyalkylbenzenes with iodine and with iodine monochloride show that this is actually the case. Working independently in this Laboratory we also found this to be true, and our results on the interaction of several polyalkylbenzenes with iodine offer interesting comparison with the data of Andrews and Keefer.

The equilibrium constant of the complex, *K*, and the molar extinction coefficient of the complex, ϵ_c, were determined from the equation first derived by Benesi and Hildebrand.[7]

$$\frac{(I_2)l}{d_c} = \frac{1}{K\epsilon_c} \times \frac{1}{N_a} + \frac{1}{\epsilon_c}$$

The notation for this equation is similar to that which has been employed by Andrews and Keefer.[8] Plots of $(I_2)/d_c$ *versus* $1/N_a$ (based on at least four points for each aromatic compound) gave straight lines. Since ϵ_c and K are sensitively dependent upon the line drawn through the experimental points, the equation for the line was determined by the method of least squares and the values of ϵ_c and

TABLE I

WAVE LENGTHS OF MAXIMUM ABSORPTION, MOLAR EXTINCTION COEFFICIENTS AND EQUILIBRIUM CONSTANTS OF IODINE–AROMATIC COMPLEXES IN CARBON TETRACHLORIDE AT ROOM TEMPERATURE

Aromatic cpd.	λ_{max}, mμ	ϵ_c × 10^{-3}	*K*
Benzene	295	14.7	1.60[a]
Mesitylene	332	10.2	5.96[a]
Isodurene	339	8.70	6.87
Pentamethylbenzene	355	7.77	9.72
Hexamethylbenzene	371	6.69	15.2
Hexaethylbenzene	375	4.57	4.58

[a] H. A. Benesi and J. H. Hildebrand (ref. 7) report for benzene λ_{max} 297 mμ, ϵ_c 15.4 × 10^3, *K* 1.72; and for mesitylene λ_{max} 333 mμ, ϵ_c 9.3 × 10^3, *K* 7.2.

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(1) From the B.S. honor's thesis of Donald Robert Virzi submitted to the chemistry department, University of Illinois, June, 1952.

(2) R. S. Mulliken, THIS JOURNAL, **74**, 811 (1952).

(3) R. S. Mulliken, *ibid.*, **72**, 600 (1950).

(4) L. J. Andrews and R. M. Keefer, *ibid.*, **71**, 3644 (1949); **72**, 5034 (1950).

(5) L. J. Andrews and R. M. Keefer, *ibid.*, **74**, 4500 (1952).

(6) In a private discussion, Professor Mulliken agreed with this prediction.

(7) H. A. Benesi and J. H. Hildebrand, THIS JOURNAL, **71**, 2703 (1949).

(8) L. J. Andrews and R. M. Keefer, *ibid.*, **72**, 4677, 5170 (1950); *ibid.* **73**, 462 (1951).

K were then calculated. These data, together with the wave length of maximum absorption of the complex, are given in Table I.

In this work as in that of Benesi and Hildebrand,[7] $K = (\mathrm{Ar{\cdot}I_2})/N_a(\mathrm{I_2})$ is a dimensionless quantity, where N_a is the mole fraction of the aromatic compound in carbon tetrachloride and $(\mathrm{Ar{\cdot}I_2})$ and $(\mathrm{I_2})$ are the molar concentrations of the complex and free iodine, respectively. The equilibrium constant, K_c, of Andrews and Keefer[5] is in units of reciprocal moles per liter, *i.e.*, $K_c = (\mathrm{Ar{\cdot}I_2})/(\mathrm{Ar})(\mathrm{I_2})$ where (Ar) is the molar concentration of the aromatic compound in carbon tetrachloride. The relative values of the equilibrium constants for the two sets of data are in fair agreement[9]; this being true also for the $\lambda_{\max}$ and ϵ_c data.

Of the polymethylbenzenes which they investigated, Andrews and Keefer found that the interaction with iodine could be correlated qualitatively with the data of McCaulay and Lien[10] who reported on the interaction of the aromatics with $\mathrm{HF{-}BF_3}$. Our result for isodurene, which was not determined by Andrews and Keefer, is in agreement with this observation.

There are several differences between the two sets of data, however, which should be mentioned. In this work it is found that the equilibrium constant for the hexaethylbenzene complex with iodine is larger than that for the benzene complex, whereas Andrews and Keefer report the opposite to be more likely correct. Furthermore, our extinction coefficient (4.57×10^3) for the hexaethylbenzene complex is the smallest of any of the complexes studied here, whereas the value of Andrews and Keefer (16.7×10^3) was the largest of the complexes investigated by them.

Also it appears that, for the data of Table I at least, an increase in K as methyl groups are introduced in the benzene nucleus is accompanied by a corresponding decrease in ϵ_c. The product of ϵ_c and $\sqrt[3]{K}$ seems to be constant,[11] except possibly for mesitylene where the result is slightly high. This is borne out in Fig. 1 in which there is plotted ϵ_c *versus* $1/\sqrt[3]{K}$.

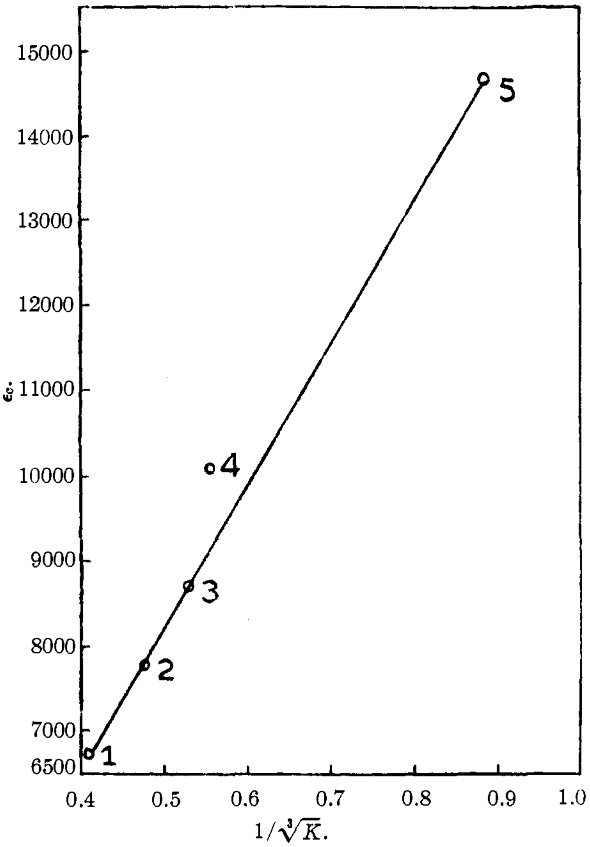

Fig. 1.—Relation between molar extinction coefficients and equilibrium constants for several aromatic–iodine complexes: 1, hexamethylbenzene; 2, pentamethylbenzene; 3, isodurene; 4, mesitylene; 5, benzene.

It was reported by Benesi and Hildebrand that increasing methyl substitution in benzene shifts the visible absorption peak of iodine dissolved in aromatic hydrocarbons toward shorter wave lengths. From the results in Table II, this effect does not seem apparent at first. The lack of shift toward shorter wave lengths for the polyalkylbenzenes may be due to the dilution of the system with carbon tetrachloride. This would cause a shift in absorption toward longer wave lengths, that is, toward the absorption in pure carbon tetrachloride. Also it may be that some overlap in the absorption curves of the free iodine and of the complex occurs since the absorption maxima of the two are not far apart. Dilution with carbon tetrachloride favors a larger free iodine to complex ratio, which may account for the shift to longer wave lengths. For the pentamethyl-, hexamethyl- and hexaethylbenzene data in Table II, the per cent. of free iodine is approximately 57, 69 and 83%, respectively.

TABLE II

VISIBLE ABSORPTION DATA

Solvent	Mole fraction in carbon tetrachloride	$(\mathrm{I_2}) \times 10^4$, moles/l.	d_0	$\epsilon_{\max}$[a]	$\lambda_{\max}$ mμ
Carbon tetrachloride	1.0000	23.22	2.10	904	517
Benzene[b]	1.0000	6.91	1.45	1050	500
Mesitylene[b]	1.0000	9.20	2.21	1200	490
Isodurene	0.3476	2.13	0.21	987	495
	.2165	4.66	0.47	1001	500
	.1554	5.18	0.50	964	505
	.0748	7.77	0.73	942	503
Pentamethylbenzene	.0770	3.80	0.33	870	503
Hexamethylbenzene	.0290	19.12	1.94	1023	506
Hexaethylbenzene	.0438	19.34	1.86	964	510

[a] Calculated by use of the Beer–Lambert equation assuming all the iodine to be free. [b] Data from Benesi and Hildebrand (ref. 7).

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(9) The ratio of (Ar) to N_a for each aromatic compound is a variable which depends upon the composition. The limiting ratio of (Ar) to N_a as $N_a \rightarrow 0$ is $1000\ \rho/M$ where ρ and M are the density and molecular weight, respectively, of carbon tetrachloride. If this constant of 10.3 is employed to convert K into K_c the following results are obtained which may be compared with those of Andrews and Keefer given in parentheses: benzene 0.15 (0.15); mesitylene 0.58 (0.82); pentamethylbenzene 0.94 (0.88); hexamethylbenzene 1.47 (1.35); and hexaethylbenzene 0.44 (0.13).

(10) D. A. McCaulay and A. P. Lien, THIS JOURNAL, **73**, 2013 (1951).

(11) Note Added to Proof.—The recent literature survey by H. McConnell, J. S. Ham and J. R. Platt (*J. Chem. Phys.*, **21**, 66 (1953)) revealed no strong correlation between the molar extinction coefficients and the equilibrium constants of the complexes.

It is of interest to note that increasing methyl substitution in benzene affects λ_{max} of the complex as well, but in this case the shift is toward longer wave lengths. If this shift were to be employed as a qualitative criterion for the change in basicity of the electron donor molecule[12] then the low result for the equilibrium constant of the hexaethylbenzene–iodine complex could be attributed to fewer, though comparatively strongly bound, associated molecules as a consequence of unfavorable steric requirements. Consideration of molecular models, as pointed out by Andrews and Keefer,[5] indicates that an ethyl group can fold back and overlap a small area above the aromatic ring.

The investigation of steric factors in the formation of iodine complexes with polymethylbenzenes cannot be considered as confirming uniquely the Mulliken model R for the $Ar \cdot I_2$ complex. Although structures in which the iodine molecule is at a corner or edge of the benzene ring (as in models L, E and O) now appear highly improbable, structures other than R in which the iodine molecule is centrally located with respect to the benzene ring (as in model A) still remain. Comparing the possibilities R and A for the hexaethylbenzene–iodine complex, the one which would be predicted the more likely to result in steric interaction between the iodine molecule and the ethyl groups is structure R. But the fact that a steric effect is observed experimentally does not necessarily eliminate model A, although it is a point in support of the Mulliken proposal.

Experimental

Materials.—Carbon tetrachloride and the liquid hydrocarbons were purified by the distillation procedure previously described.[13] Carbon tetrachloride, $n^{20}D$ 1.4609, was purified as specified by Fieser.[14] The method of Benesi and Hildebrand,[7] except for the mercury treatment, was used to purify benzene and mesitylene, $n^{20}D$ of 1.5008 and 1.4965, respectively. Isodurene (prepared by the Organic Manufacturing Laboratory at the University of Illinois) was dried over calcium chloride and distilled, $n^{20}D$ 1.5095.

Pentamethylbenzene, hexamethylbenzene and hexaethylbenzene were made available to us by Dr. A. P. Lien. Several months of standing in capped vials did not affect the purity. Prior to use the uncorrected melting points were 52–53°, 164 and 127°, respectively.

Reagent grade iodine from the General Chemicals Company was sublimed and stored over phosphorus pentoxide in a desiccator.

Procedure.—The procedure for obtaining absorption spectra data was the same as that described by Benesi and Hildebrand.[7] The instrument employed was a Cary Recording Quartz Spectrophotometer with a matched pair of 1-cm. glass-stoppered quartz cells.

A standard iodine stock solution was prepared at room temperature by dissolving a known weight of iodine (0.3105 g.) in 100 ml. of carbon tetrachloride. More dilute solutions were prepared, as required, by taking a known aliquot of the stock solution and diluting with carbon tetrachloride in a calibrated 25-ml. volumetric flask. The concentrations of the iodine solutions were checked spectrophotometrically from time to time.

A solution of each aromatic compound was prepared by dissolving a known weight of the compound in a known weight of carbon tetrachloride. The use of solutions was necessary for the solid aromatic compounds, but solutions of the liquid aromatics in carbon tetrachloride were made also in order to study the same range of concentrations. Aliquots were taken by means of calibrated pipets and each aliquot was weighed. To each was added a known weight of iodine solution, delivered through a calibrated pipet, and the absorption measurement was then made immediately. From these data, the mole fraction of the aromatic compound and the molar concentration of iodine could be calculated. The ranges of mole fractions of the aromatic compounds in the mixtures thus prepared were: benzene 0.901–0.0239; mesitylene 0.366–0.0317; isodurene 0.216–0.0748; pentamethylbenzene 0.0770–0.0254; hexamethylbenzene 0.0594–0.0196; hexaethylbenzene 0.0805–0.0253.

Acknowledgment.—We are indebted to Dr. A. P. Lien of the Standard Oil Company of Indiana for the pentamethylbenzene, hexamethylbenzene and hexaethylbenzene which he generously provided.

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[12] The data of this investigation and that of Andrews and Keefer suggest that this may apply to closely related derivatives of a parent compound. It does not appear to apply to unrelated compounds. Note Added to Proof.—McConnell, Ham and Platt[11] have shown that there is an inverse linear relationship between the ionization potential, I_p, of the electron donor molecule and the wave length of maximum absorption, λ_{max}, of its complex with iodine. The ionization potential increases in the order: mesitylene < *o*- or *m*- xylene < toluene < benzene. This is the same order for decreasing stability of the complex. Since the magnitude of the equilibrium complex, K, is regarded as an indication of basic strength (barring steric factors) as well as a measure of stability, there is some justification for relating K with λ_{max}. A plot of ϵ_c *versus* λ_{max} for benzene and its methyl derivatives (data of Table I) gives a smooth curve except for mesitylene which, as was noted previously, does not lie on the ϵ_c *versus* $1/\sqrt[3]{K}$ graph of Fig. 1.

There is some doubt at present that the K and λ_{max} values for the iodine complexes of all electron donor molecules can be related by a single expression. Diethyl ether, which lies on the linear I_p *versus* λ_{max} plot, has an ionization potential which is considerably greater than that for benzene. If taken to mean that the equilibrium constant for the diethyl ether–iodine complex is less than that for the benzene–iodine complex, this would constitute an unusual reversal of expected basic characteristics. There is a need for additional data for the K values of iodine with other electron donors. But until such data are forthcoming, it seems best to restrict the use of λ_{max} as a qualitative measure of basicity to closely related compounds.

[13] M. Tamres, THIS JOURNAL, **74**, 3375 (1952).

[14] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1935, p. 309.

The Reaction of Trifluoroacetone with Acetylene

BY PAUL TARRANT, D. A. WARNER AND R. E. TAYLOR

RECEIVED MARCH 30, 1953

It has been claimed[1] that trifluoroacetone reacts with ethynylmagnesium bromide to give a product which was dehydrated with oxalic acid to 3-trifluoromethylbutyn-1-ene-3. The acetylenic compound was then treated with hydrogen to yield 3-trifluoromethylbutadiene-1,3. No physical constants nor analyses were given for the intermediate compounds.

As part of the program in this Laboratory on the preparation of fluoroölefins for the Arctic rubber program for the Office of Quartermaster General, it seemed desirable to repeat the experiments described in the patent to obtain trifluoromethylbutadiene. Although a number of runs were carried out with trifluoroacetone and the Grignard reagent prepared from ethylmagnesium bromide, no product which could be dehydrated with either magnesium sulfate or oxalic acid was obtained. However, there was obtained some 3-trifluoromethyl-1-butyne-3-ol and a larger amount of 2,5-

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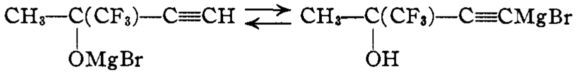
[1] H. M. Hill and E. B. Towne, U. S. Patent 2,490,753 (Dec. 6, 1949).

bis-(trifluoromethyl)-3-hexyne-2,5-diol whose properties were determined.

Since low yields of the carbinol were obtained using the Grignard reagent, a study was made of the reaction of acetylides of sodium and potassium with trifluoroacetone in various solvents. The highest yield of 3-trifluoromethyl-1-butyne-3-ol (15%) was obtained by the use of aqueous potassium hydroxide as the condensing agent; the glycol was still the chief product (37%). Apparently trifluoroacetone does not react readily in liquid ammonia since a 55% recovery was obtained when the ketone was treated with sodium acetylide in ammonia. No reaction occurred between trifluoroacetone and potassium acetylide in dibutyl cellosolve using Bergmann's procedure[2] at −40° or at −20°. The method of Smith[3] using butanol and xylene also failed to give either the alcohol or the glycol.

Evidence has been found that the formation of 3-trifluoromethyl-1-butyne-3-ol was hindered by a redistribution of the ionic charge in the salt of the alcohol which is the initial product in all of these reactions. The result of this shift is a new carbanion from the substituted acetylene. Thus in the case of the Grignard reagent, the following equilibrium may exist



$$CH_3{-}\underset{\displaystyle OMgBr}{\underset{|}{C}}(CF_3){-}C{\equiv}CH \rightleftarrows CH_3{-}\underset{\displaystyle OH}{\underset{|}{C}}(CF_3){-}C{\equiv}CMgBr$$

The position of the equilibrium could not be readily determined since the new acetylenic Grignard reagent reacted immediately with a second molecule of trifluoroacetone to give the glycol, 2,5-bis-(trifluoromethyl)-3-hexyne-2,5-diol, which was the principal product in all cases. An analogous situation exists also in the case of the alkali metal acetylides.

It was found that, in the case of the Grignard reaction, the time elapsing between the addition of the trifluoroacetone to the solution of ethynylmagnesium bromide and hydrolysis of the adduct exerted a pronounced influence on the yield of the alcohol. For example, in a run standing at 20° under an inert atmosphere for 36 hours, a 7.72% conversion to the alcohol was obtained; in a run standing for two hours, a 13.8% conversion was obtained. In each case the conversion to the glycol exceeded 32%. Froning and Hennion[4] have found that increased yields of 2,5-dimethyl-3-hexyn-2,5-diol were obtained by allowing the reaction product of acetone and sodium acetylide to stand for several days; the initial product from trifluoroacetone and acetylene seems even more sensitive to aging since overnight aging gave 32% of the glycol. Since it has been established[5,6] that a quantitative yield of HC≡CNa is obtained on the reaction of sodium with excess acetylene in liquid ammonia solution, the formation of the glycol must be a consequence of the charge redistribution in the initial adduct. Since it further appears from the evidence presented above that this redistribution is quite rapid in the anion from 3-trifluoromethyl-1-butyne-3-ol it may be concluded that the same effect is present in the Grignard synthesis with the result that a low yield of the alcohol is obtained there as well.

Experimental

Source of Reagents.—Trifluoroacetone was prepared by the Claisen type condensation of ethyl trifluoroacetate with ethyl acetate followed by decomposition of the resulting ethyl trifluoroacetoacetate with 35% sulfuric acid. The crude trifluoroacetone was distilled from phosphoric oxide to obtain anhydrous material, b.p. 21–23°.

Acetylene was delivered from a tank, scrubbed with water, 95% H_2SO_4, dried over anhydrous $CaCl_2$ and Drierite.

Anhydrous methanol was prepared by distillation of the commercial material from CaO.

The Grignard Reaction.[1]—One mole of ethylmagnesium bromide was prepared under nitrogen in a 1000-ml. three neck flask fitted with a stirrer, a Y tube carrying a gas inlet tube and an ice-water cooled reflux condenser, and a jacketed dropping funnel. Acetylene was bubbled into the stirred solution at a rate of about 100 ml. per minute for four hours; the rate was then reduced to about 20 ml. per minute while 0.80 mole of trifluoroacetone was added during one hour. The addition of acetylene was stopped and the mixture refluxed for 30 minutes. It was cooled to room temperature and poured into 100 ml. of concd. hydrochloric acid and 200 g. of ice. The water layer was separated, saturated with sodium chloride and extracted with fresh ether. The ether was stripped off and the residue steam distilled.

The liquid steam distillate was dried over magnesium sulfate followed by Drierite and rectified. If the drying process had been thorough, there was obtained 10–15 g. (9–13%) of a water-white liquid of pleasant odor, b.p. 97–98°, n^{25}_D 1.3521, d^{25}_4 1.160.

Anal. Calcd. for $C_5H_5F_3O$: MR_D, 24.52; mol. wt., 138.09; F, 41.28. Found: MR_D, 25.69; mol. wt., 139; F, 40.82; AR_F, 1.39.

In all cases, if the solid residue were recrystallized from ethylene chloride, there was obtained a 30–40% yield of the glycol as white, silky needles, m.p. 108–108.5°.

Anal. Calcd. for $C_8H_9F_6O_2$: mol. wt., 250.1; F, 45.48. Found: mol. wt., 244; F, 45.4.

Sodium Acetylide in Liquid Ammonia.—One mole of sodium acetylide was prepared in 1.2 l. of liquid ammonia according to the procedure already described.[3] The flask was then partially immersed in a bath of Dry Ice and acetone, and one mole of trifluoroacetone added in one hour. Acetylene was bubbled into the solution for an additional 15 minutes before the stirrer was stopped to allow the ammonia to evaporate overnight. The residue was covered with 150 ml. of ether while iced 35% sulfuric acid was added to dissolve the solid. From this point the procedure was that described for the Grignard reaction. Distillation yielded 62 g. of trifluoroacetone (55%), 15 g. of 3-trifluoromethyl-1-butyne-3-ol (11%) and 22 g. of the glycol (18%).

A run in which the sodium was converted to sodamide before addition of the acetylene gave almost identical results.

Potassium Hydroxide in Water.—In a 200-ml. flask fitted with a stirrer, gas inlet tube and ice-water cooled reflux condenser 0.5 mole of trifluoroacetone was added to 40 ml. of 2.5% aqueous potassium hydroxide. Acetylene was bubbled into the solution for six hours. At the end of the time 1.5 g. of sodium bicarbonate was added, followed by 10 ml. of water. The layers so formed were separated; the lower layer deposited 12 g. of glycol. The liquid portion gave 10 g. (14.5%) of alcohol on drying and distillation. An additional 5 g. of glycol was obtained on acidification of the upper layer; total conversion to glycol, 36.8%.

Potassium Hydroxide in Methanol.—One fourth mole of trifluoroacetone was cooled to 0° in a 200-ml. flask and saturated with acetylene. Sixty ml. of 2% methanolic potassium hydroxide was added dropwise while the addition of acetylene was continued. After four hours the acetylene was stopped and 1.5 g. of $NaHCO_3$ was added. The liquid was filtered and dried over Drierite. After removal of the

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[2] E. D. Bergmann, *Selecta Chim.*, No. 9, 24 (1950).

[3] E. F. Smith, U. S. Patent 2,385,547 (Sept. 25, 1945).

[4] J. F. Froning and G. F. Hennion, THIS JOURNAL, **62**, 653 (1940).

[5] T. H. Vaughn, G. F. Hennion, R. R. Vogt and J. A. Nieuwland, *J. Org. Chem.*, **2**, 1 (1937).

[6] K. N. Campbell, B. K. Campbell and L. T. Eby, THIS JOURNAL, **60**, 2882 (1938).

methanol, there remained 22 g. of undistillable material, presumably glycol (70.5%).

Acknowledgments.—We wish to acknowledge with thanks the help of the analytical section of the M. W. Kellogg Co., who ran the fluorine analysis on the 2,5-bis-(trifluoromethyl)-3-hexyne-2,5-diol. We appreciate the encouragement of Dr. J. C. Montermoso of the Research and Development Division of the Office of the Quartermaster General.

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Infrared Absorption of Some Steroid Digitonides

BY RICHARD B. TURNER

RECEIVED MARCH 16, 1953

Although formation of stable molecular compounds (digitonides) from the saponin, digitonin, and steroids possessing a C_3 hydroxyl group is known to be ultimately dependent upon a 3β-orientation of the latter group,[1] little information is available regarding the nature of the secondary valence forces responsible for complex formation. In particular, the extent to which, in polyfunctional molecules, groups other than the 3β-hydroxyl group may be involved, through hydrogen bonding or other associative phenomena, has not been ascertained. The work reported in this communication was undertaken in order to examine the effects of digitonide formation upon the characteristic infrared absorption frequencies of carbonyl groups located at various positions in the steroid nucleus. 3β-Hydroxy steroids possessing carbonyl functions at positions 6, 7, 11, 12, 17 and 20 were investigated in this connection. Two α,β-unsaturated ketonic derivatives were also included. Owing to insolubility of the digitonides and to the possibility of dissociation in solution, measurements were made on suspensions of the crystalline complexes in mineral oil. Absorption data for the free sterols in mineral oil and in carbon disulfide solution are listed for comparison (Table I).

TABLE I

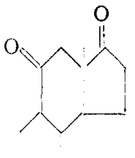
INFRARED ABSORPTION OF STEROID DIGITONIDES

No.	Compound*	Maxima, cm.$^{-1}$ (Mineral oil) Sterol	Digitonide	(CS_2 soln.) Sterol
1	6-Ketocholestanol	1692	1704	1715
2	7-Ketocholestanol[a]	1691	1700	1715
3	11-Ketoergostenol[b]	1693	1704	1709
4	Hecogenin[c]	1688	1697	1712
5	Δ^5-Androstene-3β-ol-17-one	1720	1735	1742
6	Δ^5-Pregnene-3β-ol-20-one	1673	1697	1709
7	Δ^4-Cholestene-3β-ol-6-one[a]	1666	1677	1692
8	7-Ketocholesterol[a]	1660	1675	1675

* Compounds indicated by lettered superscripts were furnished through the kindness of the following investigators: (a) L. F. Fieser, Harvard University, Cambridge, Mass. (sample no. 7 represents a highly purified preparation, m.p. 155.5–156.5°), (b) M. Tishler, Merck and Co., Rahway, N. J., (c) G. Mueller, University of Tennessee, Nashville, Tenn.

From inspection of the data (columns 1 and 2) it is clear that digitonide formation is accompanied by small, but significant, displacements (8 to 24 cm.$^{-1}$) of the carbonyl stretching maxima toward higher frequencies in all cases investigated. These displacements correspond to *increases* in the force constants of the carbon–oxygen double bonds. Since shifts to lower frequencies, associated with *decreases* in the C=O force constants, result from hydrogen bonding involving carbonyl groups,[2,3] participation of forces of this kind in stabilization of the digitonides would appear to be minimized.

High frequency displacements of the C=O stretching maxima have been observed by Jones and his collaborators[2,4] in a number of instances in which two appropriately oriented carbonyl groups occupy proximate positions in space. 11,17-Diketo steroids (I) and ketol acetates of types II and III[5] may be cited as illustrative of the several recorded examples of this phenomenon. Suppression of polar resonance structures (*cf.* IV) by mutual dipole repulsions, with consequent reinforcement of the double bond character of the respective carbonyl groups, may account for these observations.[6] However, the assumption that similar processes (for example, interactions between carbonyl groups of different molecules) are involved in the case of the digitonides, requires acceptance of a number of elaborate hypotheses.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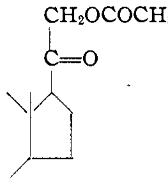
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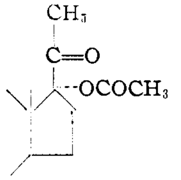
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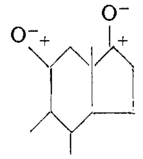
IV

A more plausible explanation for the spectral shifts encountered in the present work is based upon consideration of forces operative within the steroid crystals. The results of X-ray analyses indicate that hydrogen bonding, particularly that involving the C_3 hydroxyl group, plays an important part in determining the lattice structure of these substances.[7] Thus sterols possessing a single hydroxyl group (C_3) are doubled in the unit cell by head-to-head association of the hydroxyl functions

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[1] A discussion of digitonide formation is given by L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold Publ. Corp., New York, N. Y., 1949, pp. 102, 648.

[2] R. N. Jones, P. Humphries, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2820 (1952).

[3] R. S. Rasmussen, D. D. Tunnicliff and R. R. Brattain, *ibid.*, **71**, 1068 (1949); M. St. C. Flett, *J. Chem. Soc.*, 1441 (1948); M. M. Davies and G. B. B. M. Sutherland, *J. Chem. Phys.*, **6**, 755 (1938); W. Gordy, THIS JOURNAL, **60**, 605 (1938).

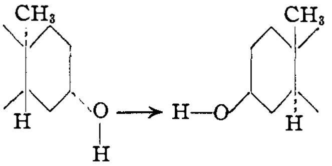
[4] R. N. Jones and K. Dobriner, *Vitamins and Hormones*, **7**, 293 (1949).

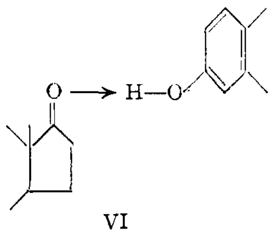
[5] R. B. Turner, THIS JOURNAL, **75**, 3489 (1953).

[6] *Cf.* A. D. Walsh, *Trans. Faraday Soc.*, **43**, 1158 (1947); R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

[7] D. Crowfoot, *Vitamins and Hormones*, **2**, 439 (1944).

of two contiguous molecules (*cf.* V). Substances, which, like estrone, possess hydroxylic and ketonic groups at opposite ends of the molecule are ordinarily propagated in the crystal by head to tail association as in VI. Disruption of these forces in solution by intervention of solvent molecules results in the expected shifts of carbonyl absorption in the direction of higher frequencies (Table I, column 3). The suggestion may be made that analogous frequency displacements in the digitonides are attributable to insulation, by the indifferent hydrocarbon nucleus of the digitonin molecule, of centers normally engaged in hydrogen bonding, with the further possibility of coördination of the 3β-hydroxyl groups with the glycosidic portion of the saponin.


V


VI

Ultraviolet absorption of 7-ketocholesterol (no. 8) and of the corresponding digitonide in alcohol solution has also been investigated. Both substances show maximum absorption at 237.5 mμ with molar extinction coefficients of 14,000 and 12,600, respectively. Interpretation of these results is unfortunately complicated by the possibility of dissociation of the digitonide in the dilute solution employed.

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Isolation and Identification of Quercetin and Some Quercetin Glycosides from Plums (*Prunus Salicina*)

BY BYRON L. WILLIAMS AND SIMON H. WENDER

RECEIVED APRIL 6, 1953

This paper reports an extension of a series of studies of the flavonols and their glycosides present in fruits. Williams, *et al.*, have previously isolated and identified quercetin (3,3',4',5,7-pentahydroxyflavone) and isoquercitrin (quercetin-3-glucoside) from grapes,[1] black currants[2] and apricots.[3] This paper reports the isolation and identification of quercetin, isoquercitrin, quercitrin (quercetin-3-rhamnoside) and a quercetin-3-arabinoside from yellow plums.

Experimental

Fifty pounds of ripe California yellow plums, *Prunus Salicina*, of the 1952 season were processed through a wet grinder with the whole fruit including the seeds and skins being ground. After 2 hours extraction with 20 gal. of distilled water at boiling temperature, the extract was filtered, then treated on an ion exchange column and later on a Magnesol column by the procedures previously used by Williams and Wender[3] for apricots. Flavonoid material was adsorbed at the top of the Magnesol column giving a zone about 40 mm. wide. The chromatogram was developed with ethyl acetate saturated with water. A zone about 30 mm. wide, yellow under ultraviolet light but not detectable in the visible, moved off the column first. The contents of this zone were found to be non-flavonoid and so were not studied further. The next zone, which will be called flavonoid fraction I, was yellow in the visible and also yellow under ultraviolet light, and its major component was later identified as quercetin. The next zone eluted, flavonoid fraction II, moved very close to the first. It was brown under ultraviolet light and yellow in the visible, and its flavonoid compound was later identified as quercetin-3-arabinoside.

The next zone eluted off the column (flavonoid fraction III) was brown in ultraviolet light and yellow in the visible, and was later shown to be a mixture of quercitrin and of a quercetin glucoside not identical with either isoquercitrin or quercimeritrin (quercetin-7-glucoside). The glucoside of fraction III has not been definitely identified as yet. The next eluted fraction (IV) was yellow in the visible and red-brown under ultraviolet light and its flavonoid was later identified as isoquercitrin. Each of the four fractions was recovered from the ethyl acetate solution by concentrating the eluate *in vacuo* to about 3 ml. and adding 10 ml. of pentane, followed by centrifugation and decantation.

Identification of Quercetin.—The quercetin zone eluted from the column was further purified as follows: The impure solid was dissolved in 10 ml. of ethyl alcohol, put on paper sheets (20 × 60 cm.) of Whatman No. 1 paper, chromatographed in 60% acetic acid–water and then air-dried for 4 hr. The resulting yellow zone on each paper at an R_f of about 0.40 was cut out and the pigment eluted with 95% ethyl alcohol in an air-tight chamber. The combined eluate from 25 sheets was concentrated to 0.5 ml. and then 10 ml. of boiling water was added. The yellow solid was separated, crystallized and identified as quercetin by the methods described in previous studies by Ice and Wender[4]; yield approximately 50 mg.

Identification of Quercetin-3-arabinoside.—The solid from fraction II was purified and then identified as quercetin-3-arabinoside by procedures similar to those reported for the isolation of this compound from the leaves of *Vaccinium myrtillus* by Ice and Wender.[4] The highly purified crystals had a m.p. 214–216°; approximate yield 16 mg.

Identification of Quercitrin.—The solid from flavonoid fraction III from the column was dissolved in 15 ml. of ethyl alcohol and put on paper strips in the manner described in previous paragraphs. The strips were first chromatographed using 15% acetic acid–water. The yellow zone at R_f about 0.6 (approximately 5 cm. wide) was cut out and eluted. Inasmuch as this zone was more dispersed than usual for the quantity recovered, a sugar analysis was made. Three mg. of the solid was hydrolyzed by refluxing for 2 hr. with 2% sulfuric acid, then the filtrate was neutralized and chromatographed as described under fraction II. By this procedure, both rhamnose and glucose were found to be present. Since the known quercetin disaccharides do not readily move on a Magnesol adsorption column with wet ethyl acetate as the chromatographing agent, and zone III did, this would indicate that zone III was most likely a mixture of a quercetin glucoside and a quercetin rhamnoside. This solid was, therefore, dissolved in ethyl alcohol once more and again put on fresh paper strips and chromatographed in 5% acetic acid–water. Each strip was loaded with 0.5 mg. of solid as before, but this time the strips were allowed to run for 14 hours. This brought the forward end of the zone to the lower end of the strip. The zone was about 10 cm. wide. The strips were allowed to air dry 3 hours, then a strip 1 cm. wide was cut out of the center of this zone and discarded. The forward part of the zone was eluted with ethyl alcohol in a leaching chamber, the alcohol evaporated, and the solid recrystallized as described under

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[1] B. L. Williams and S. H. Wender, THIS JOURNAL, **74**, 4372 (1952).

[2] B. L. Williams, C. H. Ice and S. H. Wender, *ibid.*, **74**, 4566 (1952).

[3] B. L. Williams and S. H. Wender, *Arch. Biochem. Biophys.*, **43**, 319 (1953).

[4] C. H. Ice and S. H. Wender, THIS JOURNAL, **75**, 50 (1953).

fraction II. Hydrolysis and subsequent sugar analysis by paper chromatography now showed rhamnose to be the only sugar present. The processing of the back part of the zone will be discussed in the next section. The yellow solid obtained from the combined eluates from the first (forward) part of the zone was recrystallized three times, then dried at 100° for 1 hr. It had a m.p. 183–184°, as did authentic quercitrin. No lowering of the melting point occurred on admixture of the two, and the isolated quercitrin showed no separation from authentic quercitrin by paper chromatography. One of the components (the forward portion) of fraction III from the column has, therefore, been identified as quercitrin; yield approximately 12 mg.

Properties of a Quercetin Glucoside.—The back part of the zone from the paper strips mentioned above was eluted, placed back again on fresh paper strips as before, and the strips chromatographed in 5% acetic acid. After 14 hours the new zone was about 5 cm. wide. The forward 2 cm. was cut off and discarded. The back 3 cm. was eluted and the ethyl alcohol evaporated and the solid hydrolyzed by refluxing for 2 hr. with 2% sulfuric acid. A sugar analysis made as described above showed glucose to be present as the predominant sugar with only a trace of rhamnose left from the quercitrin. The solid formed in the hydrolysis was identified as quercetin in the same manner as described for fraction I. Lack of sufficient material prevented further meaningful characterization of this compound. It may be identical with the quercetin glucoside reported, but not positively identified, from apricots.[3] It does show separation from both isoquercitrin and quercimeritrin on paper chromatograms processed in 15% acetic acid. Final yield of slightly impure product was about 5 mg.

Identification of Isoquercitrin.—The solid from flavonoid fraction IV was dissolved in 10 ml. of ethyl alcohol and put on strips by the procedure already described. The strips were processed in 15% acetic acid, air-dried for 3 hr., and the zone at R_f 0.45 was cut out and eluted with ethyl alcohol in an air-tight chamber. A total of 40 strips was processed, and after evaporation of the alcohol the solid was recrystallized eight times from hot water by cooling. The solid was dried at 110° for 1 hr. yielding a m.p. of 225–227°. It was identified as isoquercitrin by the methods previously described for this compound in *Vaccinium myrtillus*[4]; yield approximately 20 mg.

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The Preparation of Nicotinyl Chloride

BY H. N. WINGFIELD, JR., W. R. HARLAN AND H. R. HANMER

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Procedures for the preparation of nicotinyl chloride now in use seem to be modifications of the method of Meyer and Graf.[1] Salts of nicotinic acid are treated in various solvents and under varying conditions with thionyl chloride, and the product is vacuum distilled from pyridine or quinoline. The processes are tedious and often unsatisfactory.

We have now developed a more convenient method of preparation based upon the work of Adams and Ulich.[2] Potassium nicotinate suspended in benzene is treated with oxalyl chloride. The by-products, potassium chloride, carbon dioxide and carbon monoxide, are insoluble in benzene or are gases. No hydrogen chloride is formed and hence no hydrochloride. The nicotinyl chloride may be used immediately in the reaction flask in benzene solution, or siphoned off under anhydrous conditions, or distilled under vacuum after removal of the solvent.

Experimental

Sixteen and one-tenth grams of potassium nicotinate, which had been ground to pass a 100-mesh sieve and dried in an oven at 135°, and 75 ml. of anhydrous benzene was placed in a three-necked flask which was equipped with a stirrer and reflux condenser closed with a drying tube. The flask and contents were chilled in an ice-bath, and then 12.5 g. of oxalyl chloride in 25 ml. of anhydrous benzene was added at such a rate that the temperature remained low. Stirring was continued and 15 to 20 minutes after all the oxalyl chloride had been added, the unmelted ice in the bath was removed. The bath was allowed to come to room temperature, and heating was begun at a rate such that the bath began to simmer in about 30 minutes. After an additional 30 minutes heating at this temperature, the flask was allowed to cool. The cooled solution was siphoned off under anhydrous conditions and fractionated. The oily residue distilled at 75–90° (10–12 mm.). The yield was 85% or better.

Anal. Calcd. for C_6H_4ClNO: Cl, 24.70. Found: Cl, 24.82. On exposure to the air the oily chloride soon solidified to nicotinic acid hydrochloride.

Anal. Calcd. for $C_6H_6ClNO_2$: Cl, 22.01. Found: Cl, 22.09. A sample of the oily acyl chloride treated with absolute ethanol formed ethyl nicotinate, b.p. 222–224°.

The preparation was successful using 0.5 molar proportions. Sodium nicotinate did not give as good results as the potassium salt.

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[1] H. Meyer and R. Graf, *Ber.*, **61**, 2205 (1928).

[2] Roger Adams and L. H. Ulich, THIS JOURNAL, **42**, 599 (1920).

The Neutron Irradiation of Crystalline Vitamin B_{12}

BY D. T. WOODBURY AND CHARLES ROSENBLUM

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Vitamin B_{12} is a hexacovalent coördination complex of cobalt with the empirical formula[1,2] $C_{61-64}H_{86-92}N_{14}O_{14}PCo$. It is labeled[3,4] with radioactive cobalt by adding cobalt 60 to the fermentation medium in which it is produced. Direct activation of cobalt in crystalline vitamin B_{12} by neutron irradiation in a pile was thought to be improbable because of the relatively high temperatures of such a nuclear reactor, and because the high γ-ray recoil energy[5] involved in the formation of a cobalt 60 atom is far in excess of normal bond energies and should result in ejection of the radioactive cobalt atom. Radioactivation by exchange with the free Co^{60} atom is also unlikely because of the exchange stability[6] of the central cobalt atom.

In view of a report[7] that such direct activation was possible, two 21-mg. samples of crystalline vitamin were irradiated in evacuated, sealed quartz ampules in the Brookhaven National Laboratories pile for $\simeq$ 48 hours and 138

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[1] N. G. Brink, D. E. Wolf, E. Kaczka, E. L. Rickes, F. R. Koniuszy, T. R. Wood and K. Folkers, THIS JOURNAL, **71**, 1854 (1949).

[2] J. F. Alicino, *ibid.*, **73**, 405 (1951).

[3] L. Chaiet, C. Rosenblum and D. T. Woodbury, *Science*, **111**, 601 (1950).

[4] C. Rosenblum and D. T. Woodbury, *ibid.*, **113**, 215 (1951).

[5] A. C. Wahl and N. A. Bonner, "Radioactivity Applied to Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 245.

[6] R. N. Boos, C. Rosenblum and D. T. Woodbury, THIS JOURNAL, **73**, 5446 (1951).

[7] R. C. Anderson and Y. Delabarre, *ibid.*, **73**, 4051 (1951).

hours at average fluxes of 3.2×10^{12} and 2.6×10^{12} neutrons/cm.^{2}/sec., respectively, and the products examined for their radioactive vitamin content. The nominal specific activities due to radioactive cobalt produced were 0.18 and 1.7 μc./mg., as determined by γ-ray comparison with a Bureau of Standards Co^{60} standard. The presence of P^{32} was also demonstrated by β-ray range and decay measurements.

Absorption spectra of the capsule contents in aqueous solution indicated losses of B$_{12}$ amounting to 5 and 19%, respectively, for the 2-days and 6-day irradiated samples. That the induced radioactivity was not necessarily associated with residual vitamin was demonstrated by treating the aqueous solutions buffered to pH 6 with a carbon tetrachloride solution of dithizone to remove free cobalt, and by extracting free B$_{12}$-like materials with benzyl alcohol after addition of $(NH_4)_2SO_4$ to the aqueous solutions. Thus extraction of aliquots of the 2-day sample with dithizone and with benzyl alcohol showed that 80% of the radioactivity was present as free cobalt and that only 20% was extractable by the alcohol. These measurements were made by gamma ray counting of evaporation residues with a thin window Geiger tube through a thick aluminum absorber (848 mg./cm.^{2}), and represent only Co^{60}. The sample irradiated for 6 days contained only $\simeq 26\%$ of the radioactivity in the form of free cobalt, which is interpreted as indicating secondary reactions of liberated cobalt, such as complex formation or isotope exchange, with decomposition products from the vitamin.

The bulk of the latter (6-day) sample was treated with cyanide to convert any B$_{12a}$ or other analogs possibly present to vitamin B$_{12}$, and subjected to extensive purification involving, in succession free cobalt removal, solvent extraction, precipitation, chromatography on alumina and crystallization from acetone. At no stage was a material with constant specific activity obtained. Thus the product eluted with methanol from alumina with an over-all yield of 65% had a low activity of 0.069 μc./mg.; and the crystallized material, obtained in 49% yield, had the still lower specific activity of 0.045 μc./mg. The latter material was subjected further to an 8-tube countercurrent distribution in the system water–benzyl alcohol. Color and radioactivity measurements are shown in Table I as per cent. of total. These fignres are based on the absorbancies of solutions at 3610 Å., and upon the β-ray activities of evaporation residues determined with a thin window Geiger tube after decay of P^{32} activity. It is obvious from these fignres that no correlation exits between the vitamin and radioactivity concentrations. Although the color distribution was essentially normal, the bulk of the radioactivity concentrated in the first tube. The nominal specific activity of the contents of the fourth tube, in which pure vitamin concentrates, was down to 0.015 μc./mg.; and even this value is evidently fictitiously high. Obviously our purification procedures have reduced the specific activity to an insignificant figure. In all likelihood, additional treatment would lead to still further reductions in specific activity. It is clear from these results that the extent of activation of vitamin B$_{12}$ is negligible, if it occurs at all, under the irradiation conditions employed.

TABLE I

COUNTERCURRENT DISTRIBUTION OF CRYSTALLIZED PRODUCT

Tube	Theoret. % of total	Color distribution Ratio[a]	% of total	Radioactivity distribution Ratio[a]	% of total
1	1.44	4.75	3.18	41.0	50.4
2	8.38	1.53	7.88	4.75	10.6
3	21.0	1.24	17.8	1.85	8.04
4	29.1	1.16	24.6	1.20	8.42
5	24.3	1.04	22.2	0.93	7.54
6	12.1	0.89	13.9	.71	5.76
7	3.37	0.58	6.7	.40	4.48
8	0.40	0.24	3.7	.09	5.34

[a] Ratio of water to benzyl alcohol concentrations.

Smith[8] has irradiated 20 mg. of vitamin B$_{12}$ for 4 weeks at a low neutron flux of 0.5×10^{11} neutrons/cm.^{2}/sec. From an initial specific activity of 0.2 μc./mg., he reports the isolation of vitamin B$_{12}$ fractions with a specific activity of 0.0065–0.012 μc./mg. The countercurrent test was not applied. This corresponds to a specific activity retention of 3.3–6% as compared to the low value of $<<0.9\%$ attained in our case after subjecting similar material to countercurrent distribution. This difference, if real, may reflect differences in neutron energies utilized. In any case, a retention[7] of 80% as reported elsewhere for the neutron irradiation of vitamin B$_{12}$ is highly unlikely.

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[8] E. Lester Smith, *Biochem. J.*, **52**, 384 (1952).

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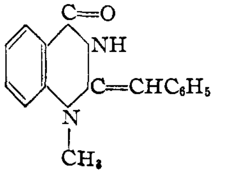
COMMUNICATIONS TO THE EDITOR

CONSTITUTION AND SYNTHESIS OF GLYCOSIN, THE NEW ALKALOID OF *GLYCOSMIS PENTAPHYLLA*, RETZ. DC.

Sir:

Glycosin, $C_{16}H_{14}N_2O$, m.p. 155°, one of the alkaloids of *Glycosmis pentaphylla*,[1-3] Retz, DC. has been proved to be a 1-methyl-4-quinazolone compound from the studies of its ultraviolet and infrared absorption spectra and hydrolysis characteristics.[1] On catalytic hydrogenation glycosin forms a dihydro derivative, $C_{16}H_{16}N_2O$, m.p. 196° (*Anal.* Calcd. for $C_{16}H_{16}N_2O$: C, 76.19; H, 6.35; N, 11.11. Found: C, 76.32; H, 6.31; N, 11.23), which also has been obtained from the base by its reduction with LiAlH$_4$ in tetrahydrofuran at room temperature. On reduction with LiAlH$_4$ in boiling tetrahydrofuran glycosin yields, however, a product different from dihydroglycosin. Further investigation of the reduction product is in progress. On ozonolysis and on oxidation with periodic acid glycosin liberates benzaldehyde which has been identified as its 2,4-dinitrophenylhydrazone, m.p. 235°. From the collective review of these experimental results it is now established that glycosin is a 2-benzylidine-1-methyl-4-quinazolone (I)



(I)

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[1] Asima Chatterjee and S. Ghosh Majumdar, *Science and Culture*, **18**, 604 (1953).

[2] Asima Chatterjee and S. Ghosh Majumdar, *ibid.*, **18**, 505 (1953).

[3] Asima Chatterjee and S. Ghosh Majumdar, *ibid.*, **17**, 306 (1952).