$$BrO_3^- + 9I^- + 6H^+ = 3I_3^- + Br^- + 3H_2O,\ \Delta H_7^0 = -132.02 \text{ kcal./mole} \quad (7)$$

Using Bureau of Standards heat data[3] we calculated $\Delta H_f^0 = -18.70$ kcal./mole for BrO_3^-. Similarly from reactions (1) and (6) we obtain

$$BrO_3^- + 8Br^- + 6H^+ = 3Br_3^- + 3H_2O,\ \Delta H_8^0 = -51.93 \text{ kcal./mole} \quad (8)$$

from which we calculate $\Delta H_f^0 = -17.82$ kcal./mole. Combining the average value of ΔH_f^0 (-18.3 kcal./mole) with the entropy of formation,[3] we calculate $\Delta F_f^0 = 2.1$ kcal./mole. The close agreement with Sammet's[2] value may be fortuitous, as may be seen from a careful examination of the iodine and bromine heat data.

The Bureau of Standards value for ΔH_f^0 of I_2(aq) (5.0 kcal./mole) is based on the temperature coefficient of fifty-year old solubility data. We calculate from more extensive and more recent data[15] the value 5.6 kcal./mole (corrected for hydrolysis). For the heat of iodide complexing of iodine (reaction (2)), the following values have been reported in the literature: $\Delta H_2^0 = -4.30,^{16} -3.87,^{10} -5.10^{17}$ kcal./mole. All of these are based on the temperature coefficients of the equilibrium constant measured in different ways. From the Bureau of Standards heat data[3] one calculates the value -4.03 kcal./mole. It is apparent that the considerable uncertainty in ΔH_f^0 of I_3^- causes three times this uncertainty in ΔH_f^0 for BrO_3^- (see reaction (7)).

In the case of bromine some calorimetric measurements have been made for the heat of solution of Br_2(l) and for ΔH_4. Again, however, the data are old, rather limited, and not obtained at 25°. Calculations from solubility data[17] lead to ambiguous results, so we must say that at least as much uncertainty exists in the Bureau of Standards value for ΔH_f^0 of Br_3^- as does in the I_3^- value, with the correspondng uncertainty existing in ΔH_f^0 for BrO_3^- calculated from equation (8). (Presumably, I^-, Br^- and H_2O heats of formation are accurately enough known so that they will not introduce significant error.)

From this discussion it should therefore be evident that our final calculations of ΔH_f^0 for BrO_3^- from both types of reductions may be uncertain by as much as several kcal./mole. This uncertainty arises at least as much from the uncertainty in the heats of formation of triiodide and tribromide as from our own experimental uncertainties.

VII. Conclusion

We will take as our final values for the heat and free energy of formation of BrO_3^- our calculated averages: $\Delta H_f^0 = -18.3 \pm 2$ kcal./mole and $\Delta F_f^0 = 2.1 \pm 2$ kcal./mole. Additional evidence for these values is provided by Myers[18] who has recently determined ΔF_f^0 to be 2.5 ± 0.3 kcal./mole from kinetic measurements.

[15] A. Seidell, "Solubilities of Inorganic and Metal Organic Compounds," 3rd edition, D. Van Nostrand Co., Inc., New York, N. Y., 1940.

[16] Calculated by Davies and Gwynne[10] from the data of G. Jones and B. B. Kaplan, THIS JOURNAL, **50**, 1845 (1928).

[17] A. D. Awtry and R. E. Connick, *ibid.*, **73**, 1842 (1952).

[18] O. Myers, private communication.

BERKELEY, CALIF.

NOTES

Isolation of Palmitic, Stearic and Linoleic Acids from Guayule Resin[1]

BY THOMAS F. BANIGAN, JR., AND JAMES W. MEEKS

RECEIVED APRIL 4, 1953

In processing guayule, *Parthenium argentatum* Gray, for the isolation of high-quality natural rubber[2] an acetone extract, termed guayule resin, is obtained as a principal by-product. Earlier investigations[3,4] on the composition of this material revealed the presence of parthenyl cinnamate, the ester of a sesqui-terpene tertiary alcohol whose structure was subsequently determined by Haagen-Smit and Fong.[5] A hard "wax-like" compound was also reported[4] and its distribution in the growing shrub determined.[6] The essential oil which constitutes about 3–5% of the resin was shown[7] to contain α-pinene, 60%; dipentene, 9%; cadinene, 8%; and smaller percentages of sesqui-, di-, tri- and higher terpenaceous hydrocarbons and alcohols.

Studies conducted in this Laboratory have now revealed the presence of linoleic, stearic and palmitic acids, and confirmed the presence of cinnamic acid[3,4] in the resin saponifiables. α-Linoleic acid, isolated and purified by solvent extractions and low-temperature crystallizations, has been found to be a major resin component (*ca.* 37%). Palmitic (4%) and stearic acids (1.6%) were isolated as the 72.5:27.5 mole per cent. eutectic, a mixture often encountered[8] when these two acids are obtained from natural sources. Linolenic acid (0.5%) was isolated only as a bromine addition product. Oleic

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

[2] F. E. Clark, T. F. Banigan, Jr., J. W. Meeks and I. C. Feustel, *Ind. Eng. Chem.*, **45**, 572 (1953).

[3] P. Alexander, *Ber.*, **44**, 2320 (1911).

[4] E. D. Walter, THIS JOURNAL, **66**, 419 (1944).

[5] A. J. Haagen-Smit and C. T. O. Fong, *ibid.*, **70**, 2075 (1948).

[6] T. F. Banigan, Jr., J. W. Meeks and R. W. Planck, *Botanical Gazette*, **113**, 231 (1951).

[7] A. J. Haagen-Smit and R. Siu, THIS JOURNAL, **66**, 2068 (1944).

[8] J. C. Smith, *J. Chem. Soc.*, **625** (1936).

acid, although not actually identified, may be present in minor amount.

Experimental

Saponification of Guayule Resin.—Four kilograms of crude resin, obtained as a by-product from the acetone deresination of guayule rubber[2] reacted with a solution of 400 g. of sodium hydroxide (25 mole per cent. excess based on sapn. equiv. 498) in 5 liters of water. After two hours stirring at a bath temperature of 95° the emulsion was diluted with water, cooled and extracted twice with low-boiling petroleum ether and three times with diethyl ether. Concentration of the petroleum ether extract *in vacuo* yielded 638 g. of viscous yellow oil from which parthenio1 and other crystalline terpenes (uncharacterized) were isolated by chromatography (activated alumina) and recrystallization from hexane solutions. On solvent removal the diethyl ether extract yielded 1245 g. of viscous reddish oil, making a total of 1883 g. of unsaponifiable material, whose composition is a subject of future investigation.

The saponified fraction was neutralized with dilute hydrochloric acid to liberate over two liters of thick black oil, which was hot-water washed repeatedly to remove cinnamic acid. The color of the oil was lightened by treatment of a solution in diethyl ether with activated charcoal. The residue oil obtained by filtration and solvent evaporation was dissolved in four gallons of petroleum ether. After two hours standing, the supernatant liquid was decanted from 104 g. of black tar. Considerable color clarification resulted from a charcoal treatment of the decantate which was filtered, solvent evaporated, and the residue redissolved in four gallons of methanol. With several hours standing, 16 g. of an oily non-acidic substance was precipitated. The decantate was again treated with charcoal, filtered and concentrated to yield 1920 g. of pale yellow oil (crude fatty acids).

Fractionation of Fatty Acids by Low Temperature Crystallization.—A 400-g. portion of the crude fatty acids, dissolved in 3.6 kg. of acetone, was subjected to a temperature of −20° for several hours. The supernatant solution was then removed by filter stick from a white waxy precipitate. The latter was redissolved in acetone (10% solution) at room temperature, and the solution again cooled to −20° enabling the saturated fatty acids to precipitate.[9] Following a third recrystallization from a 10% solution in acetone, a crystalline fatty acid fraction of 30 g. was obtained. The original filtrate was then chilled to −40° and (after standing) was filtered to yield an additional 11 g. of saturated acids. This fraction was subjected to several separate recrystallizations at −20°, combined with the main (30 g.) fraction, and the total recrystallized repeatedly from hexane to yield 35 g. of white waxy crystals (palmitic–stearic acid eutectic), m.p. 54–54.5°.

The original filtrate was then cooled slowly through two lower temperature stages, −55 and −75°, causing the deposition of unsaturated acid fractions weighing 134 g. and 91 g. With several low temperature recrystallizations, these two fractions appeared to be similar hence were combined and recrystallized, twice each from acetone and hexane at −60°. A yield of 160 g. of pale yellow oil (linoleic acid) was obtained. An additional 122 g. of linoleic acid (total yield 282 g.) and 50 g. of unsaponifiables were isolated from the combined filtrates.

Identification of α-Linoleic Acid.—In Table I are summarized the evidences for the presence of α-linoleic acid in guayule resin.

The tetrabromide, prepared according to Markley,[9] yielded, on repeated recrystallization from benzene, a small portion of a less soluble hexabromide (62.5% Br), m.p. 183–184°. The melting point of hexabromostearic acid is reported[9] as 185.5–186°. This points to the presence of about 1.4% of linolenic acid in the linoleic acid fraction.

The data characterizing guayule unsaturated acid as linoleic acid (Table I) do not preclude the presence of small amounts of oleic acid, especially in view of the indicated presence of about 1.4% of linolenic acid. The slightly low values reported for density, percentage carbon and particularly iodine number (more than cancelling effects of linolenic acid) suggest the presence of more highly saturated material than linoleic acid.

TABLE I

IDENTIFICATION OF α-LINOLEIC ACID IN GUAYULE RESIN

Property	α-Linoleic acid	Guayule unsaturated acid
M.p., °C.	−6.5[9]	−8.5
Carbon, %	77.09	76.5
Hydrogen, %	11.50	11.4
Density, d^{20}_4	0.9025[10]	0.9036
n^{20}_D	1.4699[11]	1.4704
Mol. wt. (neut. equiv.)	280.4	281
Iodine no. (Hanus)	181	175
Tetrabromide, m.p., °C.	115.5[9]	114–114.5
Bromine, %	53.27	53.22
Hydrogenation	Stearic acid	Stearic acid

Identification of Palmitic and Stearic Acids.—Table II summarizes the evidences for the presence of palmitic and stearic acids in guayule resin.

TABLE II

IDENTIFICATION OF A 72.5:27.5 MOLE PER CENT. EUTECTIC OF PALMITIC AND STEARIC ACIDS IN GUAYULE RESIN

Property	Eutectic	Guayule saturated acids
M.p., °C.	55[8]	54–54.5
Carbon, %	75.23	75.4
Hydrogen, %	12.63	12.7
Mol. wt., (neut. equiv.)	264.1	269
Iodine no. (Hanus)	0.0	1.1

The resolution of this eutectic of palmitic and stearic acids, sometimes confused in the past with margaric acid which is now known to be absent in natural fats and oils, has been accomplished elsewhere[12] by columnar partition chromatography. Our preliminary efforts to separate this binary mixture by differential migration with solvents on paper have engendered some promise. Encouraging results were obtained by employing an ascending micro technique[13] with 80% aqueous acetone as mobile solvent on untreated Whatman No. 1 paper with 1% aqueous potassium permanganate for developer. The use of a stearatochromic chloride[14] or a methyltrichlorosilane[15] treated paper offered doubtful improvement and increased the difficulty of obtaining a satisfactory stain. In no case was complete separation of these two acids realized. However, with each of the eluting solvents tested including 80% aqueous acetone, 90% aqueous methanol and *n*-butanol satd. with ammonia–ammonium carbonate buffer solution, there was a pronounced resemblance of pattern between the known fatty acid eutectic and that isolated from guayule resin. This similarity of chromatographic behavior serves to confirm the other data supporting the identification.

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(9) K. S. Markley, "Fatty Acids," Interscience Publishers, Inc., New York, N. Y., 1947.

(10) "Handbook of Chemistry & Physics," 29th ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1945.

(11) A. W. Ralston, "Fatty Acids and their Derivatives," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 129.

(12) L. L. Ramsey and W. I. Patterson, *J. Assoc. Offic. Agri. Chemists*, **31**, 441 (1948).

(13) L. B. Rockland and M. S. Dunn, *Science*, **109**, 539 (1949).

(14) D. Kritchevsky and M. Calvin, THIS JOURNAL, **72**, 4330 (1950).

(15) T. F. Banigan, Jr., *Science*, **117**, 249 (1953).

U. S. NATURAL RUBBER RESEARCH STATION
SALINAS, CALIFORNIA

Some Disubstituted Pyridines Related to 2,6-Lutidine

BY RODERICK A. BARNES AND HENRY M. FALES

RECEIVED APRIL 1, 1953

In a recent synthesis of the 3,9-diazabicyclo(3.3.1)nonane ring system[1] several attempts were made

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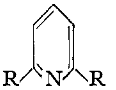
(1) R. A. Barnes and H. M. Fales, THIS JOURNAL, **75**, 975 (1953).

to convert the methyl groups of 2,6-lutidine (I) into substituents which would be suitable for further transformations toward the desired bicyclic system. Oxidation to dipicolinic acid was the only procedure which gave satisfactory yields of a useful intermediate. The transformations described in this report produced interesting substances but the yields were very low.

The dilithium salt of 2,6-lutidine reacted with bromine in ether to form small amounts of 2,6-di-(bromomethyl)-pyridine (II) and large quantities of an acid-soluble brown polymer. The reaction of N-bromosuccinimide with I also produced II along with some 6-bromomethyl-2-methylpyridine (III). Although Buu-Hoi[2] has stated that side-chain brominations in the heterocyclic series proceed easily with N-bromosuccinimide we have been able to obtain II in only 2% yield by this procedure.

When diethyl dipicolinate (IV) was reduced with lithium aluminum hydride a low yield of 2,6-di-(hydroxymethyl)-pyridine (V) was formed. Conversion of this diol to the dibromide II with hydrobromic and sulfuric acids served to confirm the structure of II.



I, R = CH_3
II, R = CH_2Br
IV, R = $COOC_2H_5$
V, R = CH_2OH

Dibromide II, even when analytically pure, melted over a range of 10 to 30° depending on the rate of heating. Melting was accompanied by the formation of a red color which remained after the sample cooled. It is believed that intermolecular quaternization may be taking place as the sample is heated. An attempt to hydrolyze II using silver oxide in aqueous ethanol did not yield diol V but a red substance similar to that obtained by heating II.

Experimental[3]

Diethyl Dipicolinate (IV).—Dipicolinic acid (25.0 g.) prepared by permanganate oxidation of 2,6-lutidine[4] was refluxed with 150 ml. of absolute ethanol while dry hydrogen chloride was introduced in a steady stream. When the acid had completely dissolved the excess ethanol was quickly distilled. The residual oil was then slowly heated on an oil-bath under full aspirator-vacuum until the product abruptly evolved hydrogen chloride.

The acid-free residue was distilled at 158° (1 mm.) to yield 20.0 g. (60%) of a sweet-smelling solid which melted at 41–42°.[5]

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87. Found: C, 59.22; H, 5.90.

2,6-Di-(bromomethyl)-pyridine (II). A.—A solution of phenyllithium in ether was prepared from 14.7 g. (2.12 moles) of lithium and 157 g. (1.0 mole) of bromobenzene. Fifty-five ml. (0.51 mole) of 2,6-lutidine was added to the ethereal solution and stirred overnight. To this mixture, cooled to 10°, 160 g. (1 mole) of bromine was rapidly added with vigorous stirring. Filtration from the solids and polymer left a very lachrymatory ethereal solution which was evaporated at room temperature to yield a dark oil. Rapid distillation at 0.5 mm. produced a white solid consisting of the dibrominated base and biphenyl. Four recrystallizations from petroleum ether produced about 750 mg. (1%) of pure 2,6-di-(bromomethyl)-pyridine which melted with decomposition from 66 to 76° or 66 to 99° depending on the rate of heating.

Anal. Calcd. for $C_7H_7NBr_2$: C, 31.73; H, 2.66; Br, 60.32. Found: C, 31.76; H, 2.64; Br, 60.37.

B.—A suspension of 62 g. (0.35 mole) of N-bromosuccinimide in 200 ml. of dry carbon tetrachloride was heated under reflux and illumination with 20 ml. (0.18 mole) of 2,6-lutidine. Boiling was continued for 15 hours while 1.2 g. of benzoyl peroxide was added in 4 portions. The remaining succinimide was filtered and the filtrate washed quickly with cold sodium bisulfite solution and water. Evaporation of the solvent left an oil which was distilled at 0.5 mm. The partially crystallized distillate was chilled, sucked as free as possible from adhering liquors and recrystallized three times from petroleum ether. About 1 g. (2%) of product was obtained which melted from 66 to 92°. A mixture of the dibromide and that prepared in (A) above, melted from 66 to 92° at the same rate of heating.

6-Bromomethyl-2-methylpyridine Picrate.—The adhering liquors from the crude dibromide II were dissolved in diethyl ether and an ethereal solution of picric acid was added until precipitation ceased. The picrate melted at 143° after four recrystallizations from ethanol.

Anal. Calcd. for $C_{13}H_{11}N_4O_7Br$: C, 37.61; H, 2.67; N, 13.49; Br, 19.25. Found: C, 38.18, 38.17; H, 2.90, 2.82; N, 13.50; Br, 19.12.

2,6-Di-(hydroxymethyl)-pyridine (V).—Diethyl dipicolinate (55.7 g., 0.25 mole) was added to a solution of lithium aluminum hydride (0.4 mole) in diethyl ether. An orange-red color developed immediately. The mixture was stirred overnight and water added to decompose the excess hydride. The ethereal layer was separated and evaporated leaving no residue. Carbon dioxide was passed into the aqueous suspension of solids to precipitate the lithium. The resulting suspension retained a yellow-colored substance which was polymeric. Filtration and distillation of the water-phase left a viscous oil (2 g., 5%) which crystallized upon the addition of ethyl acetate. Recrystallization from this solvent and a single sublimation produced the pure diol which melted at 114–118°. The diol was completely soluble in water and insoluble in dry ether.

Anal. Calcd. for $C_7H_9O_2N$: C, 60.41; H, 6.52. Found: C, 60.49; H, 6.43.

The hydrochloride, after being crystallized from methanol and sublimed, melted with decomposition at 153–160°.

Anal. Calcd. for $C_7H_{10}O_2NCl$: C, 47.87; H, 5.74. Found: C, 47.42; H, 5.66.

The diol was converted to the dibromide by the action of hydrobromic and sulfuric acids. After a small sample was boiled with an excess of 48% hydrobromic and concentrated sulfuric acids for 4 hours, the mixture was poured over ice-water, neutralized with dilute sodium hydroxide, and quickly extracted with ether. Removal of the dried solvents left the dibromide, which after recrystallization from petroleum ether melted from 66 to 74° with decomposition. A mixture of this dibromide and that prepared in (A) above melted from 63 to 76°.

SCHOOL OF CHEMISTRY
RUTGERS UNIVERSITY
NEW BRUNSWICK, N. J.

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(2) N. P. Buu-Hoi, *Ann.*, **556**, 1 (1944).

(3) Microanalyses were by W. Manser, Zurich, Switzerland. All melting points are corrected and were determined using the Kofler Hot Stage.

(4) G. Black, E. Depp and B. B. Corson, *J. Org. Chem.*, **14**, 17 (1949).

(5) G. Crippa, M. Long and E. de Martini, *Gazz. chim. ital.*, **64**, 83 (1934), reported a m.p. of 28° for this compound. The difference may have been due to the presence of traces of moisture which appear to lower the m.p. markedly.

Studies in the Wagner Rearrangement. VII.[1] The Dehydration of 2-Phenyl-1-acenaphthenol-1-C^{14}

BY WILLIAM A. BONNER AND CLAIR J. COLLINS

RECEIVED JANUARY 21, 1953

Several isotopic investigations have been reported[2] in which migration ratios for various sub-

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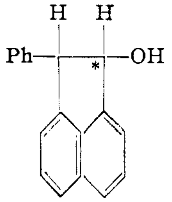
(1) This document is based upon work performed under Contract Number W-7405-eng-26 for the Atomic Energy Commission at the Oak Ridge National Laboratory.

(2) C. J. Collins and B. M. Benjamin, THIS JOURNAL, **75**, 1644 (1953) and previous papers.

stituted phenyl groups have been studied under the dehydrating conditions of the Wagner rearrangement. We have now attempted to extend these studies to the dehydration of the *cis*- and *trans*-isomers of 2-phenyl-1-acenaphthenol-1-C^{14} (I). The acenaphthene system appeared attractive because of the known migration[3-5] of phenyl caused by the action of acid on the 1,2-diphenyl-1,2-acenaphthenediols, the unusual *cis*-elimination observed in certain of its carbanion reactions[6] and the possibility that further information regarding symmetrical phenonium ions[7] might be obtained.

It was proposed to study the extent of phenyl migration during the dehydration of I by degradation of the dehydration product, 1-phenylacenaphthylene (II), to 8-benzoyl-1-naphthoic acid (III).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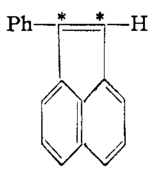
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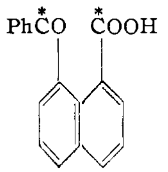
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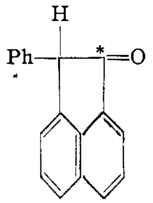

IV

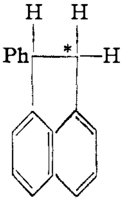
Decarboxylation of the latter would give products whose radioactivity assay would establish unambiguously the carbon-14 distribution in II.

One of the desired isomers of the carbinol I was formed by the lithium aluminum hydride reduction of 2-phenylacenaphthenone-1-C^{14} (IV) in the manner previously described.[8]

The action of phosphorus pentoxide on our isomer of carbinol I in inert solvent at elevated temperature led to immediate dehydration. The desired olefin II, however, was not the only product formed, and, in fact, could be isolated only in low yield. The bulk of the product was an amorphous yellow material of higher molecular weight and of apparently polymeric nature, from which the desired olefin II could be separated by fractional crystallization of its picrate. Decomposition of the picrate gave pure crystalline II having physical properties in agreement with those recorded in the literature. When an attempt was made to oxidize the olefin II to the acid III with neutral potassium permanganate no crystalline product could be obtained. The crude product was predominantly a neutral orange sirup, probably resulting from polymerization of the olefin II. Ozonization of II, however, followed by oxidative degradation of the ozonide led to the desired acid III in good yield. Decarboxylation of the acid so obtained yielded 1-benzoylnaphthalene containing 7.5% of the radioactivity of the parent acid. Thus phenyl migration occurred during or after the dehydration, I → II, to the extent of 7.5%.

Since the lithium aluminum hydride reduction of ketones is generally non-stereospecific in nature,[9] we have attempted to establish the geometrical configuration of our carbinol I and to prepare the second isomer by other means.

The experiments undertaken with these objectives are summarized as follows: (1) Catalytic reduction of the ketone IV with Adams catalyst or Raney nickel produced the same carbinol I obtained by means of lithium aluminum hydride reduction of the ketone. In the Raney nickel reduction a small amount of 1-phenylacenaphthene (V) also was formed. (2) Treatment of the ketone IV with alcoholic alkali led to a deep purple solution, presumably the consequence of the enolate anion VI and its resonance forms. Upon catalytic reduction these solutions absorbed far more than equimolar proportions of hydrogen, but no crystalline derivative could be isolated. (3) When the ketone IV was dissolved in pyridine an orange solution was formed, apparently owing to enol formation. This solution had a color identical with solutions of the olefin II. Treatment of such a solution with acetic anhydride led to the isolation of the enol acetate VII, an orange sirup capable of characterization through its crystalline picrate.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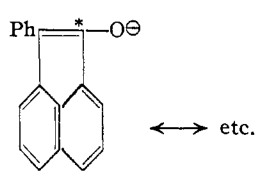
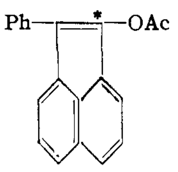

VI


VII

The structure of VII was confirmed by its ozonization in good yield to 8-benzoyl-1-naphthoic acid (III). Catalytic reduction of the enol acetate VII with Raney nickel produced only the hydrocarbon V. Similarly, the action of Raney nickel on the acetate of the carbinol I resulted in the hydrocarbon V, although the carbinol I itself was stable under similar conditions. (4) Reduction of the enol acetate VII using Adams catalyst led to a mixture of the hydrocarbon V and the acetate of the carbinol I. Thus the same geometrical isomer of I was produced by lithium aluminum hydride reduction and catalytic reduction of the ketone IV as by catalytic reduction of the enol acetate VII.

In view of the known *cis*-addition of hydrogen to olefins,[10,11] it was hoped that the catalytic reduction of the enol acetate VII would lead unambiguously to the *cis*-isomer of I. In the absence of the second geometrical isomer, however, we are unable to state that our isomer of I possesses the *cis*-configura-

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(3) P. D. Bartlett and R. F. Brown, This Journal, **62**, 2927 (1940).

(4) R. F. Brown, *ibid.*, **74**, 428 (1952).

(5) R. F. Brown, J. B. Nordmann and M. Madoff, *ibid.*, **74**, 432 (1952).

(6) S. J. Cristol, *ibid.*, **74**, 2193 (1952).

(7) D. J. Cram, *ibid.*, **71**, 3863 (1949), and subsequent papers.

(8) W. A. Bonner and C. J. Collins, *ibid.*, **75**, 2308 (1953).

(9) L. W. Trevoy and W. G. Brown, *ibid.*, **71**, 1675 (1949); W. G. Brown, "Organic Reactions," Vol. VI, J. Wiley and Sons, New York, N. Y., 1951, p. 474.

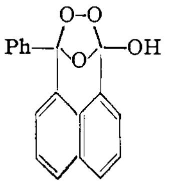
(10) R. P. Linstead and co-workers, This Journal, **64**, 1985, 1991, 2003, 2006, 2014, 2022 (1942).

(11) C. C. Price and J. V. Karabinos, *ibid.*, **62**, 1159 (1940).

tion, due to the possibility of *cis* → *trans* isomerization of I on the catalyst surface.

Our inability to obtain unequivocal evidence as to the configuration of our isomer of carbinol I, as well as our observation[12] that olefins formed by phosphoric anhydride dehydration may themselves undergo further rearrangement under conditions of the Wagner rearrangement, make it impossible for us to offer an unambiguous mechanistic interpretation of the present dehydration.

One point regarding the ozonization of VII is noteworthy. Assuming a normal structure for the ozonide, hydrolysis of the latter should yield an intermediate such as VIII. The structure VIII is vaguely suggestive of a hemiacetal, and might be expected to undergo spontaneous decomposition with loss of oxygen to give 8-benzoyl-1-naphthoic acid (III) directly. When the ozonide of the enol acetate was warmed with dilute alkali a gas was evolved and the acid III could be isolated by mere acidification, no oxidative treatment of the ozonide being necessary.



VIII

Experimental

1-Phenylacenaphthylene.—Phenylmagnesium bromide (20% excess) was prepared from bromobenzene (7.50 ml.) and magnesium (1.74 g.) in ether (100 ml.). To this solution was added dropwise with stirring over a 20-minute period a solution of acenaphthenone[13] (10.0 g.) in a mixture of benzene (70 ml.) and ether (40 ml.). The mixture was stirred for one hour under reflux, cooled slightly, and decomposed by the dropwise addition of excess water. The magnesium salts were filtered (Celite), and rinsed twice by slurrying with ether and refiltering. After washing and drying, the light orange ether layer was evaporated to yield 14.1 g. of yellow sirup. This was dissolved in hot ethanol (90 ml.) and treated with a solution of picric acid (14.2 g.) in hot ethanol (60 ml.). Crystallization was rapid, yielding 12.8 g. of 1-phenylacenaphthylene picrate, m.p. 122–123° in agreement with the recorded value.[14] The picrate was decomposed by dissolving in benzene (200 ml.) and passing the solution through a 2.8 × 45 cm. column of alumina, rinsing with benzene. Solvent evaporation from the effluent left 6.5 g. of yellow oil which readily crystallized. Recrystallization from ethanol (50 ml.) gave 4.6 g. of orange needles, m.p. 59–60°. Concentration of the mother liquors to *ca.* 12 ml. produced an additional 1.3 g., m.p. 55–56.5°, over-all yield from acenaphthenone 49%. The m.p. of 1-phenylacenaphthylene previously has been recorded as 57–58°[14] and 54–55°.[15] On standing for several weeks the crystalline material became noticeably gummy, possibly due to spontaneous polymerization. It was accordingly reconverted to the picrate and stored as such.

Attempted Oxidation of 1-Phenylacenaphthylene.—The above hydrocarbon (0.25 g.) was dissolved in acetone (10 ml.) and treated with a solution of potassium permanganate (0.35 g., 1 equiv.) and magnesium chloride hexahydrate (0.23 g., 1 equiv.) in water (4 ml.). The mixture was allowed to stand one hour, after which the MnO_2 was filtered and rinsed with acetone. The filtrate was concentrated and diluted with water then treated with ether and excess sodium bicarbonate. Evaporation of the ether layer left 0.15 g. of red neutral oil which failed to crystallize when seeded with starting material. Acidification of the bicarbonate layer, followed by extraction with ether and evaporation of the extract, produced only 0.03 g. of intractable gum which failed to crystallize on seeding with 8-benzoyl-1-naphthoic acid. It appears probable that the above oxidation conditions led only to polymeric material.

Ozonization of 1-Phenylacenaphthylene.—The above hydrocarbon (0.25 g.) was dissolved in acetone (15 ml.) and ozonized on a semimicro scale.[16] Ozonization was complete in four minutes, as indicated by disappearance of the orange color. The acetone solution of the ozonide was treated with a solution of potassium permanganate (0.25 g.) in water (5 ml.) and allowed to stand at room temperature for 20 hours. The MnO_2 was filtered, rinsed with acetone, and the oxidation mixture processed as described above. The neutral fraction gave only 0.02 g. of oil. The acidic fraction produced 0.33 g. (109%) of fluffy glass. This was recrystallized twice from a mixture of ether and ligroin giving 0.10 g. of pure 8-benzoyl-1-naphthoic acid, m.p. 131.5–132.5°.

Dehydration of 2-Phenyl-1-acenaphthenol-1-C^{14}.—The material employed in the present dehydration was a sample previously described[12] having m.p. 167.2–167.7° and showing a radioactive assay of 2.326 ± 0.016 mc./mole. This material (1.5 g.) was dissolved in hot anhydrous benzene (50 ml.), and the solution was treated with *ca.* 0.75 g. of phosphorus pentoxide. The orange color characteristic of 1-phenylacenaphthylene was immediately formed. The mixture was boiled with swirling for three minutes, cooled and washed twice with water. Solvent evaporation produced 1.47 g. of orange sirup. This was boiled with ethanol (15 ml.) and the solution was decanted from 0.60 g. of insoluble, presumably polymeric gum. The ethanol solution of the soluble fraction was treated with a solution of picric acid (0.9 g.) in ethanol (8 ml.). Chilling in ice produced 0.37 g. of 1-phenylacenaphthylene picrate, m.p. 121–123°. In a similar experiment the picrate isolated at this point had a radioactive assay of 2.303 ± 0.002 mc./mole. The above picrate was dissolved in benzene and decomposed on a small column of alumina. Evaporation of the effluent and washings left 0.20 g. of oil which readily crystallized on scratching with a small seed of 1-phenylacenaphthylene. The material was ozonized without recrystallization. In a parallel experiment, however, the 1-phenylacenaphthylene produced after decomposition of the picrate was recrystallized. The purified material had m.p. 54–55° and showed an assay of 2.303 mc./mole. In the present experiment no further pure 1-phenylacenaphthylene was obtained from subsequent picrate fractions obtained from the original mother liquors.

The above crude 1-phenylacenaphthylene (0.20 g.) was dissolved in acetone (12 ml.) and ozonized as described above. The neutral fraction obtained after permanganate oxidation of the ozonide weighed 0.03 g., while the crude acidic fraction weighed 0.14 g. The latter was recrystallized from a mixture of ether and ligroin to give a sample of 8-benzoyl-1-naphthoic acid of m.p. 132.5–133.5° showing an assay of 2.340 mc./mole. In order to have sufficient material for the decarboxylation described below, this acid was diluted with a quantity of non-radioactive 8-benzoyl-1-naphthoic acid calculated to give a lower potency sample having an assay of 1.139 mc./mole.

The above diluted 8-benzoyl-1-naphthoic acid (0.198 g.) was dissolved in quinoline (3 ml.) and treated with a pinch of copper chromite. The mixture was refluxed for 20 minutes, sweeping the carbon dioxide produced into warm barium hydroxide solution with the aid of a helium stream. The barium carbonate was filtered, rinsed with boiled water, ethanol and acetone, then dried; yield 0.12 g., assay, 1.003 ± 0.005 mc./mole. This value is slightly lower than that required on the basis of the benzoylnaphthalene assay below, presumably because of unavoidable contamination of the barium carbonate. The quinoline solution remaining after decarboxylation was cooled, poured into excess dilute hydrochloric acid, and the resulting mixture was continuously extracted with ether for 1.75 hours. The ether extract was treated with Norit and evaporated to give 0.17 g. of amber oil. The latter was crystallized from methanol (2 ml.) to give a sample of 1-benzoylnaphthalene having m.p. 76–77° and showing a radioactivity assay of 0.0852 ± 0.0000 mc./mole. This figure permits calculation that the extent of phenyl migration during or after the dehydration of 2-phenyl-1-acenaphthenol-1-C^{14} was 7.5%.

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[12] To be published in detail in the near future.

[13] L. F. Fieser and J. Cason, *ibid.*, **62**, 434 (1940).

[14] B. R. Brown and D. L. Hammick, *J. Chem. Soc.*, 1395 (1948).

[15] E. Ghigi, *Ber.*, **73B**, 677 (1940).

[16] W. A. Bonner, *J. Chem. Educ.*, in press.

1-Acetoxy-2-phenylacenaphthene-1-C^{14}.—2-Phenyl-1-acenaphthenol-1-C^{14} (0.20 g.) was dissolved in pyridine (5 ml.) and the solution treated with acetic anhydride (4 ml.). After standing at room temperature for 24 hours the mixture was poured into water, and the resulting solid extracted into ether. The ether extract was washed with water, dilute hydrochloric acid, more water, and then sodium bicarbonate solution. Solvent evaporation produced 0.24 g. of white solid. Two recrystallizations from ethanol gave a sample of m.p. 122.5–123°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.32; H, 5.59. Found: C, 83.35, 83.24; H, 5.67, 5.70.

Hydrogenation of 2-Phenylacenaphthenone-1-C^{14}.—The ketone (0.3 g.) was dissolved in ethanol (12 ml.) and treated with Raney nickel (*ca.* 0.6 g.). The mixture was stirred magnetically overnight under a 35 p.s.i. hydrogen atmosphere. Catalyst filtration and solvent evaporation produced a white solid which was fractionally crystallized from a mixture of acetone and ligroin. A total of 0.13 g. of 2-phenyl-1-acenaphthenol-1-C^{14} was obtained, m.p. 166–168°, no depression when admixed with an authentic sample. After removal of several intermediate impure fractions from the mother liquors, a small quantity of 1-phenylacenaphthene was isolated, m.p. 100–101°.

When 0.25 g. of 2-phenylacenaphthenone-1-C^{14} was reduced in ethanol using Adams catalyst, a total of 0.14 g. of 2-phenyl-1-acenaphthenol-1-C^{14}, m.p. 166–167° was obtained.

Action of Raney Nickel on 2-Phenyl-1-acenaphthenol-1-C^{14} and its Acetate.—The carbinol (0.14 g.) was dissolved in ethanol (18 ml.) and the solution treated with Raney nickel (*ca.* 1 g.). On stirring for 19 hours under 1 atmosphere of hydrogen, 17.5 ml. of hydrogen was consumed. On processing the hydrogenation mixture for products, 0.07 g. of unchanged starting material was recovered. While the mother liquors may have contained 1-phenylacenaphthene, none of this could be isolated in crystalline form.

The above 1-acetoxy-2-phenylacenaphthene-1-C^{14} (0.08 g.) was dissolved in ethanol (10 ml.) and treated with Raney nickel (0.6 g.). On stirring for 19 hours under one atmosphere of hydrogen, 8.0 ml. of hydrogen was consumed. The catalyst was filtered and rinsed, and the filtrate was evaporated to dryness. The resulting 0.06 g. of oil crystallized on scratching, and was recrystallized from 1.5 ml. of ethanol. The resulting needles, m.p. 103–104°, showed no mixed m.p. depression with 1-phenylacenaphthene.

Enol Acetate of 2-Phenylacenaphthenone-1-C^{14}.—2-Phenylacenaphthenone-1-C^{14} (0.50 g., radioactivity assay, 2.322 ± 0.002 mc./mole) was dissolved in pyridine (3 ml.) to give an orange solution. The latter was treated with acetic anhydride (2 ml.), and the mixture permitted to stand for about two hours, then diluted with excess water and allowed to stand about 15 minutes. The orange oil was extracted into ether, and the ether extract was washed with water, dilute hydrochloric acid, again with water, and finally with sodium bicarbonate solution. Solvent evaporation led to a quantitative yield of the sirupy enol acetate. A sample of this sirup (0.32 g.) was dissolved in hot ethanol (4 ml.) and treated with a solution of picric acid (0.30 g.) in hot ethanol (1 ml.). Formation of red needles of the picrate was almost instantaneous. These were filtered, 0.44 g., m.p. 144.5–146°. Recrystallization from ethanol (5 ml.) gave 0.33 g. of product having m.p. 145–146° and showing a radioactivity assay of 2.342 mc./mole.

Anal. Calcd. for $C_{26}H_{17}O_9N_3$: C, 60.60; H, 3.33; N, 8.16. Found: C, 60.15; H, 3.56; N, 8.26.

Ozonization of Enol Acetate of 2-Phenylacenaphthenone-1-C^{14}.—The above sirupy enol acetate (0.36 g.) was dissolved in ethanol (15 ml.) and ozonized on a semi-micro scale. Ozonization was complete in about 8 minutes, as indicated by disappearance of the original orange color. To the alcoholic solution of the ozonide was slowly added 10% sodium hydroxide solution (10 ml.), causing the gentle evolution of a gas, presumably oxygen. The solution was heated to boiling on the steam-bath, after which the solvent was evaporated in an air stream. The residue was diluted with water and the solution extracted with ether. Evaporation of solvent from the ether layer gave 0.05 g. of neutral gum which was not investigated. The alkaline layer was acidified with hydrochloric acid, extracted with ether, and the extract decolorized with Norit and evaporated to dryness to give 0.24 g. of amber glass. Crystallization from a mixture of ether and ligroin gave 0.16 g. of pure 8-benzoyl-1-naphthoic acid, m.p. 131–132°, unchanged on admixture with an authentic sample.

Hydrogenation of Enol Acetate of 2-Phenylacenaphthenone-1-C^{14}.—The above sirupy enol acetate (0.62 g.) was dissolved in ethanol (15 ml.) and Raney nickel added. Hydrogenation at atmospheric pressure and room temperature for 1.75 hours resulted in the uptake of 71 ml. of hydrogen and disappearance of the orange color.

Customary processing led to 0.47 g. of amber sirup which crystallized completely when scratched with 1-phenylacenaphthene. Three recrystallizations from methanol gave a sample of 1-phenylacenaphthene-2-C^{14} of m.p. 102–102.5°, radioactivity assay, 2.330 ± 0.010 mc./mole.

Anal. Calcd. for $C_{18}H_{14}$: C, 93.87; H, 6.13. Found: C, 93.30, 93.43; H, 6.18, 6.10.

This material showed no mixed m.p. depression with authentic 1-phenylacenaphthene, m.p. 103–104°, prepared by the Raney nickel catalyzed hydrogenation of our above sample of 1-phenylacenaphthylene. The m.p. for 1-phenylacenaphthene has been previously reported[14] as 105–106°. The structure of the above reduction product was further confirmed by the fact that it could be oxidized to 8-benzoyl-1-naphthoic acid with neutral permanganate in acetone.

In another experiment 0.59 g. of the above sirupy enol acetate was dissolved in 15 ml. of ethanol and treated with *ca.* 0.15 g. of freshly reduced Adams catalyst. Reduction was fairly rapid at room temperature and one atmosphere pressure. After an hour 61 ml. of hydrogen was consumed (theory, 57 ml.), and some orange color was left. The catalyst was filtered, rinsed with ethanol, and the filtrate was evaporated to dryness. Ligroin (25 ml.) was added to the residue, causing partial crystallization. The solution was evaporated to 8 ml. and the crystals filtered, 0.18 g., m.p. 115–118°. The filtrate was diluted with ligroin to 25 ml. and passed through a 1 × 20 cm. alumina column. The column was rinsed with ligroin (100 ml.) and the clear effluent was evaporated to dryness. There resulted 0.11 g. of oil which slowly crystallized. This was recrystallized from 2.5 ml. of ethanol to yield 0.04 g. of 1-phenylacenaphthene, m.p. 103–104°, mixed m.p. with an authentic sample undepressed. The alumina column was then rinsed white with ethanol (50 ml.) and the effluent was evaporated to 4 ml. Seeding with the above material of m.p. 115–118° produced 0.05 g. of solid, m.p. 112–114°. Evaporation of the filtrate gave 0.17 g. of orange oil, presumably unreduced enol acetate. The combined solid materials were recrystallized from a mixture of ethanol (2.5 ml.) and ligroin (3 ml.) to produce 0.11 g. of white needles, m.p. 122–123°, mixed m.p. with the above sample of 1-acetoxy-2-phenylacenaphthene, 121–122°.

For further characterization of the acetoxy product obtained on reduction of enol acetate, deacetylation was undertaken. Impure acetate (0.17 g.) from the recrystallization mother liquors of the above and a parallel reduction were dissolved in ether (10 ml.) and added to a stirred slurry of excess lithium aluminum hydride in ether. After stirring for 10 minutes the excess anhydride was destroyed by the cautious addition of acetone, then of water, and hydrochloric acid. The ether layer was decolorized (Norit) and evaporated to give 0.13 g. (90%) of crude 2-phenyl-1-acenaphthenol. Recrystallization from 3 ml. of ethanol gave 0.06 g. of needles, m.p. 165.5–167°, mixed m.p. with authentic carbinol 166.5–167.5°.

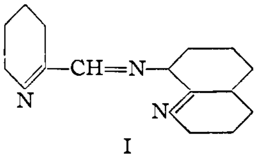
CHEMISTRY DIVISION
OAK RIDGE NATIONAL LABORATORY
OAK RIDGE, TENNESSEE

The Resolution of a Bis-Tridentate Iron(II) Complex

BY F. P. DWYER, N. S. GILL, E. C. GYARFAS AND F. LIONS

RECEIVED APRIL 4, 1953

It is generally agreed that in the bis-2,2′,2″-terpyridyl metal complexes the two tridentate chelate groups are arranged in two equatorial planes at right angles so that the complex cation has a plane of symmetry.[1] The Schiff base (1) from 8-aminoquinoline and pyridine-2-aldehyde is structurally analogous to 2,2′,2″-terpyridyl and models show a high probability of similar coördination about metallic atoms. Since this molecule is a dissymmetrical tridentate chelate the complex cation should exist in enantiomeric forms. The addition of an alcoholic solution of (1) to aqueous ferrous sulfate was found to give such an intense green color that as little as one part of iron in two million could be detected by the reaction. The iron complex was resolved through the *d*-antimonyl tartrate. The enantiomeric iodides were stable at room temperature but racemized in two minutes at 100°.



I

It is noteworthy that the sequence —N=C—C=N—C—C=N— in (1) is the same as in 2,2′,2″-terpyridyl so that similar possibilities exist for resonance and double bonding of the nitrogen and metal atoms. In the same way it can be inferred that the Schiff bases from pyridine-2-aldehyde and primary amines such as aniline and ethylenediamine should act, respectively, as bidentate and quadridentate molecules similar to 2,2′-dipyridyl and 2,2′,2″,2‴-tetrapyridyl. These compounds are being investigated.

Experimental

8-(α-Pyridylmethyleneamino)-quinoline.—Pyridine-2-aldehyde (5.35 g.) was added to a solution of 8-aminoquinoline (7.0 g.) in ethanol (5.4 ml.) and the mixture warmed for a few minutes on the water-bath. After cooling, ether was added and the product crystallized from ethanol. The minute cream needles melted at 123.5°. *Anal.* Calcd. for $C_{15}H_{11}N_3$: C, 77.2; H, 4.8; N, 18.0. Found: C, 76.2; H, 4.7; N, 18.3.

***d,l*-Bis-(8-(α-pyridylmethyleneamine)-quinoline) Iron (II) Iodide, Dihydrate.**—Ferrous sulfate heptahydrate (1.39 g.) in water (25 ml.) was treated with the tridentate (2.35 g.) in hot methanol (50 ml.) and the mixture heated to 70°. After dilution with 80 ml. of water, the intensely green colored solution was filtered and the iodide precipitated by the addition of sodium iodide. Recrystallized from hot water it gave fine black prisms. The perchlorate, sparingly soluble black needles, could not be oxidized to the iron(III) complex without complete decomposition. *Anal.* Calcd. for $C_{30}H_{26}N_6O_2I_2Fe$: C, 44.4; H, 3.2; N, 10.4; Fe, 6.9; I, 31.3. Found: C, 44.8; H, 3.5; N, 10.6; Fe, 6.9; I, 31.4.

***l*-Bis-(8-(α-pyridylmethyleneamino)-quinoline) Iron(II) Iodide Dihydrate.**—The *d,l*-iodide (2.0 g.) in hot water (40 ml.) was shaken with excess of freshly precipitated silver chloride. Filter pulp was added and the mixture filtered, washing the silver halide precipitate with a little hot water. The volume of the dark green solution was adjusted to 60 ml. and the substance cooled to 4°. Potassium *d*-antimonyl tartrate (0.9 g.) in water (15 ml.) was added with scratching of the sides of the vessel. The fine black precipitate was filtered off, washed with a little ice-water and dissolved in 10% sodium acetate solution (50 ml.) at 35–40°. After filtration the levo iodide was precipitated by the very slow addition of 10% sodium iodide solution. The active iodide which was much less soluble than the *d,l*-iodide was crystallized several times from warm methanol by the addition of ether, to give dark green nodular prisms. A 0.0025% solution in water gave α_D −0.05°, whence $[\alpha]^{20}_D$ −2000°, and $[M]^{20}_D$ −16,000°; a 0.005% solution gave α^{20}_{5461} −0.03°, whence $[\alpha]^{20}_{5461}$ −600°, and $[M]^{20}_{5461}$ −5,000°. *Anal.* Calcd. for $C_{30}H_{26}N_6O_2I_2Fe$: C, 44.4; H, 3.2; N, 10.4; I, 31.3. Found: C, 44.7; H, 3.3; N, 10.5; I, 31.4.

***d*-Bis-(8-(α-pyridylmethyleneamino)-quinoline) Iron (II) Iodide Dihydrate.**—The filtrate from the antimonyl tartrate precipitation was treated very slowly with 10% sodium iodide solution and the resulting precipitate of the impure *d*-iodide crystallized as above from warm methanol and ether.

A 0.0025% solution in water gave α_D +0.05°, whence $[\alpha]^{20}_D$ +2000°. *Anal.* Calcd. for $C_{30}H_{26}N_6O_2 \cdot I_2Fe$: C, 44.4; H, 3.2; N, 10.4; I, 31.3. Found: C, 44.7; H, 3.3; N, 10.5; I, 31.4.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF SYDNEY
N.S.W., AUSTRALIA

Thermal Decomposition of Chlorate–Chloride Mixtures

BY A. VANDEN BOSCH AND A. H. W. ATEN, JR.

RECEIVED MARCH 2, 1953

As a result of kinetic measurements Glassner and Weidenfeld have recently suggested[1] that the formation of potassium perchlorate during the thermal decomposition of potassium chlorate should be due to a transfer of atomic oxygen from the chlorate ion to a chloride ion. If this assumption were correct, decomposition of ordinary chlorate in the presence of radioactive chloride would lead to the formation of labeled perchlorate.

We have performed experiments of this type, using sodium chlorate and sodium chloride because we encountered difficulties in the rapid recrystallization of potassium perchlorate formed in this way. A mixture of 5 g. of $NaClO_3$ with 0.6 to 0.8 g. of NaCl was kept at 505° during 30 minutes. The $NaClO_3$ had been dried at 120° and the NaCl had been irradiated with a mixed beam of slow and fast neutrons and contained both Cl^{34} and Cl^{38}. As irradiation of the chloride crystals is reported to influence the course of the chemical reaction[1] the NaCl was melted before use. The reaction mixture was dissolved in water, perchlorate was precipitated as $KClO_4$ by addition of KNO_3 and chloride was isolated as AgCl. Activities were measured with a mica window counter and corrections for the natural activity of potassium and for self-absorption were applied, although these were of minor importance. In four experiments at the end of the reaction period the mixture contained 15–22% of the total chlorine as ClO_4^-, 76–82% as Cl^- and 2–4% as ClO_3^-. For the ratio of the specific activities of the chlorine in ClO_4^- and in Cl^- from the reaction mixture the following successive figures were found: 0.013, 0.015, 0.004, 0.010.

In case the mechanism of Glasner and Weidenfeld were correct and if all the chloride ions in the mixture have an equal chance of participating in the reaction, this ratio should have been > 1. At the start of the reaction the perchlorate would have originated from the undiluted labeled chloride. However, as the reaction proceeded, the original radioactive chloride would have been diluted by new inactive chloride formed in the decomposition of the chlorate and therefore at the end the specific activity of the Cl^- in the reaction mixture should be lower than the specific activity of the chlorine in the perchlorate. (Both in our experiments and in those of Glasner and Weidenfeld part of the chloride may have remained solid from the start of the reaction, but at least an appreciable fraction must have been present in the melt. Incomplete melting of the chloride might have lowered the ratio to a value slightly less than unity, but not to a small fraction of 1.)

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[1] G. T. Morgan and F. H. Burstall, *J. Chem. Soc.*, 1649 (1937).

[1] A. Glasner and L. Weidenfeld, THIS JOURNAL, **74**, 2464 (1952).

Finally we may point out that our figures do not only disprove this theory but that they also show that during the reaction an exchange of labeled chlorine between Cl^- and ClO_3^- or between Cl^- and ClO_4^- does not occur to an appreciable extent.

We are glad to thank the Foundation for Fundamental Research of Matter (F.O.M.) and the Netherlands Organization for Pure Research (Z.W.O.) for their support of this investigation. Thanks are also due to the personnel of the Philips' cyclotron who performed the necessary irradiations. We also wish to express our gratitude to the Technische Commissie van het Belgisch-Nederlands Cultureel Accoord, who enabled one of us (A. Van den Bosch, Laboratorium voor Physische Chemie, Rijksuniversiteit, Ghent) to take part in this investigation.

INSTITUUT VOOR KERNPHYSISCH ONDERZOEK
AMSTERDAM, NETHERLANDS

Preparation of N-Alkyl-2-methylcyclohexylamines

BY L. E. CRAIG AND I. J. RESSA

RECEIVED FEBRUARY 2, 1953

Adkins and Cramer[1] found that N-ethylcyclohexylamine is produced in excellent yield when aniline is hydrogenated in ethanol in the presence of a nickel catalyst. This apparent nickel-catalyzed alkylation of an amine with an alcohol was subsequently confirmed[2] by heating cyclohexylamine and ethanol at 200° under hydrogen at 75 atm. and in the presence of the nickel catalyst, N-ethylcyclohexylamine being produced as the main product along with small amounts of cyclohexylamine, N,N-diethylcyclohexylamine and dicyclohexylamine. The reaction was studied as a preparative method with several amines and alcohols, but no appreciable reaction was found to occur with cyclohexylamine, methanol and isopropyl alcohol.

TABLE I

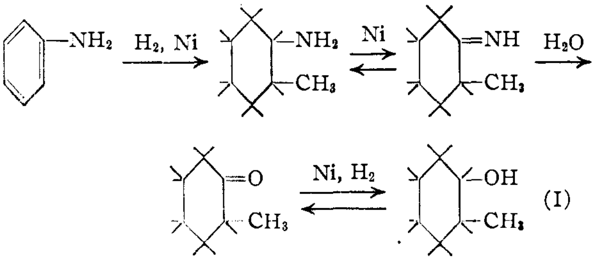
HYDROGENATIONS OF *o*-TOLUIDINE IN ALCOHOL

Alcohol	Alcohol, ml.	*o*-Toluidine, moles	Catalyst, g.	Temp., °C.	Time, hr.	Products (% yield)
CH_3OH	1000	5	50	200	29	2-Methylcyclohexanol (8.8)
						2-Methylcyclohexylamine (4.8)
						N,2-Dimethylcyclohexylamine (6.0)
						cis- (or *trans*)-N,N,2-Trimethylcyclohexylamine (33.5)
						trans- (or *cis*)-N,N,2-Trimethylcyclohexylamine (6.5)
						Unreacted *o*-toluidine (7.7)
C_2H_5OH	400	2	20	180	16	2-Methylcyclohexanol (15.8)
						N-Ethyl-2-methylcyclohexylamine (49.1)
						N,N-Diethyl-2-methylcyclohexylamine (17.1)
$(CH_3)_2CHOH$	200	0.5	5	180	14	N-Isopropyl-2-methylcyclohexylamine (67.8)
n-C_4H_9OH	200	0.5	5	180	10	N-Butyl-2-methylcyclohexylamine (64.3)
$C_4H_9\overset{C_2H_5}{\overset{\vert}{C}}HCH_2OH$	500	1	30	200	9	2-Methylcyclohexylamine (35.4)
						N-(2-Ethylhexyl)-2-methylcyclohexylamine (14.2)
						Unreacted *o*-toluidine (9.9)

This paper reports the preparation of N-alkyl-2-methylcyclohexylamines in good yields by ring-hydrogenation of *o*-toluidine in various alcohols. The reaction conditions used and the products obtained are summarized in Table I; the physical properties of the novel 2-methylcyclohexylamines and derivatives are summarized in Table II. The catalyst was a commercially available nickel-on-kieselguhr catalyst, Harshaw Ni-0104T 1/8″. One experiment was carried out with Raney nickel catalyst with results comparable to those with the nickel-on-kieselguhr catalyst, but no other catalysts were investigated.

The hydrogenations in methanol and ethanol produced both N-alkyl- and N,N-dialkyl-2-methylcyclohexylamines, the latter being the main product in methanol. Two isomers, undoubtedly *cis-trans* isomers, of N,N,2-trimethylcyclohexylamine were isolated; this is the only case where *cis-trans* isomers were isolated, although such isomers of all the 2-methylcyclohexylamines are possible.

The 2-methylcyclohexanol produced in hydrogenations in methanol and ethanol formed constant-boiling mixtures with certain of the amines. It was necessary to remove the 2-methylcyclohexanol before isolation and purification of the products by fractional distillation. It seems probable that the 2-methylcyclohexanol is formed from 2-methylcyclohexylamine and water by nickel-catalyzed reactions of the types



(I)

The formation of the imine is in accord with the mechanism suggested by Winans and Adkins[2] for the formation of secondary amines from primary amines in the presence of hydrogenation catalysts.

As evidence for the over-all reaction I, cyclohexylamine and water at 180° in the presence of the nickel catalyst were found to give cyclohexanol. The addition of a mutual solvent, tetrahydrofuran, was found to be beneficial, 62% of the cyclohexylamine reacting to give cyclohexanol in 84.8% yield.

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[1] H. Adkins and H. I. Cramer, THIS JOURNAL, **52**, 4349 (1930).

[2] C. F. Winans and H. Adkins, *ibid.*, **54**, 306 (1932).

TABLE II

N-ALKYL-2-METHYLCYCLOHEXYLAMINES

Compound	B.p.,[a] °C.	Mm.	n^{25}_D	d^{25}_4	M_D Calcd.	M_D Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Picrate M.p., °C.	Picrate Nitrogen, % Calcd.	Picrate Nitrogen, % Found
N,2-Dimethylcyclohexylamine	162	747	1.4525	0.8497	40.54	40.36	75.52	75.37	13.47	13.32	11.01	11.02			
cis- (or *trans*)-N,N,2-Trimethylcyclohexylamine[b]	170	748	1.4500	.8399	45.35	45.13	76.53	76.70	13.56	13.57	9.92	9.61	157–158	15.13	15.02
trans- (or *cis*)-N,N,2-Trimethylcyclohexylamine[c]	180.5	749	1.4663	.8648	45.35	45.18	76.53	76.43	13.56	13.78	9.92	9.89	210–211 (dec.)	15.13	15.13
N-Ethyl-2-methylcyclohexylamine	177.5	760	1.4504	.8421	45.35	45.04	76.53	76.48	13.56	13.45	9.92	9.93	118–120	15.13	15.03
N,N-Diethyl-2-methylcyclohexylamine	112	50	1.4420	.8227	54.74	54.66	78.00	78.22	13.71	13.54	8.28	8.40			
N-Isopropyl-2-methylcyclohexylamine	186	754	1.4440	.8266	49.78	49.80	77.41	77.39	13.55	13.72	9.03	9.11	149–151	14.58	14.59
	82.4	10													
N-Butyl-2-methylcyclohexylamine	218.4	747	1.4503	.8365	54.74	54.65	78.04	78.13	13.69	13.71	8.27	8.10	143–144	14.06	14.19
	88.2	10													
N-(2-Ethylhexyl)-2-methylcyclohexylamine	135.5	10	1.4513	.8466	72.87	71.59	79.92	79.94	13.86	13.82	6.21	6.23			

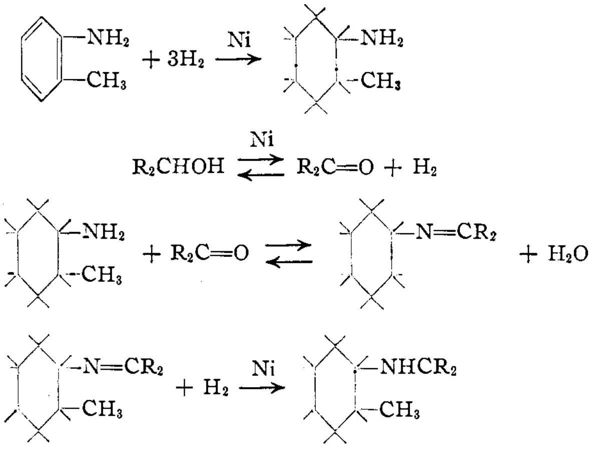
[a] All boiling points are corrected. [b] Methiodide, m.p. 218–219° (dec.). *Anal.* Calcd.: N, 4.94. Found: N, 5.08. [c] Methiodide, m.p. 238–238.5° (dec.). *Anal.* Calcd.: N, 4.94. Found: N, 5.07.

The formation of cyclohexanol in the hydrogenation of aniline was not noted by Adkins and Cramer.[1] In the work described herein, anhydrous alcohols were not used. However, a molecule of water is split out in the alkylation reaction II, and therefore water becomes available for reaction I in any case.

$$RNH_2 + R'OH \xrightarrow{Ni} RNHR' + H_2O \qquad (II)$$

Hydrogenation of *o*-toluidine in isopropyl alcohol and in *n*-butanol produced the corresponding N-alkyl-2-methylcyclohexylamine in good yield. No other products were isolated. The excess alcohol, in each of these cases, was removed at reduced pressure from the acidified reaction product and any 2-methylcyclohexanol would have been removed also. Hydrogenation in 2-ethylhexanol gave 2-methylcyclohexylamine as the main product, although some N-(2-ethylhexyl)-2-methylcyclohexylamine was produced.

The yields obtained suggest that this reaction would be an acceptable preparative method for making various substituted cyclohexylamines by hydrogenation of aromatic amines in alcohols. The reaction probably proceeds by the steps



The products reported herein are in accord with those formed by reductive alkylation of amines with aldehydes and ketones.[3] That is, amines and formaldehyde readily give the tertiary amine, whereas higher aldehydes give mainly the secondary amine and ketones give only the secondary amine.

Experimental

Hydrogenation of *o*-Toluidine.—The hydrogenations summarized in Table I were carried out in an Aminco rocker-type bomb. The catalyst was Harshaw Ni-0104T 1/8", which is a prereduced, stabilized nickel-on-kieselguhr pelleted catalyst supplied by the Harshaw Chemical Company. The *o*-toluidine, alcohol and catalyst were charged into the bomb, the bomb flushed with nitrogen and then with hydrogen, and hydrogen introduced to 2500 p.s.i.g. The temperature was raised to 180–200° with shaking, the hydrogen pressure rising to 3000–3500 p.s.i.g. In some cases it was necessary to add more hydrogen during the course of the hydrogenation. The theoretical amount of hydrogen had been absorbed in the times indicated in Table I. After cooling, the catalyst was removed by filtration and the products isolated as described below.

In the first reactions with methanol and ethanol, most of the alcohol was removed by distillation, the residue treated

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[3] R. Adams, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 174.

with a large volume of water, and the mixture extracted exhaustively with low boiling petroleum ether. In the distillation of the residue from these extracts, constant-boiling azeotropes of 2-methylcyclohexanol and certain of the products were obtained. The azeotrope of 2-methylcyclohexanol and N,N,2-trimethylcyclohexylamine (about 60% 2-methylcyclohexanol) had a b.p. of 162° (736 min.) (cor.), $n^{25}\text{D}$ 1.4570, the azeotrope with N,N-diethyl-2-methylcyclohexylamine (about 40% 2-methylcyclohexanol) had a b.p. of 192° (cor.), $n^{25}\text{D}$ 1.4500. In order to avoid these azeotropes, an excess of hydrochloric acid was added to the residue from the petroleum ether extracts, the 2-methylcyclohexanol removed by steam distillation, and the amines isolated by making the solution basic, extracting, and fractionally distilling.

The higher alcohols were removed by distillation under reduced pressure after adding an excess of acid to the reaction product. The residue was then made basic, the resulting mixture extracted with ether, and the products isolated by fractional distillation. All distillations were carried out in a 6 ft. × 13 mm. Podbielniak column except the product from 2-ethylhexanol which was distilled through a 3 ft. × 13 mm. Podbielniak column. The products isolated and yields are summarized in Table I.

Cyclohexanol from Cyclohexylamine.—A mixture of 50 g. (0.5 mole) of cyclohexylamine, 200 ml. of water and 5 g. of Harshaw Ni-0104T $^1/_8$" was placed in an Aminco bomb and, after flushing with nitrogen and venting, heated for 10 hours at 180° (no hydrogen was used). The catalyst was removed by filtration and the reaction product extracted exhaustively with low boiling petroleum ether. The extracts were dried and the solvent removed by distillation. Analysis[4] of the residue indicated that it contained 42.8% alcohol calculated as cyclohexanol, 38.6% primary amine calculated as cyclohexylamine, and 7.8% secondary amine calculated as dicyclohexylamine. This would indicate that cyclohexanol was produced in 50% yield, based on reacted cyclohexylamine.

In another experiment carried out under the same conditions, except that 100 ml. of tetrahydrofuran was added as a solvent for the reaction, analysis of the product indicated that 62% of the cyclohexylamine reacted to give cyclohexanol in 84.8% yield. Cyclohexanol was isolated by extracting an acidified aliquot of the reaction product with ether and distilling (b.p. 157–158°) (uncor.), $n^{26}\text{D}$ 1.4631[5] and further identified by its 3,5-dinitrobenzoate, m.p. 112–113°.[6]

Acknowledgment.—The authors are indebted to Mr. L. J. Lohr for the distillations and to Dr. S. Siggia and Mr. L. J. Fraunefelder for analyses.

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(4) S. Siggia, J. G. Hanna and I. R. Kervenski, *Anal. Chem.*, **22**, 1295 (1950); S. Siggia and I. R. Kervenski, *ibid.*, **23**, 117 (1951).

(5) Reported b.p. 161°, K. K. Kelley, THIS JOURNAL, **51**, 1400 (1929); reported $n^{25}\text{D}$ 1.4642, G. S. Hiers and R. Adams, *ibid.*, **48**, 2385 (1926).

(6) Reported m.p. 112–113°, T. Reichstein, *Helv. Chim. Acta*, **9**, 799 (1926).

GENERAL ANILINE AND FILM CORP.
CENTRAL RESEARCH LABORATORY
EASTON, PENNSYLVANIA

Oxidations with Ruthenium Tetroxide

BY CARL DJERASSI AND ROBERT R. ENGLE[1]

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Osmium tetroxide has been used widely in organic chemistry as a catalyst in oxidations[2] and particularly for the hydroxylation[3] of olefins. The latter reaction is usually carried out by mixing stoichiometric quantities of the olefin and osmium tetroxide in an inert solvent such as ether, with or without traces of pyridine, and proceeds in good yield to the corresponding *cis*-glycol *via* a cyclic osmate ester which has to be cleaved.[3] Osmium tetroxide is expensive and very poisonous, and it seemed of interest, therefore, to investigate the behavior of the corresponding ruthenium derivative, since ruthenium appears immediately above osmium in the periodic table. Ruthenium tetroxide has been prepared a number of times,[4] but its behavior toward organic compounds has not been investigated except for the observation[4] that it is reduced rapidly by alcohol, acetaldehyde and the like. Ruthenium is more readily available than osmium and there exist *a priori* two reasons why ruthenium tetroxide might be preferred to the osmium analog. Although its vapors cause irritation when inhaled, it is not poisonous to the eyes[4,5] in contrast to this very serious danger with osmium tetroxide. Furthermore, recovery problems are simplified by the fact that combustion of ruthenium dioxide in air will not yield the volatile tetroxide in contrast to the analogous osmium derivative and organic impurities can thus be removed readily. In view of the fact that the present investigation had to be interrupted,[1] we should like to report briefly our observations on the behavior of ruthenium tetroxide with some organic compounds.

The much greater oxidizing action of ruthenium tetroxide as compared to osmium tetroxide was already demonstrated in initial qualitative experiments when a search was made for suitable solvents in which the oxidations could be conducted. Thus ether, benzene and pyridine, solvents which have been found very useful in the case of osmium tetroxide,[3] reacted violently and instantaneously with ruthenium tetroxide and thus proved completely useless. Of the common organic solvents, only carbon tetrachloride and chloroform were satisfactory[6] and the former was employed throughout our experiments. In view of the very high vapor pressure of ruthenium tetroxide, the solid usually has to be stored over potassium hydroxide in an ice cooled desiccator and it was found advantageous, therefore, to keep the reagent in carbon tetrachloride solution in which it was stable for a period of over one year. The ruthenium tetroxide content was established readily in an aliquot portion by reduction with an organic compound to the insoluble solvated ruthenium dioxide and reduction of the latter with hydrogen to ruthenium metal which could be weighed.

Since phenanthrene reacts slowly (2–7 days) with osmium tetroxide[3] in benzene solution to afford in good yield the osmate ester which upon cleavage leads to the crystalline 9,10-dihydrophenanthrene-9,10-diol, this example was selected first for comparison purposes. When a carbon tetrachloride solution of ruthenium tetroxide was added to an ice-cold solution of phenanthrene, a black pre-

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(1) American Platinum Works Predoctoral Fellow at Wayne University, 1952.

(2) *Inter al.*, K. A. Hofmann, *Ber.*, **45**, 3329 (1912); N. A. Milas and S. Sussman, THIS JOURNAL, **58**, 1302 (1936).

(3) *Cf.* R. Criegee, *Ann.*, **522**, 75 (1936); R. Criegee, B. Marchand and H. Wannowius, *ibid.*, **550**, 99 (1942).

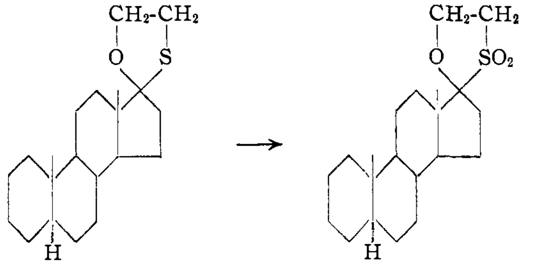
(4) First prepared by C. Claus, *J. prakt. Chem.*, **79**, 28 (1860); the most recent reference is that by F. S. Martin, *J. Chem. Soc.*, 2683, 3055 (1952).

(5) W. M. Latimer and J. H. Hildebrand, "Reference Book of Inorganic Chemistry," The Macmillan Co., New York, N. Y., 1940, p. 418.

(6) This observation was also made by Martin (ref. 4) who measured the partition coefficient of ruthenium tetroxide between water and carbon tetrachloride and found it to be 59 in favor of the latter.

cipitate separated rapidly which appeared to consist chiefly of ruthenium dioxide rather than a ruthenate ester since conventional[3] cleavage with sodium sulfite yielded only a small amount of 9,10-dihydrophenanthrene-9,10-diol. The bulk of the product was in the original carbon tetrachloride solution and consisted of 9,10-phenanthrenequinone accompanied by some unreacted phenanthrene. Whether the formation of the quinone is due to direct oxidation at the 9,10-position or involves further oxidation of an intermediate ruthenate ester cannot be decided with the information at hand and further work on the oxidation of polycyclic aromatic hydrocarbons with this reagent is contemplated.

Attention was next turned to the behavior of sulfides since they appear to be essentially inert to osmium tetroxide[7,8] under ordinary conditions. In marked contrast to osmium tetroxide,[8] diphenyl sulfide was oxidized rapidly by ruthenium tetroxide at ice-bath temperature and afforded the corresponding sulfone accompanied by some sulfoxide. That diphenyl sulfoxide was probably the intermediate in this reaction was shown by the nearly quantitative conversion of the sulfoxide to the sulfone by ruthenium tetroxide. The oxidation was not limited to a diaryl sulfide since methyl *p*-tolyl sulfide and methyl benzyl sulfide were also oxidized to the corresponding sulfones; no sulfoxide could be isolated in these instances. A steroidal hemithioketal, androstan-17-one ethylene hemithioketal (I)[9] was similarly oxidized rapidly to the corresponding sulfone II in somewhat better yield as compared to perphthalic acid[9] where some cleavage to the parent ketone is observed.



I II

In view of this ready conversion of sulfides to sulfones or sulfoxides by means of ruthenium tetroxide under essentially neutral conditions, it seemed pertinent to investigate the behavior of triphenylmethyl phenyl sulfide toward this reagent. Knoll[10] claimed the formation of the sulfoxide by chromium trioxide oxidation of the sulfide, a reaction which could not be substantiated by Gregg and co-workers,[11] who observed that only triphenylcarbinol,[12] diphenyl disulfide and benzenesulfonic acid were formed. In spite of the fact that the entire reaction was carried out in carbon tetrachloride rather than acid solution, the main product (41%) of the ruthenium tetroxide oxidation was also triphenylcarbinol and no evidence for the presence of a sulfoxide or sulfone could be detected even after chromatography.

Acknowledgment.—We are indebted to the American Platinum Works, Newark, New Jersey, for support in the form of a fellowship and generous supplies of ruthenium compounds, and to Mr. Frank A. Meier of that company for helpful suggestions.

Experimental[13]

Stability of Ruthenium Tetroxide in Various Solvents.—A small amount of ruthenium tetroxide[14] (*ca.* 10 mg.) was tested with the following solvents: anhydrous ether—small explosion, followed by yellow flame; benzene—vigorous explosion; pyridine—no explosion, only flame; carbon tetrachloride and chloroform—reddish-orange solution, which was quite stable if preserved in stoppered flasks uncontaminated by organic matter. When a carbon tetrachloride solution (rather than the solid) of ruthenium tetroxide was added to benzene or ether, no fire or explosion was produced but an instantaneous appearance of a black precipitate of ruthenium dioxide was noted. The same observation was made when the reaction was conducted in an atmosphere of nitrogen.

Determination of Ruthenium Tetroxide in Carbon Tetrachloride Solution.—For storage or shipping purposes, ruthenium tetroxide is best handled in carbon tetrachloride solution and the following method of determination was employed. To a 4-cc. aliquot portion of the standard solution was added dropwise diphenyl sulfide or ethanol until no more black precipitate was formed. After centrifugation, the supernatant liquid was tested for the presence of unreacted tetroxide by the addition of a few drops of diphenyl sulfide and the precipitate was washed several times with carbon tetrachloride–ether. The solvated ruthenium dioxide was then transferred to a tared Rose crucible as a slurry in carbon tetrachloride (this was done to avoid losses rather than as a safety precaution since ruthenium dioxide is stable and harmless), the latter was blown off and the dioxide was reduced to ruthenium metal at red heat for 20 minutes in a slow current of hydrogen. After cooling in an atmosphere of hydrogen, the crucible was again weighed in order to determine the weight of ruthenium and the concentration of ruthenium tetroxide could thus be established accurately. A typical duplicate run gave values of 17.62 and 17.65 mg. per cc. and the accuracy of this method was tested initially with solutions of ruthenium tetroxide of known concentration.

Reaction of Phenanthrene with Ruthenium Tetroxide.—To an ice-cold solution of 2.0 g. (0.0112 mole) of phenanthrene in 100 cc. of carbon tetrachloride[15] was added dropwise with stirring over a period of 15 minutes 55 cc. of a carbon tetrachloride solution of ruthenium tetroxide containing 0.972 g. (0.0058 mole) of the tetroxide. A black precipitate formed upon addition of the first drop. After 24 hours at −5°, the precipitate was centrifuged, washed several times with carbon tetrachloride and ether, and finally was extracted with ether in a Soxhlet extractor to ensure complete removal of soluble products. The combined organic solutions were evaporated to dryness and the residue, dissolved in 100 cc. of hexane–benzene (1:1) was chromatographed on 80 g. of alumina. Unreacted **phenanthrene** (0.958 g., 48%) was eluted with the original solvent combination, while the chloroform eluates after evaporation and recrystallization from benzene afforded 0.34 g. (28% based on ruthenium tetroxide) of **9,10-phenanthrenequinone** with m.p. 206–208°, undepressed upon ad-

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[7] G. Stork, E. E. van Tamelen, L. J. Friedman and A. W. Burgstahler, THIS JOURNAL, **75**, 384 (1953).

[8] Unpublished observation from this Laboratory.

[9] C. Djerassi and M. Gorman, THIS JOURNAL, **75**, 3704 (1953).

[10] R. Knoll, *J. prakt. Chem.*, **113**, (N.F.), 40 (1926).

[11] D. C. Gregg, K. Hazelton and T. F. McKeon, *J. Org. Chem.*, **18**, 36 (1953), and earlier papers.

[12] It is noteworthy that the reported melting point (ref. 10) for the presumed sulfoxide (m.p. 163°) is nearly the same as that of triphenylcarbinol (m.p. 162°).

[13] Melting points are uncorrected. Infrared absorption spectra were measured in chloroform solution with a Baird Associates double beam recording infrared spectrophotometer using a 0.1-mm. cell thickness.

[14] Obtained from American Platinum Works, Newark, New Jersey.

[15] The carbon tetrachloride in this and all other experiments was purified as indicated by L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath & Co., New York, N. Y., 1941, p. 365.

mixture with an authentic specimen. Identity was established further by comparison of the infrared spectra and formation of a quinoxaline derivative, m.p. 218–220°.

In another experiment,[16] the reaction was carried out as above except that equimolar proportions were used, and there was isolated 18% of phenanthrenequinone. The original black precipitate was refluxed with sodium sulfite[3] in dilute ethanol for two hours, filtered, and the filtrate was extracted thoroughly with ether. The ether residue after recrystallization from hexane–acetone furnished 11% of **9,10-dihydrophenanthrene-9,10-diol** with m.p. 175–177°, undepressed upon admixture with a sample prepared with osmium tetroxide.[3]

Reaction of Diphenyl Sulfide with Ruthenium Tetroxide.—A large excess of sulfide was employed in order to isolate any intermediate oxidation product.

An ice-cold solution of 4.798 g. (0.0257 mole) of diphenyl sulfide in 150 cc. of carbon tetrachloride was treated exactly as described above with 25 cc. of a carbon tetrachloride solution of ruthenium tetroxide (containing 1.043 g., 0.0063 mole of tetroxide). Precipitation of ruthenium dioxide started immediately and after 14 hours in the refrigerator, the precipitate was centrifuged and washed thoroughly with carbon tetrachloride and ether. The residue after evaporation of the organic solvents was chromatographed on 100 g. of alumina. The unreacted sulfide was removed by the original hexane–benzene (7:3) eluates, while **diphenyl sulfone** (0.58 g., 42%) with m.p. 124.5–125.5° was obtained from the hexane–benzene (1:9) fractions. Identity was established by a mixture melting point and infrared comparison with an authentic sample; the two typical sharp sulfone bands[17] at 8.65 and 9.0 μ were present.

Anal. Calcd. for $C_{12}H_{10}O_2S$: C, 66.05; H, 4.62. Found: C, 66.32; H, 4.91.

Evaporation of the benzene and benzene–ether (1:1) eluates to dryness and recrystallization from benzene–petroleum ether furnished 0.4 g. (32%) of **diphenyl sulfoxide** with m.p. 68–69°. Identity was established in the usual manner including infrared comparison (typical[18] sulfoxide band at 9.6 μ).

Anal. Calcd. for $C_{12}H_{10}OS$: C, 71.28; H, 4.99. Found: C, 71.18; H, 5.28.

When an equimolar ratio of diphenyl sulfoxide and ruthenium tetroxide was mixed in carbon tetrachloride solution and worked up in the above manner, a 93% yield of diphenyl sulfone was realized.

Reaction of Methyl *p*-Tolyl Sulfide with Ruthenium Tetroxide.—Methyl *p*-tolyl sulfide (3.90 g., 0.0281 mole) was oxidized with 1.165 g. (0.007 mole) of ruthenium tetroxide exactly as indicated for diphenyl sulfide and purified by chromatography. **Methyl *p*-tolyl sulfone** was obtained in 31% yield, m.p. 85–86° (lit.[19] m.p. 86–87°) but no sulfoxide could be detected in the later eluates of the chromatogram.

Anal. Calcd. for $C_8H_{10}O_2S$: C, 56.46; H, 5.92. Found: C, 56.35; H, 5.82.

Reaction of Methyl Benzyl Sulfide with Ruthenium Tetroxide.—The oxidation was carried out in the above described manner with 0.0252 mole of methyl benzyl sulfide and 0.0067 mole of ruthenium tetroxide. **Methyl benzyl sulfone** was isolated in 58% yield, m.p. 125–126°,[20] but no sulfoxide was found in the latter chromatogram fractions.

Anal. Calcd. for $C_8H_{10}O_2S$: C, 56.46; H, 5.92. Found: C, 55.98; H, 5.69.

Reaction of Triphenylmethyl Phenyl Sulfide and Ruthenium Tetroxide.—The oxidation of the triphenylmethyl phenyl sulfide[11] was carried out in the standard manner except that equimolar amounts were employed. As in the above-described cases, ruthenium dioxide separated immediately upon addition of the tetroxide. After centrifugation, the carbon tetrachloride solution was evaporated to dryness yielding a residue with m.p. 77–87° which was partitioned between water[21] and ether. The ether solution was washed until neutral, dried, evaporated and dissolved in warm cyclohexane from which 33% of triphenylcarbinol (m.p. 160–162°) separated. The filtrate was evaporated and the residue was chromatographed on alumina yielding 13% of recovered sulfide and an additional 8% of triphenyl carbinol. No disulfide[11] was found in any chromatogram fractions. Acidic products formed were not investigated.

Reaction of Androstan-17-one Ethylene Hemithioketal (I) and Ruthenium Tetroxide.—A mixture of 0.48 g. (0.0011 mole) of the hemithioketal (I)[9] and 0.34 g. (0.0021 mole) of ruthenium tetroxide in carbon tetrachloride was left in the refrigerator overnight. After centrifugation the supernatant liquid was evaporated to dryness and triturated with acetone yielding 0.35 g. of the **sulfone** II with m.p. 187–190°. Two recrystallizations from acetone raised the m.p. to 199–200°, undepressed upon admixture with an authentic sample[9] prepared by perphthalic acid oxidation of I. The infrared spectra of the two specimens were identical.

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[16] This experiment was performed at the University of Mexico with Dr. Alberto Sandoval.

[17] K. C. Schreiber, *Anal. Chem.*, **21**, 1168 (1949).

[18] D. Barnard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).

[19] R. Otto, *Ber.*, **18**, 154 (1885).

[20] Reported, m.p. 124.5° (A. Freiman and S. Sugden, *J. Chem. Soc.*, 263 (1928)).

[21] The ruthenium tetroxide probably contains a small amount of water since it is obtained by co-distillation with water. It is therefore not necessary to postulate that the hydrogen necessary for the formation of triphenylcarbinol is furnished during the ether–water partition. Indeed, direct chromatography of the carbon tetrachloride residue gave essentially the same results.

DEPARTMENT OF CHEMISTRY
WAYNE UNIVERSITY
DETROIT 1, MICHIGAN

Δ^5-Pregnen-20-one[1]

BY MARGARET A. DAUS AND H. HIRSCHMANN

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In a study of the hydrogenolyses of toluenesulfonates with lithium aluminum hydride Schmid and Karrer[2] observed that the tosylate of cholesterol yielded both Δ^5-cholestene and 3,5-cyclocholestane. In contrast reduction of the tosylate of Δ^5-pregnen-3β-ol-20-one followed by reoxidation of the 20-hydroxy group furnished only a single pure product[3] of the composition $C_{21}H_{32}O$. This was held probably to be the hitherto undescribed[4] Δ^5-pregnen-20-one, as it showed a well-defined infrared absorption maximum in the region of the bending vibrations of hydrogen attached to a trisubstituted double bond. However, the spectrum which possessed absorption maxima near 12.67 and 12.37 μ failed to conform to the generalizations which had emerged from a study of the spectra of Δ^5-unsaturated steroids.[5] These compounds showed in general two maxima in this region that could be associated with the presence of the double bond. If no functional group other than one at C-3 was present in the vicinity of the double bond one of these peaks was close to 12.50 μ (800 cm.$^{-1}$) while the position of the other depended on the nature and the configuration of the substituent at C-3. Since Δ^5-cholestene showed maxima at 12.52, 12.37 (w) and 12.01 μ (799, 809, 833 cm.$^{-1}$) an absorption peak near 12.50 μ was to be expected also for the spectrum of Δ^5-pregnen-20-one. As it

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[1] Supported by grants from the Hanna Research Fund and from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

[3] P. Karrer, H. Asmis, K. N. Sareen and R. Schwyzer, *ibid.*, **34**, 1022 (1951).

[4] The preparation of this substance has been recorded in the patent literature (R. E. Marker and E. L. Wittle, U. S. Patents 2,397,424, 2,397,425 and 2,397,426). However, the product was not characterized in any way.

[5] H. Hirschmann, THIS JOURNAL, **74**, 5357 (1952).

seemed important to ascertain whether the spectrum of this compound was indeed anomalous we undertook its preparation by an unambiguous route.

3β-Chloro-Δ^5-pregnen-20-one was prepared from Δ^5-pregnen-3β-ol-20-one with phosphorus pentachloride and reduced with sodium and propanol. The resulting mixture of the two Δ^5-pregnen-20-ols was oxidized according to the method of Bladon, *et al.*,[6] which proved superior to the customary procedure with bromination of the 5–6 double bond. The reaction product was identified as Δ^5-pregnen-20-one by its composition, its rotation, and by its conversion to the known allopregnan-20-one. It is clearly different from the product described by the Swiss workers as shown by a comparison of the infrared spectra and the melting points. The absorption maxima of our preparation (12.54 (v.s.), 12.36 (w), and 12.02 (v.s.) μ (798, 809, 832 cm.$^{-1}$) in carbon disulfide, and near 12.50, 12.34 and 11.95 μ (800, 811, 837 cm.$^{-1}$) in Nujol) were in close accord with the corresponding peaks of Δ^5-cholestene[5] and of 20α-acetoxy-Δ^5-pregnene. Since no peaks of comparable height were seen in the reduction products[7] cholestane[6] and allopregnan-20-one it is probable that all three frequencies are characteristic of Δ^5-unsaturated steroids that lack a substituent at C-3 and are not subject to disturbing influences from other vicinal groups.

The results serve to re-emphasize that the presence even of a strong maximum in the 12 μ range is insufficient proof for the presence of a trisubstituted double bond and indicate the greater reliability of a spectral comparison with closely related structures.

Experimental[8]

Δ^5-Pregnen-20-one.—A solution of 62 mg. of phosphorus pentachloride in 2.8 cc. of dry chloroform was added dropwise to a stirred solution of 37 mg. of Δ^5-pregnen-3β-ol-20-one in 4.6 cc. of the same solvent (50 minutes at −15°). The mixture was stirred at 0° for 10, and at room temperature for 60 minutes and worked up in the usual manner.[9] The resulting 3β-chloro-Δ^5-pregnen-20-one which was purified by chromatography on alumina and by recrystallization from dilute methanol and from petroleum ether melted at 148.5–150.5°; lit.[10] m.p. 146.5° uncor. The absorption peaks at 13.15, 12.51 and 12.18 μ (760, 799, 821 cm.$^{-1}$) are in good accord with the corresponding maxima of other Δ^5-3β-chlorosteroids.[11] Another strong peak was at 12.10 μ (827 cm.$^{-1}$). A solution of 46.8 mg. of 3β-chloro-Δ^5-pregnen-20-one in 8 cc. of propanol was reduced with 540 mg. of sodium as described for other 3-chlorosteroids.[9] The crude diols (42.3 mg.) in 6 cc. of acetone were oxidized with 0.13 cc. of 8 *N* chromic acid reagent[6] for 5 minutes at 34°. The excess oxidant was reduced by adding immediately a mixture of 110 mg. sodium bisulfite, 1.2 cc. of *N* sulfuric acid and 6.4 cc. of acetone. The reaction mixture was distributed between ether and water. The ether layer was washed with potassium carbonate and water. The ether residue (35.7 mg.) was freed of a high melting impurity which was rather insoluble in petroleum ether and recrystallized from this solvent and from methanol; yield of Δ^5-pregnen-20-one 16.2 mg., m.p. 133–135°, $[\alpha]^{27}\text{D}$ +6° (*c* 0.5, chloroform) $[M]\text{D}$ +18° ($[M]\text{D}$ calcd. +26° from $[M]\text{D}$ for cholesterol[12] −154°, Δ^5-cholestene[12] −207° and of Δ^5-pregnen-3β-ol-20-one[12] +79°); carbonyl peak at 5.86 μ (1706 cm.$^{-1}$).

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74. Found: C, 83.81; H, 10.72.

Allopregnan-20-one.—A mixture of 8.7 mg. of Δ^5-pregnen-20-one, 200 mg. of prereduced palladium–calcium carbonate catalyst and 8.5 cc. of 95% ethanol were shaken in an atmosphere of hydrogen. The uptake of gas ceased after 15 minutes. The reduction product was isolated in the usual manner[9] and recrystallized from methanol to give 5.3 mg. of allopregnan-20-one. The m.p. (136.5–137.5°) remained unchanged by admixture with a specimen[13] prepared from allopregnane-3,20-dione. The infrared spectra of both preparations were in good agreement. In the 12 μ region allopregnan-20-one showed very weak peaks near 12.56 and 12.09 μ (796, 827 cm.$^{-1}$). The ketone peak was at 5.86 μ (1706 cm.$^{-1}$). The compound has been prepared by a variety of methods. Several of these are cited by Mancera, *et al.*[14]

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[6] P. Bladon, J. M. Fabian, H. B. Henbest, H. P. Koch and G. W. Wood, *J. Chem. Soc.*, 2402 (1951).

[7] This is in contrast to the peaks seen near 12.0 μ in many Δ^5-3β-acetoxy steroids. These weaker maxima were considered to be unrelated to the presence of the double bond since reduction caused little or no spectral change (*cf.* Fig. 1 in ref. 5).

[8] All m.p.'s reported are corrected. Details on spectrographic technique have been given previously.[5] The solvent was carbon disulfide unless indicated otherwise. Weak bands are designated as (w), very strong ones as (v.s.). The analysis is by Dr. E. W. D. Huffman, Wheatridge, Colorado.

[9] H. Hirschmann and F. B. Hirschmann, *J. Biol. Chem.*, **184**, 259 (1950).

[10] A. Butenandt and W. Grosse, *Ber.*, **70**, 1446 (1937).

[11] H. Hirschmann, *Ciba Foundation Colloquia*, in press.

[12] D. H. R. Barton and J. D. Cox, *J. Chem. Soc.*, 783 (1948).

[13] H. Hirschmann, F. B. Hirschmann and M. A. Daus, *J. Biol. Chem.*, **178**, 751 (1949).

[14] O. Mancera, G. Rosenkranz and C. Djerassi, *J. Org. Chem.*, **16**, 192 (1951).

DEPARTMENT OF MEDICINE
WESTERN RESERVE UNIVERSITY AND THE
LAKESIDE HOSPITAL
CLEVELAND 6, OHIO

β-Fattyalkylaminopropionaldehydes[1]

BY KENDRICK R. EILAR AND OWEN A. MOE

RECEIVED APRIL 8, 1953

It has been found that aliphatic amines having long chain (twelve or more carbon atoms) alkyl groups undergo the Mannich reaction[2] with formaldehyde and other lower aldehydes which contain α-hydrogen atoms in much the same manner as do the lower alkylamines. The products are obtained in good yields (81–92%) in every case except those involving primary fatty amines and acetaldehyde; in such cases mixtures are obtained which are difficult if not almost impossible to separate.

The aldehyde function of the β-fattyalkylaminopropionaldehydes is singularly unreactive for an aldehydo group. It is noteworthy that all attempts to prepare the usual aldehyde derivatives (2,4-dinitrophenylhydrazone, semicarbazone and oxime) were unsuccessful, although positive Tollens tests[3] were obtained. However, the elemental analyses, the mode of formation, and the infrared spectrum of one of the compounds (α,α-dimethyl-β-didodecylaminopropionaldehyde; bands at 880, 1100, 1310, 1730 and 2700 cm.$^{-1}$) constitute strong evidence in favor of the β-alkylaminopropionaldehyde structure.

Experimental

α,α-Dimethyl-β-didodecylaminopropionaldehyde.—Didodecylamine (71 g.) was dissolved in 95% ethanol (100 ml.)

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[1] Paper No. 148, Journal Series, General Mills Research Laboratories.

[2] C. Mannich, U. S. Patent 1,824,676; Blicke, in "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303.

[3] S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945, p. 133.

and formalin (16.2 g.) was added. The resulting solution was stirred for a few minutes and isobutyraldehyde (14.4 g.) was added and the resulting reaction mixture was refluxed for a period of one hour. After cooling the reaction mixture separated into two distinct phases. The lower (ethanol) phase was removed, leaving a slightly cloudy, colorless liquid (93 g.). The volatile impurities were removed by evacuation at 0.2 mm. for three hours at 40°. A small amount of finely divided solid material was removed by filtration, yielding 81 g. (92%) of a clear, colorless liquid, $n^{30}\text{D}$ 1.4544, neutral equivalent, 422.

An analytical sample was prepared by adding 0.108 g. of oxalic acid (in 50 ml. of ether) to 5 g. of the above material in 30 ml. of ether. The ether was removed by evaporation, and the residue was extracted with Skellysolve B in which the Mannich base was soluble but didodecylammonium oxalate was insoluble. Filtration and removal of the solvent left 4.8 g. of a clear, colorless liquid, $n^{30}\text{D}$ 1.4547.

Anal. Calcd. for $C_{29}H_{59}NO$: C, 79.56; H, 13.58; N, 3.20; neut. equiv., 438. Found: C, 80.01; H, 13.38; N, 3.62; neut. equiv., 428.

α,α-Dimethyl-β-dodecylaminopropionaldehyde.—Dodecylamine (74 g.) was dissolved in 95% ethanol (100 ml.). The resulting solution was warmed to 50° and formalin (32.4 g.) was added over a period of 15 minutes. Isobutyraldehyde (28.8 g., 0.40 mole) was then added, and the solution was refluxed for one hour, and finally allowed to cool to 25°. The lower phase, 102 g., was removed and combined with an additional 5 g. obtained by adding water to the ethanol layers. The product was evacuated at 0.35 mm. for 4 hours at 40° leaving a clear, colorless oil, wt. 101 g. (88%), $n^{30}\text{D}$ 1.4568.

Anal. Calcd. for $C_{17}H_{35}NO$: N, 5.20; neut. equiv., 270. Found: N, 5.18; neut. equiv., 273.

A portion (20 g.) of this material was dissolved in 150 ml. of dioxane, 0.20 g. of Adams catalyst was added, and the mixture was placed in a low pressure hydrogenation shaker at 45 lb. p.s.i. and 30°. No pressure drop occurred during 2.5 hours. The mixture was heated to 80°, but no pressure drop occurred during 2 hours. No further attempt was made to reduce the compound to the amino alcohol.

β-Didodecylaminopropionaldehyde.—This compound was prepared from didodecylamine, formalin and acetaldehyde by a procedure similar to those described above; yield 81%, $n^{30}\text{D}$ 1.4661.

Anal. Calcd. for $C_{27}H_{55}NO$: N, 3.42; neut. equiv., 410. Found: N, 3.32; neut. equiv., 416.

α-Methyl β-Octadecylaminopropionaldehyde.—This compound was prepared from octadecylamine, formaldehyde and propionaldehyde by a procedure similar to those described above. The product crystallized from the reaction mixture; m.p. 32–33°, yield 88%.

Anal. Calcd. for $C_{22}H_{45}NO$: N, 4.16; neut. equiv., 340. Found: N, 4.46; neut. equiv., 342.

GENERAL MILLS RESEARCH LABORATORIES
MINNEAPOLIS, MINNESOTA

The Permanganate Oxidation of Uracil and 5-Nitrouracil

BY J. L. FAIRLEY, L. L. DAUS AND B. KRUECKEL

RECEIVED DECEMBER 11, 1952

The reaction of uracil with potassium permanganate in slightly acidic solution to yield carbon dioxide and oxaluric acid has been of considerable use in the degradation of the pyrimidine ring.[1,2] Edmonds, Delluva and Wilson have presented good evidence, although somewhat indirect in nature, suggesting that neither the carbon dioxide nor the oxaluric acid represent specific carbon atoms of the uracil. In this work synthetic orotic acid-4-C^{14} was supplied to a yeast and after a period of metabolic activity radioactive uracil was isolated.[3] The logical assumption was made that the conversion of the orotic acid to uracil by the yeast involved only the loss of the carboxyl group, resulting in uracil labeled only in the 4-position. Reaction of the uracil with permanganate, however, led to the finding that radioactivity was present in both the carbon dioxide and oxaluric acid fractions, indicating the lack of specificity of the oxidation.

Behrend and Offe[4] have described experiments, however, which have been interpreted as indicating that the course of the reaction varies with the nature and position of the substituent groups, and that 5-nitrouracil reacts in such fashion that the carbon atoms of the oxalic acid portion of the oxaluric acid fragment are derived from carbons 4 and 5 of the pyrimidine.

Lagerkvist[5] has applied these conclusions to the interpretation of the data resulting from experiments on the biosynthesis from radioactive bicarbonate of the nucleic acid pyrimidines of the rat. In this work the isolated uracil was converted to 5-nitrouracil prior to permanganate oxidation. It was concluded from the observed radioactivity of the reaction products and the assumption that carbons 4 and 5 of the nitrouracil gave rise to the oxaluric acid that bicarbonate was a direct precursor of carbon 6 of nucleic acid pyrimidines.

In view of the current interest in the biosynthesis of the nucleic acid components and the potential importance of Lagerkvist's results, it was felt that the course of the reaction of 5-nitrouracil with permanganate should be re-examined. It was deemed desirable at the same time to attempt a direct test of the conclusions of Edmonds, *et al.*,[2] concerning the oxidation of uracil.

Accordingly, both uracil-4-C^{14} and 5-nitrouracil-4-C^{14} were synthesized and subjected to permanganate oxidation. The distribution of radioactivity in the carbon dioxide and oxaluric acid fractions was then determined. The results, presented in Table I for typical experiments, were very similar for both pyrimidines and were in excellent agreement with those of Edmonds, *et al.*,[2] for uracil. High percentages of the isotope were found in both fractions, indicating that ring cleavage had occurred rather indiscriminately between carbons 4 and 5 and between carbons 5 and 6 of the pyrimidine ring.

TABLE I

PERMANGANATE OXIDATION OF URACIL-4-C^{14} AND 5-NITROURACIL-4-C^{14}

Compound	Amt. used, mg.	Amt. recovered (as $BaCO_3$), mg.	Total activity, c./min.
Uracil-4-C^{14}	75		24.7×10^5
Carbon dioxide		115	9.1×10^5
Oxalic acid		160	10.6×10^5
5-Nitrouracil-4-C^{14}	47.5		21.6×10^4
Carbon dioxide		53	7.1×10^4
Oxalic acid		72	8.2×10^4

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(1) M. R. Heinrich and D. W. Wilson, *J. Biol. Chem.*, **186**, **447** (1950).

(2) M. Edmonds, A. M. Delluva and D. W. Wilson, *ibid.*, **197**, 251 (1952).

(3) The numbering of the pyrimidine ring throughout this article is in conformance with the current usage of *Chemical Abstracts*.

(4) R. Behrend and G. Offe, *Ann.*, **353**, 267 (1907).

(5) U. Lagerkvist, *Acta Chem. Scand.*, **4**, 1151 (1950).

It must be concluded that the oxidation with permanganate of 5-nitrouracil, as well as of uracil itself, under the conditions used does not yield fractions representing specific carbon atoms of the ring system. The conclusions of Lagerkvist,[5] therefore, concerning the role of bicarbonate as a precursor of carbon 6 of uracil must be viewed with considerable doubt.

Experimental

Uracil-4-C^{14}.—The method of Davidson and Baudisch[6] was used for the synthesis of uracil from urea and a sample of malic acid-4-C^{14} prepared in this Laboratory by methods recently described.[7] The identity and purity of the twice-recrystallized uracil-4-C^{14} were established by the determination of the ultraviolet absorption spectrum in 0.01 N hydrochloric acid. Both the ϵ_{max} and the ratio of optical densities at 260 and 280 mμ agreed to within 1% with published data.[8]

5-Nitrouracil-4-C^{14}.—The isotopic nitrouracil was prepared by the method of Johnson and Matsuo[9] from a portion of the uracil-4-C^{14} diluted somewhat with non-radioactive uracil. The increase in weight during this process was 94% of that required by theory. The material was recrystallized once from water.

Oxidation of Uracil-4-C^{14}.—The procedures described by Heinrich and Wilson[1] for the cleavage of the pyrimidine ring, collection of the carbon dioxide, hydrolysis of the oxaluric acid, separation of the calcium oxalate and its subsequent oxidation to carbon dioxide were followed closely, except that the *p*H was maintained between 5 and 7 with the aid of a *p*H meter.

Oxidation of 5-Nitrouracil.—The method of Behrend and Offe[4] was followed for the oxidation step, followed by procedures similar to those mentioned above for uracil.

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RADIATION LABORATORY AND DEPARTMENT OF CHEMISTRY[10]
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIF.

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(6) D. Davidson and O. Baudisch, THIS JOURNAL, **48**, 2379 (1926).

(7) E. C. Jorgensen, J. A. Bassham, M. Calvin and B. M. Tolbert, *ibid.*, **74**, 2418 (1952).

(8) J. M. Ploeser and H. S. Loring, *J. Biol. Chem.*, **178**, 431 (1949).

(9) T. B. Johnson and I. Matsuo, THIS JOURNAL, 41, 782 (1919).

(10) The work described in this paper was sponsored by the Atomic Energy Commission.

A Convenient Preparation of Ethyl 2-Pyridylacetate

BY NEWTON N. GOLDBERG, BRUNO M. PERFETTI AND ROBERT LEVINE

RECEIVED MARCH 5, 1953

The following three methods are reported in the literature for the preparation of ethyl 2-pyridylacetate (I): (1) the alcoholysis of 2-pyridylacetanilide, which was prepared by the Beckmann rearrangement of 2-phenacylpyridine oxime,[1,2] (2) in 25% yield by the reaction of the potassium derivative of 2-picoline (prepared from the tar base and potassium amide) with diethyl carbonate[3] and (3) in 35–40% yield by the esterification of the lithium salt of 2-pyridylacetic acid, which was prepared by the carbonation of 2-lithiopyridine, which was in turn prepared from phenyllithium and 2-picoline.[4] These three methods have the common disadvantage that they are lengthy processes.

We have now found that by modifying the method developed in this Laboratory for the acylation of the lithium derivatives of methylated tar bases,[5,6] I may be prepared in 44.5% yield by the addition of a dilute ethereal solution of 2-picolyl lithium to a dilute ethereal solution of diethyl carbonate over a five-hour period. In addition to I, a small amount of di-2-picolyl ketone was isolated as its dipicrate.

Procedure.—2-Picolyllithium (0.4 mole) in 800 ml. of absolute ether was prepared as described previously[5] by the interaction of 0.4 mole of phenyllithium (prepared from 0.8 mole of lithium ribbon[7] and 0.4 mole (62.8 g.) of bromobenzene) and 0.4 mole (37.2 g.) of 2-picoline and was added over a five-hour period to a rapidly stirred cold (ice–salt-bath) solution of diethyl carbonate (0.2 mole, 23.6 g.) in 700 ml. of anhydrous ether. The ether was not allowed to reflux during the addition of the 2-picolyllithium. After the addition of the 2-picolyllithium was complete, the cooling bath was removed. The reaction mixture was heated to reflux, poured onto 200 g. of ice and extracted with several 200-ml. portions of ether. The combined ethereal phases were dried and concentrated and the residue fractionated to give 14.7 g. (44.5%) of ethyl 2-pyridylacetate, b.p. 110–113° (6 mm.); picrate, m.p. 138.8–139.2°.[5] The tarry residue was extracted for 18 hours with petroleum ether, b.p. 60–70°, in a Soxhlet extractor to give a small amount (< 0.1 g.) of a semi-solid material, which contained di-2-picolyl ketone, as indicated by the analysis of its dipicrate, m.p. 190–191° (from 95% ethanol) (undepressed by the dipicrate of the ketone obtained by the carbonation of 2-picolyllithium).

Anal. Calcd. for $C_{25}H_{18}O_{15}N_8$: N, 16.72. Found: N, 16.51.

Acknowledgment.—The authors gratefully acknowledge the support of the U. S. Atomic Energy Commission during the course of this work.

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(1) M. P. Oparina, *Khim Farm. Prom.*, No. 4, 15 (1934); (*C. A.*, **29**, 1820 (1935)).

(2) M. P. Oparina, *J. Gen. Chem.* (*U.S.S.R.*), **5**, 1699 (1935); (*C. A.*, **30**, 2567 (1936)).

(3) M. J. Weiss and C. R. Hauser, THIS JOURNAL, **71**, 2023 (1949).

(4) R. B. Woodward and E. C. Kornfeld, *Org. Syntheses*, **29**, 44 (1949).

(5) N. N. Goldberg, L. B. Barkley and R. Levine, THIS JOURNAL, **73**, 4301 (1951).

(6) N. N. Goldberg and R. Levine, *ibid.*, **74**, 5217 (1952).

(7) The lithium ribbon was generously supplied by the Metalloy Corporation.

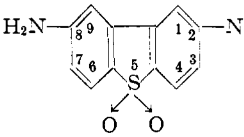
CONTRIBUTION NO. 904
CHEMISTRY DEPARTMENT
THE UNIVERSITY OF PITTSBURGH
PITTSBURGH 13, PA.

Some Brominated Dibenzothiophene Derivatives

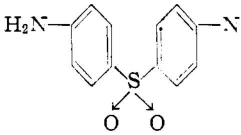
BY HENRY GILMAN AND ROBERT K. INGHAM

RECEIVED MARCH 16, 1953

Dibenzothiophene derivatives, especially the substituted 5-dioxides, are closely related to substituted diphenyl sulfones; several compounds possessing high antituberculous activity are diphenyl sulfone derivatives. In view of this relationship and the demonstrated activity of 2-halo-7-aminodibenzofurans[1] the preparation of 2-bromo-



2,8-Diaminodibenzothiophene-5-dioxide



p,p'-Diaminodiphenyl sulfone

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(1) V. C. Barry, L. O'Rourke and D. Twomey, *Nature*, **160**, 800 (1947).

7-aminodibenzothiophene-5-dioxide was undertaken.

The preparation of 2-bromodibenzothiophene-5-dioxide has been reported by Courtot,[2] the compound being obtained by oxidation of 2-bromodibenzothiophene with potassium dichromate; however, no experimental details were given. The only other report is that of Muth and Putzer,[3] who report the chromic acid oxidation of 2-bromodibenzothiophene. During the present investigation, the oxidation of the bromo derivative with hydrogen peroxide was found to be convenient and to give moderate yields of the desired product.

An attempted catalytic reduction of 2-bromo-7-nitrodibenzothiophene-5-dioxide was not successful. The compound was readily reduced by tin and hydrochloric acid. The results of pharmacological rests of the 2-bromo-7-aminodibenzothiophene-5-dioxide will be reported elsewhere.

Since the 2,8-substituted dibenzothiophenes may be regarded as "closed models" of the *p*,*p*′-substituted diphenyl sulfides, the preparation and testing of 2-bromo-8-aminodibenzothiophene appeared desirable. The 2-bromo-8-nitro- and 2-bromo-8-aminodibenzothiophenes have been reported,[4] but no experimental details were included in this report.

A procedure for the preparation of 3-bromodibenzothiophene from the 3-amino analog has been reported.[5] In addition to the repetition of this method, the 3-bromo compound was also synthesized by the reduction of 3-bromodibenzothiophene-5-dioxide with lithium aluminum hydride. It is noteworthy that reduction of the dioxide was effected without replacement of the bromine atom. The method may prove useful for the reduction of other substituted dibenzothiophene-5-dioxides either for structure proof or for the synthesis of otherwise difficultly obtainable derivatives.

Experimental[6]

2-Bromodibenzothiophene-5-dioxide.—Fifteen grams (0.058 mole) of 2-bromodibenzothiophene was suspended in 200 ml. of glacial acetic acid. To this solution was slowly added 30 ml. of 30% hydrogen peroxide, and the mixture was then slowly warmed to reflux temperature. On warming, the solid entirely dissolved, a precipitate forming shortly thereafter. The mixture was refluxed for one hour, cooled, filtered and the precipitate washed well with water. The white sulfone melted at 261–262° and weighed 16.0 g. (93.5%). Courtot[2] reports a m.p. of 266–267°; Muth and Putzer[3] report a m.p. of 256°. After digestion with absolute ethanol the 2-bromodibenzothiophene-5-dioxide melted at 261.5–262°.

2-Bromo-7-nitrodibenzothiophene-5-dioxide.—Into a three-necked, 250-ml. flask was placed 15.0 g. (0.051 mole) of 2-bromodibenzothiophene-5-dioxide. Fifty milliliters of concentrated sulfuric acid was added, forming a thick paste, and then 33 ml. of fuming nitric acid (sp. gr. 1.50) was added slowly. The stirred mixture was warmed to 80° and there maintained for two hours. Upon cooling, the reaction mixture was filtered and immediately washed well with water to stop action of the concentrated acids. The crude yield was 14.0 g. (80%) of a light yellow solid, melting over the range from 250–300°. Three recrystallizations from glacial acetic acid gave 9.0 g. (52%) of pale yellow needles, melting at 319–321°. After one recrystallization the m.p. range was 295–315°; after the second, 315–320°; and following the third, 319–321°.

Anal. Calcd. for $C_{12}H_6O_4SNBr$: S, 9.43. Found: S, 9.39, 9.39.

2-Bromo-7-aminodibenzothiophene-5-dioxide.—An attempted catalytic reduction employing Raney nickel and an ethanolic suspension of the nitro compound was unsuccessful, only starting material being obtained. Nine grams (0.0264 mole) of 2-bromo-7-nitrodibenzothiophene-5-dioxide was suspended in 175 ml. of absolute ethanol. To this mixture were added 17.0 g. of granular tin and 175 ml. of concentrated hydrochloric acid. The mixture was stirred at reflux temperature for two hours. Complete solution did not occur; however, the suspended precipitate soon changed in coloration from yellow to white. The amine hydrochloride was filtered, suspended in water and decomposed with ammonium hydroxide. There was thus obtained 7.0 g. of yellow solid, melting from 315–320°. A mixed m.p. with starting material was greatly depressed. Two recrystallizations from acetone–methanol gave 5.5 g. (67%) of a yellow solid (Norit A did not lessen the intensity of the yellow coloration), melting at 331–333°, with some decomposition.

Anal. Calcd. for $C_{12}H_8O_2SNBr$: Br, 25.77. Found: Br, 25.47, 25.54.

2-Bromo-8-nitrodibenzothiophene.—Ten grams (0.038 mole) of 2-bromodibenzothiophene was partially dissolved in 100 ml. of glacial acetic acid, and 15 ml. of fuming nitric acid (sp. gr. 1.50) was added dropwise. No noticeable change occurred; the reaction mixture was warmed to 50°, and the suspended solid slowly turned yellow. The mixture was stirred at this temperature for 1.5 hours and then filtered directly. There was thus obtained 10.0 g. of solid melting from 160–200°. Recrystallization from glacial acetic acid raised the m.p. range to 170–207°. The product was digested for two hours with refluxing ethanol and then again recrystallized from glacial acetic acid; the m.p. range was 233–242°. Two additional recrystallizations from this solvent gave 3.0 g. (25.5%) of pale yellow needles, melting at 254–256°.

2-Bromo-8-aminodibenzothiophene.—To a suspension of 2.5 g. (0.0081 mole) of 2-bromo-8-nitrodibenzothiophene in 50 ml. of absolute ethanol was added about 0.5 g. of Raney nickel catalyst. The initial reaction pressure was 40 lb./sq. in. After shaking overnight, 4 lb./sq. in. had been absorbed. The solution was filtered free from catalyst and diluted with water to give 2.0 g. of a light violet solid melting from 100–130°. Three recrystallizations from ethanol gave 1.0 g. (45%) of solid, melting at 149–150°.

3-Bromodibenzothiophene. (A) **From 3-Aminodibenzothiophene.**—The previously published procedure[5] was followed, with one exception. The method called for a thorough extraction of the reaction product with ether; however, the residue was found to be quite soluble in this solvent. The ether was evaporated and the residual material dissolved in hot ethanol; filtration and dilution of the cooled filtrate with water gave light brown platelets, melting from 82–91°. Two recrystallizations from ethanol gave a 39% yield of product, melting from 93–96°.

(B) **From 3-Bromodibenzothiophene-5-dioxide.**—3-Bromodibenzothiophene-5-dioxide (0.5 g., 0.0017 mole) and 0.2 g. (0.005 mole) of lithium aluminum hydride were placed in a 250-ml., three-necked flask, and 100 ml. of anhydrous ether was added. The reaction mixture was refluxed for 1.5 hours, with stirring. The cooled mixture was then hydrolyzed by the dropwise addition of water. Dilute hydrochloric acid was added to dissolve the resulting precipitate; the layers were separated and the aqueous layer was extracted twice with ether. The combined ether solutions were evaporated, leaving a light yellow gum. The residue was extracted with hot ethanol; dilution of the ethanolic extract with water gave a white solid melting from 40–63°. Three recrystallizations from absolute ethanol gave 0.2 g. (44.5%) of white needles melting at 98–99°. A mixed m.p. with the 3-bromodibenzothiophene prepared from 3-aminodibenzothiophene showed no depression.

The reduction of dibenzothiophene-5-dioxide with lithium aluminum hydride has been reported.[7] The 3-bromodiben-

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(2) C. Courtot, *Compt. rend.*, **198**, 2260 (1934).

(3) F. Muth and B. Putzer, PBL 63936. (Enlargement Print of Frames 1004-10.0 of FIAT microfilm Reel C 60, PB 17657.) March 1933. 7 pp. *Photo Ger.*, **5**, 568a, No. 7 (May 16, 1947).

(4) C. Courtot, L. Nicolas and T. H. Liang, *Compt. rend.*, **186**, 1624 (1928).

(5) G. Illuminati, J. F. Nobis and H. Gilman, THIS JOURNAL, **73**, 5887 (1951).

(6) All melting points are uncorrected.

(7) F. G. Bordwell and W. H. McKellin, THIS JOURNAL, **73**, 2251 (1951).

zothiophene-5-dioxide sample was prepared by H. A. Pacevitz.[8]

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[8] H. Gilman, A. L. Jacoby and H. A. Pacevitz, *J. Org. Chem.*, **3**, 120 (1938).

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

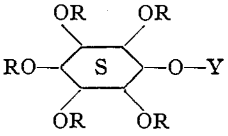
Pentamethyl and Triacetyl Derivatives of *myo*-Inositol[1]

BY G. E. McCASLAND AND STEPHEN BOUTSICARIS

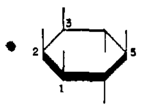
RECEIVED FEBRUARY 5, 1953

To facilitate another investigation which is still in progress we have prepared the partially alkylated or acylated inositols described below.

In 1947 McGowan[2] reported the preparation of the first pentamethyl ether of *myo*-inositol (I, R = CH_3, Y = H). His product was a sirup but did yield a crystalline monoacetate of m.p. 101°. By saponification of this monoacetate we have now obtained the pentamethyl ether itself in crystalline form, m.p. 51°. We have further characterized the ether by converting it to its monobenzoate, m.p. 133°.



I



II

Such a pentaalkyl ether (or its monoester) can have only a single structure I, but twenty diastereomers are possible. However, the configuration II of the starting material here used limits the possible diastereomers to four, since no inversions of configuration would be expected.

In 1915 Griffin and Nelson[3] reported a procedure for conversion of *myo*-inositol to acetylated mono- and dimethyl ethers. While repeating this procedure we isolated a previously unreported by-product of m.p. 71°. This compound is apparently the first crystalline triacetate[4] of *myo*-inositol, as indicated by its analysis, and its transformation into the known hexaacetate on further acetylation.

Three structures are possible for an inositol triacetate, and ten diastereometric configurations are probable when the starting material II is used.

Each product here reported appears to consist of a single pure isomer, but the configurations (and structure for the triacetate) remain undetermined.

Experimental

M.p.'s (corrected) were taken on Köfler micro-block; microanalyses by Mr. R. S. Pyke.

***myo*-Inositol Pentamethyl Ether Monoacetate of M.P. 101°.**—Fifty grams of anhydrous *myo*-inositol when methylated by the procedure of West and Holden,[5] as modified by McGowan,[2] gave 10 g. of crude pentamethyl ether (colorless sirup, b.p. 123–145° (150 μ)), which on acetylation as described[2] gave 7.0 g. (22%) of the pentamethyl monoacetate, m.p. 100–101° (reported[2] 101°).

***myo*-Inositol Pentamethyl Ether of M.P. 51°.**—A solution of the pentamethyl ether monoacetate (7.0 g.) in 140 ml. of 1 *N* sodium hydroxide was kept at 25° for one hour, then neutralized with 12 *M* hydrochloric acid. The solution was saturated with potassium carbonate and extracted repeatedly with chloroform. The dried extract on evaporation left 6.0 g. of brown sirupy residue, which on vacuum-distillation gave 3.0 g. of a colorless viscous sirup, b.p. 127° (150 μ). The sirup solidified on standing overnight at 5°. The solid product was recrystallized twice from ligroin (b.p. 80–100°) giving 2.5 g. (42%) of *myo*-inositol pentamethyl ether, colorless crystals, m.p. 50–51°. The crystals are soluble in water, alcohol, or benzene.

Anal. Calcd. for $C_{11}H_{22}O_6$: C, 52.78; H, 8.86. Found: C, 52.38; H, 8.49.

On reacetylation of the crystalline pentamethyl ether, the monoacetate of m.p. 101° was again obtained.

***myo*-Inositol Pentamethyl Ether Monobenzoate of M.P. 133°.**—To the pentamethyl ether (0.60 g.) in 3.0 ml. of dry pyridine was added with stirring 0.50 ml. of benzoyl chloride. After five minutes the crystals which had separated were collected, washed with water, with 0.5 *M* sodium carbonate, and again with water, and dried. By recrystallization from ligroin, 0.65 g. (76%) of *myo*-inositol pentamethyl ether monobenzoate, colorless crystals, m.p. 132–133°, were obtained. The crystals are soluble in alcohol or benzene.

Anal. Calcd. for $C_{18}H_{26}O_7$: C, 61.00; H, 7.40. Found: C, 60.99; H, 7.31.

***myo*-Inositol Triacetate of M.P. 71°.**—*myo*-Inositol (20 g.) was treated by the methylation and acetylation procedure[3] of Griffin and Nelson. The filtered ethereal mother liquors, from which the acetylated mono- and dimethyl ethers had already crystallized, on long standing formed a third crop of crystals. This third crop was recrystallized from ethanol, giving 0.30 g. (0.8%) of colorless crystals, m.p. 70–71°. The crystals are soluble in chloroform but not in water. Analysis indicates that the new compound is a triacetate of (unmethylated) *myo*-inositol.

Anal. Calcd. for $C_{12}H_{18}O_9$: C, 47.06; H, 5.92. Found: C, 47.49; H, 5.89.

The triacetate (0.27 g.) on further acetylation with 5 ml. of hot acetic anhydride containing 0.1 g. of zinc chloride gave the expected *myo*-inositol hexaacetate (0.30 g., 79%) of m.p. 212–213° (reported[6] 211–212°).

Although the use of methylating agents in the procedure may seem superfluous, no more direct method for preparing this triacetate has yet been found.

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[1] Aided by a grant from the Research Council of Ontario.

[2] J. C. McGowan, *J. Soc. Chem. Ind.*, **66**, 446 (1947).

[3] E. Griffin and G. Nelson, THIS JOURNAL, **37**, 1566 (1915).

[4] The only previously reported triacetate of *myo*-inositol was an amorphous, gummy, hygroscopic substance of unstated m.p. and uncertain purity. See H. Müller, *J. Chem. Soc.*, **101**, 1781 (1912).

[5] E. S. West and R. F. Holden, *Org. Syntheses*, **20**, 97 (1940).

[6] L. Maquenne, *Ann. Chim.*, [6] **12**, 100 (1887).

CHEMISTRY DEPARTMENT
UNIVERSITY OF TORONTO
TORONTO, CANADA

Antimony(III) Fluoride–Dioxane Addition Compound[1]

BY H. M. HAENDLER, R. H. GLAZIER AND D. W. BRECK

RECEIVED APRIL 8, 1953

Antimony(III) fluoride, which is reported to occur as a molecular crystal,[2] does not show the tendency to form addition compounds with many organic compounds that is so characteristic of the other halides of antimony(III). Solubility measurements in various organic solvents,[3] such as benzene or chlorobenzene, gave no indication of reaction. There was, however, some evidence of reac-

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[1] This research was supported by the Research Corporation and is taken in part from the M.S. thesis of R. H. Glazier.

[2] A. Byström and A. Westgren, *Arkiv. Kemi, Mineral Geol.*, **17B**, No. 2, 1 (1943); R. W. G. Wyckoff, "Crystal Structures," Interscience Publishers, Inc., New York, N. Y., 1951, Chap. V, table p. 17b.

[3] D. W. Breck, J. L. Harvey and H. M. Haendler, *J. Phys. Colloid Chem.*, **53**, 906 (1949).

tion with 1,4-dioxane, which has frequently been used with other halides.[4]

Subsequent study has shown the formation of a 1:1 addition compound by direct reaction of antimony(III) fluoride and dioxane and by reaction in methanol solution. The complex decomposes at 143° into its components and can be used as a mild fluorinating agent.

Experimental

Antimony(III) fluoride was refluxed for 15 minutes with a 14-fold excess of dioxane, filtered and cooled. Alternatively, a mixture of 15 ml. of dioxane (0.17 mole) and 15 ml. of methanol was added slowly to a solution of 19.3 g. (0.11 mole) of the fluoride in 30 ml. of methanol. After brief refluxing the solution was cooled, the crystals removed, and dried in a stream of dry air. Samples were analyzed for antimony by titration with potassium bromate,[5] using Naphthol Blue Black.[6]

Anal. Calcd. for $SbF_3 \cdot C_4H_8O_2$: Sb, 45.62. Found: Sb, 45.47, 45.54, 45.57.

The dissociation temperature was found by determining the heating curve of a 14-g. sample in a nickel cell, using copper–constantan thermocouples and a Speedomax recorder. A sharp break occurred at 143°, and a sample heated to 305° showed a break in its cooling curve at 290°, corresponding to the m.p. of the fluoride.

Benzotrichloride was fluorinated by the complex, using the apparatus and procedures given by Henne,[7] maintaining the same fluoride–chloride ratio. Both benzotrifluoride and the chlorodifluoride were formed.

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(4) M. S. Kennard and P. A. McCusker, THIS JOURNAL, **70**, 1039 (1948); C. J. Kelley and P. A. McCusker, *ibid.*, **65**, 1307 (1943).

(5) H. H. Willard and H. Diehl, "Advanced Quantitative Analysis," D. Van Nostrand Publishing Co., Inc., New York, N. Y., 1943, p. 350.

(6) G. F. Smith and R. L. May, *Ind. Eng. Chem., Anal. Ed.*, **13**, 460 (1941).

(7) A. L. Henne in R. Adams, ed., "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 62.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NEW HAMPSHIRE
DURHAM, N. H.

Ammonium Pentafluorozirconate(IV) and its Monohydrate[1]

BY HELMUT M. HAENDLER AND DEAN W. ROBINSON

RECEIVED APRIL 8, 1953

Ammonium pentafluorozirconate(IV), NH_4ZrF_5, has been reported as one of the intermediate products of the thermal decomposition of ammonium heptafluorozirconate(IV), $(NH_4)_3ZrF_7$.[2] Attempts to grow single crystals of the pentafluorozirconate from solution for X-ray structural studies led to the discovery of its monohydrate. Both compounds crystallize from a solution of zirconium oxide in hydrofluoric acid, to which has been added 75% of the theoretical quantity of ammonium fluoride. The predominant product is controlled by the rate of crystallization. Rapid crystallization favors formation of the hydrate, slow crystallization suppresses it. The monohydrate loses water spontaneously in air of low humidity to become the anhydrous compound. Powder diffraction and Weissenberg photographs of the two compounds are distinctive.

Experimental

All crystallizations were carried out with platinum or polyethylene apparatus. To obtain the monohydrate, the solution was evaporated by heating to incipient crystallization, filtered and cooled. The hydrate crystallized in clusters of clear, colorless, six-sided right prisms. These were separated mechanically from the small crystals of the anhydrous compound, the formation of which could not be prevented completely.

Anhydrous pentafluorozirconate was produced with exclusion of hydrate by allowing the solution to evaporate slowly for 2–3 weeks, or by adding a small amount of ethanol prior to the slow evaporation. This compound crystallized in small, colorless, almost square plates, with truncated faces.

X-Ray diffraction powder photographs were taken of the products obtained by heating the hydrate at 110° and from its spontaneous decomposition in air. They were identical with the pattern of the pentafluorozirconate produced in the thermal decomposition of the heptafluorozirconate.

Ammonium ion was determined by distillation from basic solution into boric acid and titration with hydrochloric acid. Zirconium was determined by digestion with sulfuric acid and ignition to the oxide. Water was determined by heating at 110°.

Anal. Calcd. for $NH_4ZrF_5 \cdot H_2O$: NH_4, 8.12; Zr, 40.94; H_2O, 8.10. Found: NH_4, 7.64; Zr, 41.15; H_2O, 8.25.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NEW HAMPSHIRE
DURHAM, NEW HAMPSHIRE

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(1) Research supported by the Atomic Energy Commission and the Research Corporation.

(2) H. M. Haendler, C. M. Wheeler and D. W. Robinson, THIS JOURNAL, **74**, 2352 (1952).

Diazonium Fluoborates as Initiators of Vinyl Polymerization[1]

BY C. S. MARVEL, H. Z. FRIEDLANDER, SHERLOCK SWANN, JR., AND H. K. INSKIP

RECEIVED JANUARY 26, 1953

In some experiments on the electrolytic generation of free radicals for the initiation of polymerization,[2] hydroquinone was added as a "shortstop" immediately after the electrolysis to prevent polymerization during the examination of the mixture. In those runs involving the electrolysis of *p*-bromobenzenediazonium fluoborate, extensive polymerization of acrylonitrile was observed after the addition of hydroquinone, but not before. Tests showed that the sulfuric acid anolyte solution and the fluoborate anion were not responsible for the polymerization. Further study demonstrated that the diazonium fluoborate in the presence of hydroquinone or ferrous ammonium sulfate caused the initiation of polymerization at 30°. In Table I are summarized the results of a number of homopolymerizations and copolymerizations initiated by substituted benzenediazonium fluoborates.

The effect of *p*H on yield and viscosity of polyacrylonitrile is demonstrated in experiments 1–6. Optimum conditions obtain at about *p*H 3. At 0° no polymer was obtained from acrylonitrile even after four days (experiments 7, 8) unless the amount of initiator was doubled over that used at 30° (experiments 9–14), and even with increase of initiator the yield and viscosity were relatively low. The effectiveness of the ferrous-salt activator in promoting polymerization of acrylonitrile at 30° is demonstrated in the 18-hour polymerizations (ex-

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(1) The work discussed herein was performed as a part of the research project sponsored by the Reconstruction Finance Corporation, Office of Synthetic Rubber, in connection with the Government Synthetic Rubber Program.

(2) H. Z. Friedlander, S. Swann, Jr., and C. S. Marvel, *J. Electrochem. Soc.*, in press.

TABLE I

POLYMERIZATIONS INITIATED BY SUBSTITUTED BENZENEDIAZONIUM FLUOBORATES[a]

Experiment no.	Monomer	Comonomer	Weight ratio, monomer/comonomer	Total monomer(s) weight, g.	Water, ml.	Initiator,[b] g.	Activator,[c] g.	*p*H[d]	Temp., °C.	Time, hr.	Conversion, %	Inherent viscosity[e]
1	Acrylonitrile	None	...	16.1	40	0.1	0.01	1.0	28	3	5.2	3.80
2	Acrylonitrile	None	...	16.1	40	.1	.01	2.0	28	3	11.9	4.52
3	Acrylonitrile	None	...	16.1	40	.1	.01	3.0	28	3	22.2	5.22
4	Acrylonitrile	None	...	16.1	40	.1	.01	4.0	28	3	20.9	3.30
5	Acrylonitrile	None	...	16.1	40	.1	.01	4.9	28	3	7.0	1.79
6	Acrylonitrile	None	...	16.1	40	.1	.01	5.3	28	3	9.4	1.89
7	Acrylonitrile	None	...	10.0	33	.1	.01	U	0	96	0	..
8	Acrylonitrile	None	...	10.0	33	.2	.01	U	0	96	19	2.01
9	Acrylonitrile	None	...	8.0	30	.1	None	U	30	18	17.5	5.50
10	Acrylonitrile	None	...	8.0	30	.1	0.002	U	30	18	100	7.11
11	Acrylonitrile	None	...	8.0	30	.1	.01	U	30	18	100	7.32
12	Acrylonitrile	None	...	8.0	30	.1	.02	U	30	18	100	5.32
13	Acrylonitrile	None	...	8.0	30	.1	.1	U	30	18	100	5.06
14	Acrylonitrile	None	...	8.0	30	.1	1.0	U	30	18	100	3.33
15	Acrylonitrile	None	...	10.0	40	.1	0.01	U	30	114	100	3.98
16	Acrylonitrile	None	...	10.0	40	.1	None	U	30	114	94	Insol.
17	Methyl acrylate	None	...	10.5	40	.1	None	U	30	114	93	0.47
18	Styrene	None	...	10.0	40	.1	None	U	30	114	75	0.41
19	Acrylonitrile	Butadiene	75/25	20.0	20	.1	0.05	U	30	69	18.5	0.54
20[f]	Acrylonitrile	Butadiene	50/50	20.0	20	.1	.05	U	30	69	24.3	0.61
21	Acrylonitrile	Butadiene	25/75	20.0	20	.1	.05	U	30	69	7.5	0.24
22[g,j]	Acrylonitrile	Butadiene	50/50	20.0	45	.2	.05	U	50	40	29.5	Insol.
23[h]	Acrylonitrile	Butadiene	50/50	20.0	45	[k]	.05	U	50	40	93.5	Insol.
24[i]	Acrylonitrile	Styrene	50/50	20.0	45	.2	.05	U	50	40	31.0	0.47
25	Acrylonitrile	None	...	10	40	.1	None	U	50	15	90	2.97
26	Acrylonitrile	None	...	10	40	.1	0.01	U	50	15	88	3.01
27	Acrylonitrile	None	...	10	40	[k]	None	U	50	15	80	3.97
28	Acrylonitrile	None	...	10	40	[k]	0.01	U	50	15	69	3.70
29	Styrene	None	...	10	40	.1	None	U	50	15	24	0.26
30	Styrene	None	...	10	40	.1	0.1	U	50	15	38	0.18
31	Methyl acrylate	None	...	10	40	.1	None	U	50	15	88	0.45
32	Methyl methacrylate	None	...	10	40	.1	None	U	50	15	100	1.82
33	Vinyl acetate	None	...	10	40	.1	None	U	50	15	0	...

[a] With the exceptions noted, the reaction medium in each experiment consisted of 2 ml. of emulsifier MP-635-S in varying amounts of redistilled water. MP-635-S consists of a mixture of alkanesulfonic acids in the C_{16} range (49.5%), unreacted hydrocarbons (10.3%), sodium chloride (0.86%), sodium sulfate (0.4%), isopropyl alcohol (3%), and the balance water. We are indebted to Dr. S. Detrick, Jackson Laboratory, E. I. du Pont de Nemours and Company, for a generous sample of this material. [b] *p*-Bromobenzenediazonium fluoborate, except where otherwise indicated. [c] Ferrous ammonium sulfate hexahydrate. [d] Either adjusted with sulfuric acid–sodium acetate, or, in the experiments marked U, unbuffered. [e] In dimethylformamide. [f] Acrylonitrile incorporation in copolymer, from N analysis, 48.7%. [g] Acrylonitrile incorporation 38.2%. [h] Acrylonitrile incorporation 60.5%. [i] Acrylonitrile incorporation 34.8%. [j] Dodecylamine hydrochloride, 2 g., was substituted for MP-635-S as emulsifier in this experiment. [k] *p*-Methoxybenzenediazonium fluoborate was substituted for the bromo compound as initiator in these experiments: 0.2 g. in experiment 23; 0.1 g. in experiments 27 and 28.

periments 9–14) and in the 114-hour polymerizations (experiments 15, 16). At 18 hours even a trace of ferrous salt caused a sixfold increase in yield, to 100%. At 114 hours, while yields were essentially quantitative both with and without the ferrous salt, only in the experiment that included activator was a soluble, non-cross-linked product obtained. At 50°, however, the activator was not needed, either with *p*-bromobenzenediazonium fluoborate (experiments 25, 26) or with the corresponding *p*-methoxy compound (experiments 27, 28). For other monomers the diazonium fluoborate was sufficiently effective to bring about polymerization in the absence of activator. Thus styrene (experiments 18, 29, 30) formed a polymer in fairly good yield provided the reaction time was of sufficient duration, while for methyl acrylate either prolonged reaction time (experiment 17) or increase in temperature (experiment 31) was effective. In the copolymerizations (experiments 19–24), it is noteworthy that replacement of the *p*-bromodiazonium salt by the *p*-methoxy salt resulted in a threefold increase in yield (experiments 22, 23); both products, however, were insoluble.

In general we found that the aryldiazonium chlorides were not effective initiators, although some small amounts of polymer were obtained in a few runs.

Our experiments lead us to believe that the polymerization at 30° is initiated by free radicals produced by the reduction of the diazonium fluoborate by either the hydroquinone or the ferrous ammonium sulfate. At 50° there is apparently enough decomposition of an aqueous solution of the fluoborate to give the free radicals necessary for initiation of polymerization. Apparently neither of these conditions produces a large concentration of radicals, for only easily polymerizable monomers seem to give polymers. It is of course known[3] that aryldiazonium salts initiate polymerizations of a variety of monomers in alkaline media, but they have apparently not been used for this purpose primarily in acid media.[4]

Experimental

Each of the polymerizations recorded in Table I was accomplished by either shaking (28 and 30° runs) or tumbling (0° and 50° runs) the indicated reaction mixture for the designated period, preliminary experiments having shown no differences in the products from these operations.

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(3) J. M. Willis, G. Alliger, B. L. Johnson and W. M. Otto, Lecture before Division of Rubber Chemistry, American Chemical Society Meeting, Buffalo, New York, October 29, 1952.

(4) After this note had been accepted for publication W. Cooper published a note in *Chemistry and Industry*, No. 17, p. 407, April 25, 1953, describing the use of *p*-nitrobenzenediazonium *p*-chlorobenzenesulfonate as an initiator for the polymerization of methyl acrylate and acrylonitrile in 2.5 *N* hydrochloric acid solution.

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

N-Acetylimesatins and Related Compounds

BY FEDERICO PARISI

RECEIVED FEBRUARY 28, 1953

In the course of researches carried out some years ago at the University of Fribourg (Switzerland) on the constitution of the products of the reaction of indigo with benzoyl chloride,[1] it was supposed that imesatins were obtained by the degradation of the products of benzoylation with aromatic amines.

This supposition has since been found to be erroneous, although the possibility of the formation of an imesatin by the treatment of Dessoulavy's compound with ammonia is still being studied.

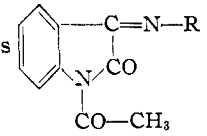
This note will serve to record the preparation of several N-acetylimesatins and of two derivatives of N-chloroacetylisatin.

The N-acetylimesatins can be prepared by the action of the corresponding amines on N-acetylisatin (prepared according to J. Büchi[2]) in absolute alcohol without the use of catalysts.

For example: 0.01 mole of N-acetylisatin, 0.02 mole of amine and 30 ml. of absolute alcohol are heated under reflux on the water-bath for an hour, cooled and allowed to stand in the refrigerator to complete the separation of the solid. The product is collected, washed with cold alcohol and then with ether and recrystallized from an appropriate solvent (often glacial acetic acid). It may be necessary to allow the liquid to stand for some days in the refrigerator in order to complete the crystallization. In Table I are given the properties of the substances prepared.

TABLE I

N-ACETYLIMESATINS



R	Crystallized from	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
C_6H_5	AcOH	177–178	10.61	10.59
1,2-$C_6H_4CH_3$	AcOH	185–186	10.07	10.13
1,3-$C_6H_4CH_3$	AcOH	169–170	10.07	9.91
1,4-$C_6H_4CH_3$	AcOH	176–177	10.07	10.07
1,2-C_6H_4OH	*i*-Pr_2O	169–170	10.00	9.89
1,4-C_6H_4OH	$Ph\cdot CH_3$	194–195	10.00	9.83
1,4-C_6H_4COOH	AcOH	224 (dec.)	9.09	8.94
1-$C_{10}H_7$	AcOH	170–171	8.92	9.01
2-$C_{10}H_7$	AcOH	189–190	8.92	9.03
$C_5H_5N_2$[a]	AcOEt	169–170	20.00	19.82
C_3N_2NS[b]	AcOEt	184–185	15.50	15.41

[a] 4-Methylpyrimidyl. [b] 2-Thiazolyl.

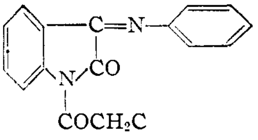
Acetylization of imesatins with acetic anhydride does not produce the corresponding N-acetylimesatins but yields resinous substances.

Derivatives of N-chloroacetylisatin have also been prepared using aniline according to Huntress.[3] In absolute alcohol as for N-acetylimesatins, N-chloroacetylphenylimesatin (I) was obtained. After crystallization from acetic acid it has m.p. 146°.

Anal. Calcd. for $C_{16}H_{11}N_2O_2Cl$: N, 9.38; Cl, 11.88. Found: N, 9.57; Cl, 11.71.

On the other hand, 0.01 mole of chloroacetylisatin refluxed with 0.02 mole of aniline in 10 ml. of pyridine for five minutes yields after cooling and diluting with an equal volume of water, half a volume of acetic acid and 8 ml. of concentrated hydrochloric acid (without passing the change point of congo red) a resinous precipitate. When stirred for some time this precipitate redissolves in the liquid leaving only a small residue. The filtrate from this, made alkaline with ammonia, gives a yellow precipitate of phenylglycylisatin (II) soluble in mineral acids, in concentrated alkalies and in ethyl alcohol. Crystallized from acetic acid, it has m.p. 197°.

Anal. Calcd. for $C_{16}H_{12}N_2O_3$: N, 9.99; Cl, nil. Found: N, 10.16; Cl, absent.



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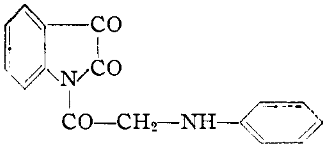

II

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RESEARCH LABORATORIES
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(1) H. de Deisbach and coll., *Helv. Chim. Acta*, **16**, 148 (1933); **17**, 113 (1934); **19**, 1213 (1936); **20**, 132 (1937); **23**, 469 (1940); **24**, 158 (1941); **26**, 1869 (1943); **31**, 724 (1948); **32**, 1214 (1949).

(2) J. Büchi and H. Humi, *Helv. Chim. Acta*, **32**, 1806 (1949).

(3) E. H. Huntress and J. Bornstein, THIS JOURNAL, **71**, 745 (1949).

Polarography of Tripositive Antimony and Arsenic. Cathodic Reduction of Antimonous in Strong Hydrochloric Acid and Anodic Oxidation of Arsenite and Stibnite in Strong Sodium Hydroxide

BY G. P. HAIGHT, JR.[1]

RECEIVED DECEMBER 17, 1952

The polarography of arsenic and antimony in acid solutions has been investigated by Lingane,[2] Kolthoff and Probst[3] and Bambach[4] who have shown that the tripositive state of each element is generally reducible while the pentavalent states are reduced only in very strong hydrochloric acid. Waves in 1.5 *M* HCl and in 1 *M* HCl plus 1 *M* tartaric acid have been found suitable for simultane-

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(1) Chemistry Department, University of Kansas, Lawrence, Kansas.

(2) J. J. Lingane, *Ind. Eng. Chem., Anal. Ed.*, **15**, 583 (1943).

(3) I. M. Kolthoff and R. L. Probst, *Anal. Chem.*, **21**, 753 (1949).

(4) K. Bambach, *Ind. Eng. Chem., Anal. Ed.*, **14**, 265 (1942).

ous polarographic determination of these elements in the tripositive state by Bambach[4] and the author.[5] The antimony wave in hydrochloric acid has the general characteristics of a reversible 3-electron process and it has been generally assumed that the $SbCl_4^-$ ion is the species being reduced. Pentavalent antimony is reduced prior to the anodic dissolution of mercury in 4 *M* or stronger HCl. Kolthoff and Probst[3] have also reported anodic waves for the oxidation of the tripositive states to the pentavalent state in potassium hydroxide solutions. The object of this paper is to throw further light on the nature of the processes producing these anodic waves and to use polarographic data to determine the actual number of chloride ions associated with tripositive antimony in concentrated HCl.

Apparatus and Materials.—A Sargent Model XX recording polarograph was used for all measurements. A conventional mercury pool polarographic cell was used, the potential of the large mercury anode being determined separately at the end of each run. In basic media the pool had HgO in contact with it and was separated from the dropping electrode by a sintered glass disc. A potentiometer attached to the pool and to the dropping mercury electrode provided accurate measurements of e.m.f. All measurements were made at 30° except where indicated. Reagent grade chemicals were used throughout.

Experimental Results. Chloro Complex of Tripositive Antimony.—It was confirmed that a plot of *E vs.* log $i/(i_d - i)$ for the cathodic wave for tripositive antimony in strong HCl yielded a straight line with a slope of −0.020, indicating reversible reduction. If the reversible character of the wave is accepted it follows that $E_{1/2} = C + 0.02\, n \log (Cl^-)$ where $E_{1/2}$ is the half-wave potential, *C* a constant, and *n* is the number of chloride ions attached to antimony in the chloroantimonous complex. Figure 1 shows a plot of $E_{1/2}$ *vs.* log (Cl^-) in solutions which were 4 *M* in hydrogen ion. The result is a straight line with a slope of 0.077 indicating that 4 chloride ions are present in the complex as has been suspected all along. At 4 *M* Cl^- the half-wave potential is independent of hydrogen ion concentration. Figure 2 shows a plot of $E_{1/2}$ *vs.* the molal activity of hydrochloric acid for 1, 4 and 6 *M* solutions which yields a straight line plot of slope 0.079 which indicates good agreement with theory for a complex containing no hydrogen and four chloride ions.

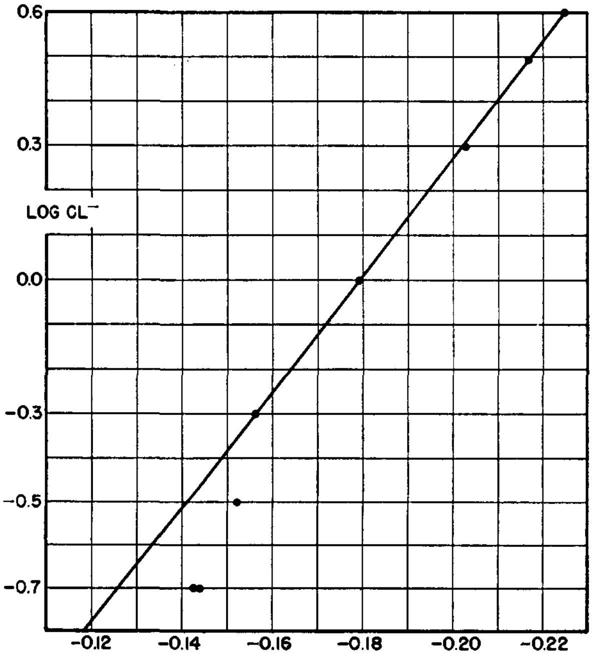

Fig. 1.—Variation of $E_{1/2}$ with (Cl^-) at constant (H^+).

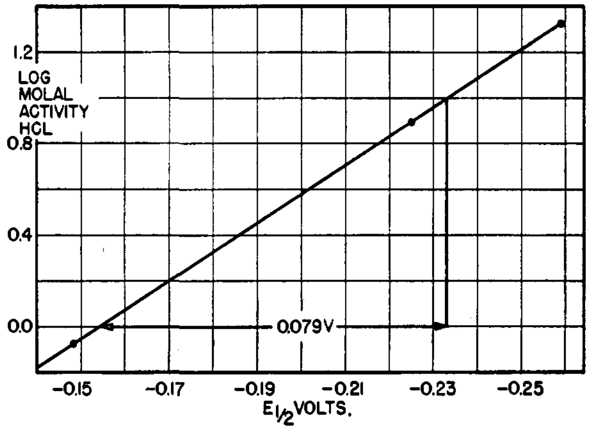

Fig. 2.—Reduction of Sb(III) to Sb^0 in HCl.

This agreement is interesting in view of the fact that individual ion activities are generally assumed to be different from average activity coefficients for salts and acids in aqueous solution. It suggests that the individual ion activity is either the same as or a linear function of the average activity coefficient of the dissolved ionic substance. If such is the case for other electrolytes, the technique illustrated in Fig. 2 might be useful in place of, or supplementary to, the technique of maintaining constant ion strength, which is exceedingly difficult to do in concentrated solutions of acids and bases. Also, in such solutions it is virtually impossible to find "inert" electrolytes which do not participate in complex formation. It was found impossible to use NaCl with NaOH in the arsenite study below, for instance. It should be noted that the points in Fig. 1 at Cl^- concentrations below 0.5 *M* show marked deviation from the other points. The H^+ concentration was maintained using $HClO_4$. Compilations of Robinson and Stokes[6] show that the HCl and $HClO_4$ activity coefficients are nearly the same up to 2 molal but begin to deviate sharply at 4 molal with the activity of $HClO_4$ increasing faster than HCl with increasing concentration. An increase in the activity coefficient of Cl^- due to promotion of their activity by high $HClO_4$ would cause the deviations observed in Fig. 1 as would change in number of Cl^- ions in the complex. The author feels that the straight line as far as is observed is rather fortuitously due to the near identity of activities of HCl and $HClO_4$ in this range. The technique of Fig. 2 has been applied to the study of the oxidation of tripositive antimony and arsenic in KOH solutions. Activities

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(5) G. P. Haight, Jr., unpublished work.

(6) R. A. Robinson and R. H. Stokes, *Trans. Faraday Soc.*, **45**, 612 (1949).

of KOH solutions were obtained from the data of Akerlof and Bender.[7]

Anodic Oxidation of Tripositive Arsenic in Potassium Hydroxide Solution.—Figure 3 shows a typical polarogram of tripositive arsenic and antimony in 1 *M* potassium hydroxide. Both are anodically oxidized to the pentavalent state while antimony is reduced to the metal as well. A plot of *E vs.* log $i/(i_d - i)$ for the arsenic wave yields a straight line of slope 0.029 corresponding to a reversible 2 electron change. Figure 4 shows a plot of $E_{1/2}$ *vs.* the logarithm of the molal activity of KOH for concentrations ranging from 0.5 to 10 *M*. The result is a straight line with a slope of 0.028, corresponding closely to a reversible two electron process involving one hydroxide ion.

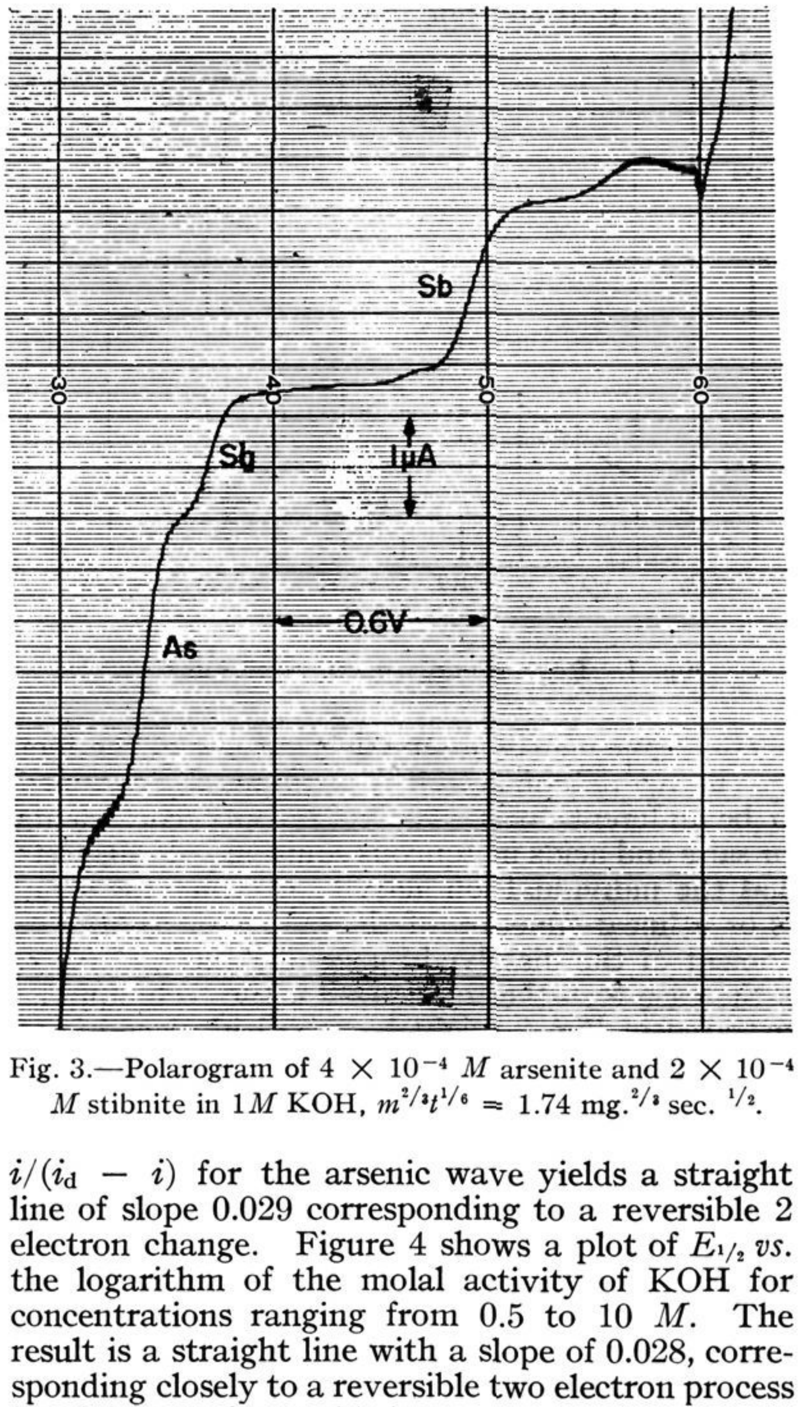

Fig. 3.—Polarogram of 4×10^{-4} *M* arsenite and 2×10^{-4} *M* stibnite in 1*M* KOH, $m^{2/3}t^{1/6} = 1.74$ mg.$^{2/3}$ sec.$^{1/2}$.

$$E_{1/2} = -0.276 - 0.029 \log A_{OH^-} \text{ vs. S.C.E.}$$

Half-wave potentials are independent of arsenic concentration. Oxidation of solutions by air is quite rapid so no precise calculation of the diffusion current constant was made although a rough idea as to its value may be obtained from Fig. 1. The hydroxide medium is unsatisfactory for analytical use unless air-free KOH is employed and all operations are carried out in an inert atmosphere. In this study, air was not excluded until just prior to taking the polarograms. Since both ortho and meta forms exist in the case of arsenite and arsenate several possible reactions involving one hydroxide ion present themselves. Both ortho- and meta-arsenates yield identical solutions shortly after dissolution in water with the meta form probably being converted to the ortho form. Precipitation reactions yield ortho-arsenites as a rule indicating that that form is predominant in solution. Some possible electrode reactions involving one hydroxide are

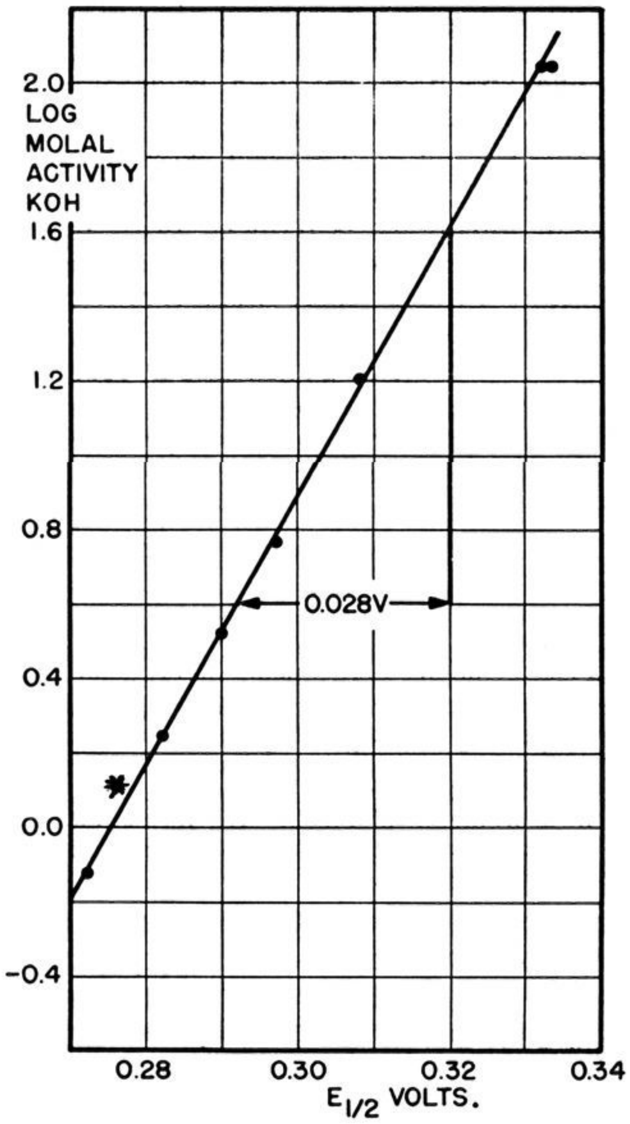

Fig. 4.—Oxidation of arsenite in KOH: *, in NaOH at 27°.

$$AsO_2^- + OH^- \longrightarrow HAsO_3 + 2e \quad (1)$$

$$AsO_3^{=} + OH^- \longrightarrow HAsO_4^{=} + 2e \quad (2)$$

$$HAsO_3^{=} + OH^- \longrightarrow H_2AsO_4^- + 2e \quad (3)$$

$$H_2AsO_3^- + OH^- \longrightarrow H_3AsO_4 + 2e \quad (4)$$

$$HAsO_3^{=} + OH^- \longrightarrow AsO_3^- + 2e + H_2O \quad \text{(proposed as most likely)} \quad (5)$$

Since "ic" acids are generally much stronger than "ous" acids it would seem unlikely that the product would contain more protons than the arsenite species originally present in strongly alkaline solution. This would rule out equations 1 to 4. The fact that ordinary arsenate solutions are not reducible would rule out the products in equations 2 to 4. Equation 5 seems the most likely description of the electrode process, the AsO_3^- produced being converted to $AsO_4^{\equiv}$ after diffusing away from the electrode. The first dissociation constant of arsenious acid is 6×10^{-10} which would indicate the presence of at least one hydrogen in the ortho form even in strongly basic solutions. Equation (5) represents a simple electrical change with the same spatial configuration of oxygen about arsenic and should be easier to accomplish electrically than conversion of ortho-arsenite to ortho-arsenate.

Anodic Oxidation of Tripositive Antimony in Potassium Hydroxide.—The analysis of the anodic

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(7) G. Akerlof and P. Bender, THIS JOURNAL, **70**, 2366 (1948).

wave for tripositive antimony reveals a somewhat more complicated situation than with arsenic. The slope of the E vs. log $i/(i_d - i)$ plot gives a straight line in all cases with a slope which varies from 0.047 to 0.037 as the hydroxide ion concentration increases from 1.0 to 10.0 moles/l. These slopes are high compared to 0.030 characteristic of a reversible 2 electron change. Raising the temperature to 40° failed to alter the slope beyond the limits of experimental error, indicating the spread wave does not result from a high activation energy for the reaction. The half-wave potential varies with the molal activity of potassium hydroxide in manner characteristic of a reversible 2 electron change involving two hydroxide ions as shown in Fig. 5. Also shown in Fig. 5 is the effect of a 10° rise in temperature on the half-wave potentials in 1 M and 10 M KOH. At 30°

$$E_{1/2} = -0.453 - 0.060 \log a_{OH^-} \text{ vs. S.C.E.}$$

The small negative shift with increasing temperature is characteristic of a reversible process. Whitney and Davidson[8] have shown that the complexes $SbCl_4^-$ and $SbCl_6^-$ interact to give a colored complex in strong hydrochloric acid. It would seem possible then that the corresponding hydroxy complexes, if formed, would interact. Such interaction would serve to decrease the concentrations of $Sb(OH)_4^-$ and $Sb(OH)_6^-$ at the surface of the mercury drop in such a way as to spread the wave out, increasing the slope of the E vs. log $i/(i_d - i)$ plot as observed. Solutions of high ionic strength might be expected to cut down interaction and the plot should show a trend toward a reversible slope with increasing ion strength as it does. The reaction $2OH^- + Sb(OH)_4^- \rightarrow Sb(OH)_6^- + 2e$ satisfies the dependence of $E_{1/2}$ on hydroxide ion activity. Since pentavalent antimony is not reduced under these conditions it would seem likely that the form produced by the oxidation would be an unusual form not normally encountered in solution. Pauling[9] and Beintema[10] have shown the existence of salts of $Sb(OH)_6^-$ but the species has not heretofore been identified in solution where it may polymerize to an irreducible form. Many other equations involving two hydroxide ions and two electrons are of course possible, but the correlation of the reaction given with other known phenomena of antimony complexes seems to favor it in the author's opinion. This proposed mechanism is very tentative and confirmation or rejection must wait on data from other types of experiments if such are possible.

Figure 3 shows that the 2nd antimony wave which is cathodic is 3/2 the height of the first as found by Kolthoff and Probst. The plot of E vs. $i/(i_d - i)$ for this wave gives a straight line with a slope of 0.076—nearly four times the value for a reversible 3 electron change. The small wave following may be partial reduction to stibine.

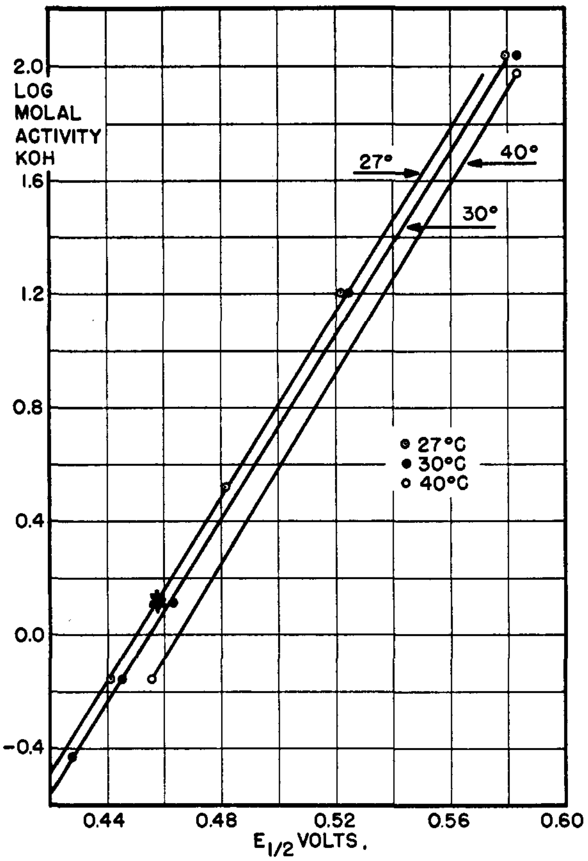

Fig. 5.—Oxidation of stibnite in KOH: *, in NaOH at 27°.

Summary.—This paper describes the nature of the chloroantimonous complex and the participation of hydroxide in the polarographic oxidation of arsenite and antimonite solutions. In addition it introduces a new technique of plotting $E_{1/2}$ vs. molal activities of ions involved in the reaction as a means for studying complexes in solutions of strong acids and bases at concentrations above 1 molal.

NAVAL RESEARCH LABORATORY
WASHINGTON, D. C.
CHEMISTRY DEPARTMENT
UNIVERSITY OF KANSAS
LAWRENCE, KANSAS

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[8] J. Whitney and N. Davidson, THIS JOURNAL, **71**, 3809 (1949).

[9] L. Pauling, *ibid.*, **55**, 1895 (1933).

[10] J. Beintema, *Rec. trav. chim.*, **56**, 931 (1937).

The Reaction of Methanesulfonyl Chloride with Alcohols in the Presence of Pyridine

BY C. R. NOLLER, C. A. LUCHETTI, E. M. ACTON AND R. A. BERNHARD

RECEIVED FEBRUARY 2, 1953

The reaction of methanesulfonyl chloride with an alcohol in the presence of pyridine might be expected to yield either the alkyl methanesulfonate or the alkyl chloride. As subsequent reactions the pyridine may remove methanesulfonic acid from the ester or hydrogen chloride from the alkyl chloride to give the olefin, or may form alkylpyridinium salts.

The reaction of methanesulfonyl chloride with an alcohol in the presence of pyridine at room temperature or below is the usual method for preparing alkyl methanesulfonates.[1] 1-Hydroxy-2-octyne does not yield the ester by this procedure, but a

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[1] V. C. Sekera and C. S. Marvel, THIS JOURNAL, **55**, 345 (1933); M. Zief, H. G. Fletcher and H. R. Kirshen, *ibid.*, **68**, 2743 (1946); M. F. Clarke and L. N. Owen, *J. Chem. Soc.*, 315 (1949); 2103, 2108 (1950).

poor yield of the chloride is obtained.[2] A double bond can be introduced into triterpenes by heating methanesulfonates with pyridine.[3]

The present work was undertaken to determine whether the decomposition of alkyl methanesulfonates by heating with pyridine may be used as a general method for preparing olefins. For this purpose the ester was not isolated, but the methanesulfonyl chloride merely was added to the alcohol in the presence of an excess of pyridine, and the resulting mixture heated.

The standard procedure adopted was the addition of 0.2 mole of methanesulfonyl chloride slowly with stirring to a solution of 0.2 mole of the alcohol in 0.4 mole of dry pyridine under a reflux condenser. During the addition the heat of reaction caused the mixture to boil. After the addition the mixture was heated on the steam-bath for 30 minutes, allowed to cool, and decomposed with water. The organic layer was separated, washed with dilute hydrochloric acid and water, dried over sodium sulfate, and distilled at 15 mm. until the residue in the flask began to decompose. A cold trap was inserted between the condenser and the vacuum pump. The distillate then was fractionated at atmospheric pressure into the lower-boiling fraction of olefin and a higher-boiling fraction, which consisted of a mixture of the chloride and, depending on the difference in the boiling points, more or less unreacted alcohol. The chloride was purified by washing with cold concentrated sulfuric acid, then with water, drying, and distilling. The olefins and halides were identified by their boiling points and refractive indexes. 2-Chlorooctane was characterized further by conversion through the Grignard reagent to the anilide of 2-methyloctanoic acid. The results are summarized in Table I.

TABLE I

Alcohol used	Yield of products, % Olefin	Yield of products, % Chloride	Alcohol used	Yield of products, % Olefin	Yield of products, % Chloride
n-Hexyl alcohol	0	59	*n*-Butyl alcohol	..	58
2-Octanol	24	28	*s*-Butyl alcohol	..	40
2-Methyl-2-heptanol	56	0	*t*-Butyl alcohol	..	0
Cyclohexanol	29	18	*i*-Butyl alcohol	..	53

For the four higher alcohols, which were chosen for the initial work because the olefins could be isolated readily, the primary alcohol gives chiefly chloride, the secondary alcohols about equal amounts of chloride and olefin, and the tertiary alcohol chiefly olefin. The butyl alcohols behave similarly since, although no attempt was made to isolate the olefins, the yield of chloride decreases from primary, to secondary to tertiary. It is of interest to note that whereas *n*-butyl alcohol is reported[1] to give a 79% yield of ester at 0°, at temperatures in the neighborhood of 100° a 58% yield of the chloride is obtained.

Although not recorded in the table, the behavior of pinacolyl alcohol also was investigated. The yield of isolable products was very low. About 14% of olefins and 4% of chloride were obtained, the remainder being high-boiling material. The olefins boiled in the range 38–73°, and fractionation and color reactions with tetranitromethane indicated that the mixture contained *t*-butylethylene, *unsym*-methylisopropylethylene and tetramethylethylene, and hence was similar to that obtained by the acid-catalyzed dehydration of pinacolyl alcohol.[4] Thus although an excess of pyridine was present at all times, a mixture of rearranged olefins was produced.

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(2) R. A. Raphael and F. Sondheimer, *J. Chem. Soc.*, 2101 (1950).

(3) F. A. Alves, Ph.D. Thesis, Stanford University, 1950; C. R. Noller and P. J. Hearst, THIS JOURNAL, **72**, 625 (1950).

(4) K. C. Laughlin, C. W. Nash and F. C. Whitmore, *ibid.*, **56**, 1395 (1934).

DEPARTMENT OF CHEMISTRY
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

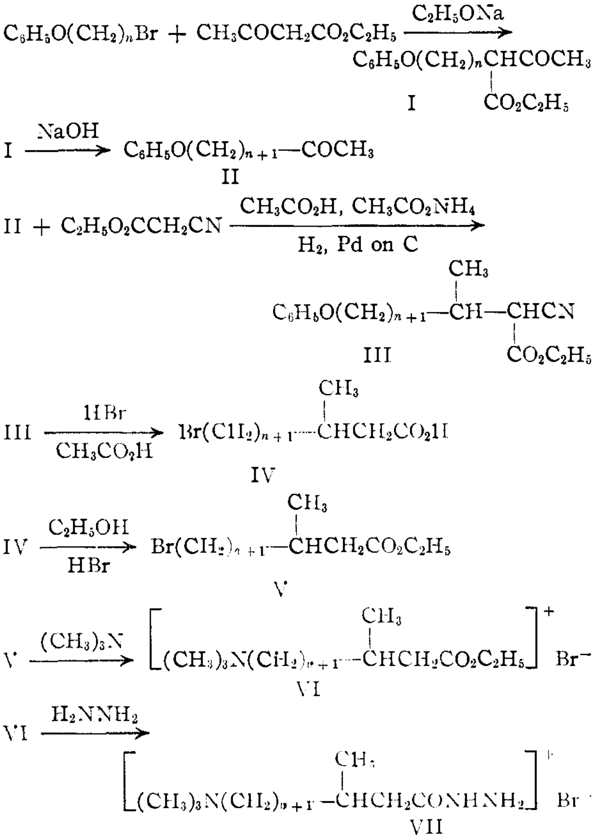
Substituted Alkyltrimethylammonium Bromides

BY NORMAN RABJOHN AND P. D. STRICKLER[1]

RECEIVED APRIL 1, 1953

It is known that branched chain fatty acids, hydrazides and quaternary ammonium salts possess properties of physiological significance and it appeared to be of interest to combine all of these functions in a single molecule.

The present work describes the methods of preparation of two such compounds as well as some related substances. The synthetic scheme employed is summarized by the equations



$$C_6H_5O(CH_2)_nBr + CH_3COCH_2CO_2C_2H_5 \xrightarrow{C_2H_5ONa} \underset{\text{I}}{C_6H_5O(CH_2)_n\underset{\substack{|\\CO_2C_2H_5}}{C}HCOCH_3}$$

$$\text{I} \xrightarrow{NaOH} \underset{\text{II}}{C_6H_5O(CH_2)_{n+1}{-}COCH_3}$$

$$\text{II} + C_2H_5O_2CCH_2CN \xrightarrow[H_2,\ Pd\ on\ C]{CH_3CO_2H,\ CH_3CO_2NH_4} \underset{\text{III}}{C_6H_5O(CH_2)_{n+1}{-}\overset{\substack{CH_3\\|}}{C}H{-}\underset{\substack{|\\CO_2C_2H_5}}{C}HCN}$$

$$\text{III} \xrightarrow[CH_3CO_2H]{HBr} \underset{\text{IV}}{Br(CH_2)_{n+1}{-}\overset{\substack{CH_3\\|}}{C}HCH_2CO_2H}$$

$$\text{IV} \xrightarrow[HBr]{C_2H_5OH} \underset{\text{V}}{Br(CH_2)_{n+1}{-}\overset{\substack{CH_3\\|}}{C}HCH_2CO_2C_2H_5}$$

$$\text{V} \xrightarrow{(CH_3)_3N} \underset{\text{VI}}{\left[(CH_3)_3N(CH_2)_{n+1}{-}\overset{\substack{CH_3\\|}}{C}HCH_2CO_2C_2H_5\right]^+ Br^-}$$

$$\text{VI} \xrightarrow{H_2NNH_2} \underset{\text{VII}}{\left[(CH_3)_3N(CH_2)_{n+1}{-}\overset{\substack{CH_3\\|}}{C}HCH_2CONHNH_2\right]^+ Br^-}$$

where $n = 3$ and 5.

The ω-phenoxy bromides were prepared by conventional procedures and caused to react with ethyl acetoacetate in the usual fashion. The resulting substituted acetoacetic esters underwent a facile hydrolysis to give the desired methyl ketones. The method of Cope and Alexander[2] was used to convert these to the α-cyano-β-methyl-ω-phenoxy

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(1) Abstracted in part from a thesis submitted by P. D. Strickler to the Graduate College of the University of Missouri, 1951, in partial fulfillment of the requirements for the Degree of Master of Arts.

(2) A. C. Cope and E. R. Alexander, THIS JOURNAL, **66**, 886 (1944).

esters. The latter were cleaved, hydrolyzed and decarboxylated in one step by means of an acetic acid solution of hydrogen bromide. This procedure was found to be more successful than a stepwise hydrolysis and decarboxylation of the cyano esters followed by cleavage of the phenoxy ethers.

The formation of the quaternary ammonium salts of the esters took place quite slowly and the products were so deliquescent that their physical properties were not determined. They were washed thoroughly with anhydrous ether and converted to the hydrazides without transferring them from the reaction flask. The hydrazides also were deliquescent in nature, but were obtained in a dry, crystalline form by allowing them to stand for extended periods in a vacuum desiccator.

As yet, no pharmacological testing has been carried out on the compounds.

Experimental[3]

ω-Phenoxyalkyl Halides.—γ-Phenoxypropyl and ε-phenoxyamyl bromides were prepared from trimethylene and pentamethylene dibromides, respectively, by the method of Marvel and Tanenbaum.[4] Commercially available tetramethylene dichloride was converted to δ-phenoxybutyl chloride by the same procedure. This in turn was changed to the corresponding iodide by means of sodium iodide in methyl ethyl ketone.[5]

Ethyl α-(ω-Phenoxyalkyl)-acetoacetates.—(a) Ethyl α-(γ-phenoxypropyl)-acetoacetate was prepared from 322 g. (1.5 moles) of γ-phenoxypropyl bromide, 195 g. (1.5 moles) of ethyl acetoacetate and 31 g. (1.35 gram atoms) of sodium, which had been dissolved in 625 ml. of absolute alcohol. The crude product (approximately 300 g.) was used without purification for the synthesis of methyl δ-phenoxybutyl ketone. (b) Ethyl α-(δ-phenoxybutyl)-acetoacetate was obtained from 125 g. (0.45 mole) of δ-phenoxybutyl iodide, 58.5 g. (0.45 mole) of ethyl acetoacetate and 9.7 g. (0.42 gram atom) of sodium, which had been dissolved in 225 ml. of absolute alcohol. There was obtained 93 g. (67%) of a pale, yellow liquid; b.p. 153–155° (1 mm.), $n^{20}\mathrm{D}$ 1.4984.

Anal. Calcd. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.94; H, 7.89.

(c) Ethyl α-(ε-phenoxyamyl)-acetoacetate was synthesized from 133 g. (0.55 mole) of ε-phenoxyamyl bromide, 72 g. (0.55 mole) of ethyl acetoacetate and 11.5 g. (0.5 gram atom) of sodium, dissolved in 250 ml. of absolute alcohol. The yield of ester was 48 g. (32%); b.p. 208–210° (1 mm.), $n^{20}\mathrm{D}$ 1.4970.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 69.59; H, 8.07.

Methyl ω-Phenoxyalkyl Ketones.—These materials were made essentially according to the method of Johnson and Hager.[6] (a) Methyl δ-phenoxybutyl ketone was obtained in 77% yield from the crude ethyl α-(γ-phenoxypropyl)-acetoacetate prepared in the previous experiment; b.p. 137–142° (1 mm.) (lit.[7] b.p. 136–137°) (1 mm.). (b) Methyl ε-phenoxyamyl ketone: from 93 g. (0.33 mole) of ethyl α-(δ-phenoxybutyl)-acetoacetate, stirred for 12 hours with 400 ml. of 5% sodium hydroxide solution, and worked up in the usual manner, there resulted 60 g. (87%) of a pale, yellow liquid; b.p. 142–144° (1 mm.), $n^{20}\mathrm{D}$ 1.5068.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.40; H, 8.99.

A 2,4-dinitrophenylhydrazone was prepared and obtained in the form of yellow plates from alcohol, m.p. 91–92°.

Anal. Calcd. for $C_{19}H_{22}O_5N_4$: C, 59.06; H, 5.74. Found: C, 59.29; H, 5.92.

(c) Methyl ζ-phenoxyhexyl ketone: from 39 g. (0.13 mole) of ethyl α-(ε-phenoxyamyl)-acetoacetate, stirred for 12 hours with 200 ml. of 5% sodium hydroxide solution, was isolated 21 g. (71%) of a colorless liquid; b.p. 162–163° (1 mm.), $n^{20}\mathrm{D}$ 1.5033.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.54; H, 9.00.

A 2,4-dinitrophenylhydrazone was prepared and crystallized as yellow needles from alcohol; m.p. 98–99°.

Anal. Calcd. for $C_{20}H_{24}O_5N_4$: C, 59.99; H, 6.04. Found: C, 60.20; H, 6.31.

Ethyl α-Cyano-β-methyl-ω-phenoxyesters.—The procedure of Cope and Alexander[2] was employed. (a) Ethyl α-cyano-β-methyl-ω-phenoxyheptanoate, 30 g. (66%) was obtained from 30 g. (0.156 mole) of methyl δ-phenoxybutyl ketone and 17.7 g. (0.156 mole) of ethyl cyanoacetate. The product boiled at 193–195° (1 mm.), $n^{20}\mathrm{D}$ 1.4981, and changed to a white solid, m.p. 39–41°, after standing for approximately six weeks.

Anal. Calcd. for $C_{17}H_{23}O_3N$: C, 70.56; H, 8.01. Found: C, 70.69; H, 8.09.

(b) Ethyl α-cyano-β-methyl-ω-phenoxycaprylate resulted from the condensation of methyl ε-phenoxyamyl ketone, 62 g. (0.3 mole), and ethyl cyanoacetate, 34 g. (0.3 mole), in 42% yield; b.p. 218–220° (1 mm.), $n^{20}\mathrm{D}$ 1.5096.

Anal. Calcd. for $C_{18}H_{25}O_3N$: C, 71.25; H, 8.31. Found: C, 71.09; H, 8.11.

(c) Ethyl α-cyano-β-methyl-ω-phenoxypelargonate was prepared in 48% yield from 36.3 g. (0.165 mole) of methyl ζ-phenoxyhexyl ketone and 18.7 g. (0.165 mole) of ethyl cyanoacetate; b.p. 210–212° (0.5 mm.), $n^{20}\mathrm{D}$ 1.5008.

Anal. Calcd. for $C_{19}H_{27}O_3N$: C, 71.89; H, 8.57. Found: C, 71.89; H, 8.72.

ω-Bromo-β-methylcarboxylic Acids and Their Ethyl Esters.—The procedure for the preparation of ω-bromo-β-methylheptanoic acid is representative of the method employed. A mixture of 68 g. (0.235 mole) of ethyl α-cyano-β-methyl-ω-phenoxyheptanoate and 300 ml. of 80% acetic acid, which contained approximately 1.5 moles of hydrogen bromide, was stirred and refluxed for about 60 hours. It was allowed to cool, poured into 1000 ml. of water and the insoluble layer was separated. The water layer was extracted with 100 ml. of ether and the extract was combined with the oil. The ethereal solution was shaken repeatedly with 5% sodium bicarbonate solution and the alkaline extracts were collected and acidified with 48% hydrobromic acid. The oil which separated was taken up in ether and the ethereal solution was dried over anhydrous magnesium sulfate. After removing the ether, there was obtained 20 g. (38%) of a light yellow oil; b.p. 130–133° (1 mm.), $n^{20}\mathrm{D}$ 1.4781.

Anal. Calcd. for $C_8H_{15}O_2Br$: C, 43.06; H, 6.73. Found: C, 43.42; H, 7.03.

The ethyl ester of this acid was prepared in 83% yield in the usual manner by heating it with a 7% solution of hydrogen bromide in ethanol; b.p. 95–96° (1 mm.), $n^{20}\mathrm{D}$ 1.4614.

Anal. Calcd. for $C_{10}H_{19}O_2Br$: C, 47.82; H, 7.62. Found: C, 48.09; H, 7.95.

ω-Bromo-β-methylpelargonic acid was obtained in 31% yield from a mixture of 63.4 g. (0.2 mole) of ethyl α-cyano-β-methyl-ω-phenoxypelargonate, 270 g. (1.6 moles) of 48% hydrobromic acid and 350 ml. of glacial acetic acid. The acid was isolated as a yellow oil; b.p. 157–160° (1 mm.), $n^{20}\mathrm{D}$ 1.4750.

Anal. Calcd. for $C_{10}H_{19}O_2Br$: C, 47.82; H, 7.62. Found: C, 48.01; H, 7.99.

The acid was esterified by means of ethanol and hydrogen bromide to the corresponding ester in 73% yield; b.p. 120–122° (1 mm.), $n^{20}\mathrm{D}$ 1.4600.

Anal. Calcd. for $C_{12}H_{23}O_2Br$: C, 51.55; H, 8.30. Found: C, 51.81; H, 8.53.

Trimethyl-ω-carbethoxyalkylammonium Bromides. (**a**) **Trimethyl-(5-methyl-6-carbethoxy)-hexylammonium** Bromide.—A solution of 8 g. of ethyl ω-bromo-β-methylheptanoate in 17 g. of an approximately 16% solution of triethylamine in anhydrous benzene was allowed to stand for 48 hours. The resulting white, crystalline precipitate was washed with a total of 250 ml. of anhydrous ether, after most of the mother liquor had been removed by decantation.

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[3] All melting points are uncorrected. The semimicro analyses were performed by one of the authors (P. D. S.).

[4] C. S. Marvel and A. L. Tanenbaum, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 435.

[5] A. H. Ford-Moore, *ibid.*, **30**, 10 (1950).

[6] J. R. Johnson and F. D. Hager, ref. 4, p. 351.

[7] G. Barger, R. Robinson and L. H. Smith, *J. Chem. Soc.*, **718** (1937).

The product was too deliquescent to make it practical to remove it from the reaction flask.

(b) **Trimethyl-(7-methyl-8-carbethoxy)-octylammonium Bromide.**—This compound was prepared in the same manner from 16.9 g. of ethyl ω-bromo-β-methylpelargonate and 39 g. of an approximately 16% solution of trimethylamine in anhydrous benzene. It also was extremely deliquescent, and after washing with 500 ml. of anhydrous ether, was used directly for the next synthesis.

Hydrazides of Trimethyl-ω-carboxyalkylammonium Bromides. (a) **Hydrazide of Trimethyl-(5-methyl-6-carboxy)-hexylammonium Bromide.**—A mixture of the crude trimethyl-(5-methyl-6-carbethoxy)-hexylammonium bromide and 7 g. of 85% hydrazine hydrate was heated to reflux for 15 minutes, enough alcohol was added to give a clear solution, and then refluxing was continued for an additional 2 hours. The solvent was removed under reduced pressure and the residual oil was washed with dry ether and chilled. There was obtained 2.5 g. (26%) of a white powder which melted at 118–122°.

Anal. Calcd. for $C_{11}H_{26}ON_3Br$: C, 44.59; H, 8.84. Found: C, 44.23; H, 9.16.

(b) **Hydrazide of Trimethyl-(7-methyl-8-carboxy)-octylammonium Bromide.**—The crude trimethyl-(7-methyl-8-carbethoxy)-octylammonium bromide, obtained previously, and 20 g. of 85% hydrazine hydrate were caused to react as described in the preceding experiment. The waxy appearing product was dissolved in hot absolute alcohol and precipitated by the addition of anhydrous ether. The solid was removed by filtration, dissolved in a small amount of hot absolute alcohol, clouded with petroleum ether (b.p. 60–68°) and allowed to solidify. There was obtained 5 g. (23%) of a hygroscopic, white powder, m.p. 136–139°.

Anal. Calcd. for $C_{13}H_{30}ON_3Br$: C, 48.13; H, 9.32. Found: C, 48.41; H, 9.60.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MISSOURI
COLUMBIA, MISSOURI

Constituents of U. S. P. Colchicine. N-Formyltrimethylcolchicinic Acid Methyl Ether[1]

BY ROBERT F. RAFFAUF,[2] ANN L. FARREN AND GLENN E. ULLYOT

RECEIVED MARCH 1, 1953

An earlier report from these laboratories[3] called attention to the presence of *ca.* 4% of 2-desmethylcolchicine[4] in commercial samples of U.S.P. colchicine. When a new sample[5] was subjected to chromatographic purification by the usual procedure[3,6] using chloroform–methanol (99:1) as eluant, an alkaloid (*ca.* 1.5% yield) having the properties of Šantavý's Substance B (N-formyltrimethylcolchicinic acid methyl ether)[7] was isolated; no 2-desmethylcolchicine was encountered. The new compound crystallized readily from ethyl acetate as pale yellow prisms which melted with decompositions at 260–262° (capillary). A comparison of this substance with Šantavý's Substance B is given in Table I.

The product was synthesized by formylation of trimethylcolchicinic acid methyl ether[8] using 98% formic acid in pyridine. Solvents were removed *in vacuo*, the residue was taken up in chloroform, washed with water and dried. Evaporation left a residue which crystallized readily from ethyl acetate to give pale yellow prisms, m.p. 260–262° dec. alone and when mixed with a sample isolated from U.S.P. colchicine.

TABLE I

	N-Formyl-trimethyl-colchicinic acid methyl ether from U.S.P. Colchicine[a]	Šantavý's Substance B	N-Formyl-iso-trimethyl-colchicinic acid methyl ether
M.p., °C., dec.	260–262 (capillary)	264–267 (Kofler block)	252–253 (capillary)
[α]D chloroform	−175 ± 1°	−171.2°	−315 ± 1°
	c 1.01, t = 25°	c 1.08, t = 22°	c 0.719, t = 25°
λ_{max} (log ε)	242.5 (4.48)	247 (4.51)	244 (4.50)
(95% ethanol)	350.0 (4.24)	350 (4.27)	342.5 (4.29)
	(c 5.22 × 10^{-5} M)		(c 5.6 × 10^{-5} M)

[a] Also synthesized from trimethylcolchicinic acid methyl ether.

Further confirmation of the configuration of our product was obtained by comparison with the iso-derivative prepared from iso-trimethylcolchicinic acid methyl ether[8] in the same manner. The product crystallized from ethyl acetate containing a little chloroform or methylene chloride as pale yellow prisms, m.p. 252–253° dec.; mixed m.p. with Substance B, 224–233° dec. For analysis it was dried to constant weight at 80° *in vacuo*.

Anal. Calcd. for $C_{21}H_{23}NO_6$: C, 65.44; H, 6.02. Found: C, 65.20; H, 5.94.

Comparative data are given in Table I; these are in agreement with previous findings[8,9] with respect to the properties of the iso- *vs.* the normal-forms in the colchicine and trimethylcolchicinic acid series.

Minor amounts of other alkaloids are present in the samples of U.S.P. colchicine which we have examined. Investigation of them will be continued. The biological effects of the N-formyltrimethylcolchicinic acid methyl ethers are being studied and will be reported elsewhere.

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(1) This investigation was supported (in part) by a research grant from the National Cancer Institute of the National Institutes of Health, U.S.P.H.S.

(2) Research Associate.

(3) R. M. Horowitz and G. E. Ullyot, *Science*, **115**, 216 (1952).

(4) F. Šantavý and M. Talaš, *Chem. Listy*, **46**, 373 (1952).

(5) U. S. P. Colchicine, S. B. Penick, Lot No. 1141-LI-A.

(6) J. N. Ashley and J. O. Harris, *J. Chem. Soc.*, 677 (1944).

(7) Šantavý and T. Reichstein, *Helv. Chim. Acta*, **33**, 1606 (1950).

(8) R. F. Raffauf, A. L. Farren and G. E. Ullyot, manuscript in preparation.

(9) R. M. Horowitz and G. E. Ullyot, THIS JOURNAL, **74**, 587 (1952).

RESEARCH AND DEVELOPMENT DIVISION
SMITH, KLINE AND FRENCH LABORATORIES
PHILADELPHIA, PENNSYLVANIA

The Characterization and Degradation of Isotopic Acetic and Lactic Acids

BY SAUL ROSEMAN

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During a study of the biosynthesis of hyaluronic acid,[1] it became necessary to characterize and degrade small quantities of isotopic acetic and lactic acids. As the procedures developed may be of general interest, details are presented here.

The chemistry of benzimidazole derivatives of aliphatic acids has been described in a recent comprehensive review.[2] In contrast to the usual technique for characterization of aliphatic acids,[3–5] the present method involves the use of a large excess of the reagent, *o*-phenylenediamine, and removal

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(1) S. Roseman, F. E. Moses, J. Ludowieg and A. Dorfman, *J. Biol. Chem.*, in press.

(2) J. B. Wright, *Chem. Revs.*, **48**, 397 (1951).

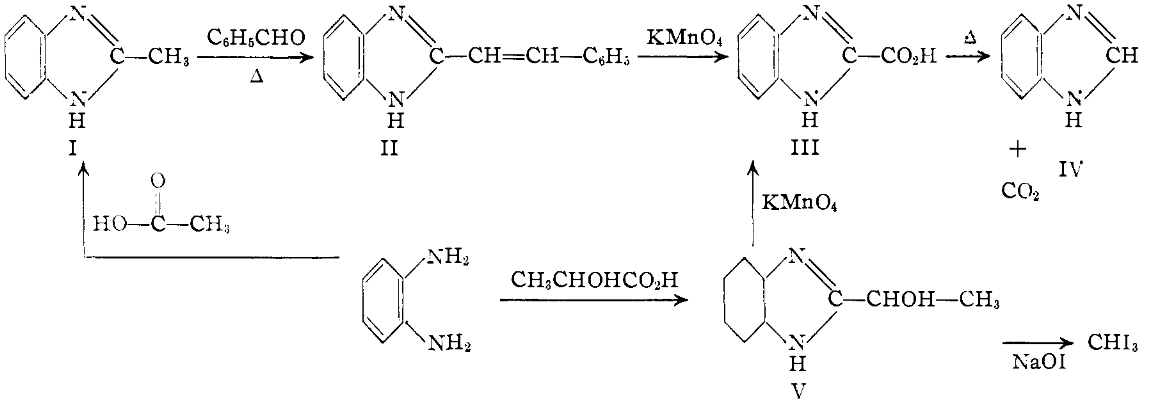
(3) E. L. Brown and N. Campbell, *J. Chem. Soc.*, 1699 (1937).

(4) R. Seka and R. B. Muller, *Monatsh.*, **57**, 97 (1931).

(5) W. O. Pool, H. J. Harwood and A. W. Ralston, THIS JOURNAL, **59**, 178 (1937).

of the excess and its highly colored decomposition products by a simple procedure. This modification thus makes the benzimidazole derivatives suitable for the characterization of micro quantities of impure acetic and lactic acids.

The derivatives are employed for degradation purposes as indicated in the reaction schemes below.[6]



Experimental

Conversion of Acetic Acid to 2-Methylbenzimidazole (I).—The procedure given below is a modification of that described by Moore and Link.[7] The molar ratio of *o*-phenylenediamine dihydrochloride to acetic acid can be varied from 2:1 to 6:1 with no change in results.

Glacial acetic acid (0.400 g.), *o*-phenylenediamine dihydrochloride (4.0 g., Eastman Kodak Co.), 10 ml. of water, 1.5 ml. of 85% phosphoric acid solution and some silicon carbide boiling chips are sealed in a glass tube and the mixture is heated for 2 hours in an oven maintained at 135°. The tube is cooled, opened and placed in an oil-bath at 135° for 2 hours. The excess reagent and its degradation products are removed from the mixture by dissolving the thick sirup in water, neutralizing with solid potassium carbonate, adjusting with glacial acetic acid to *p*H 3.5–4.0 (glass electrode) and treating 2 to 4 times with benzaldehyde. Each treatment is performed by shaking the solution with 10 ml. of benzaldehyde for approximately 30 seconds followed by three extractions with chloroform (70 ml. each). Purification is considered complete when the addition of benzaldehyde yields no color. Occasionally, filtration of the mixture is necessary for complete clarification. A final extraction of the colorless solution with petroleum ether is followed by neutralization with solid potassium carbonate. Concentrated ammonium hydroxide solution (30 ml.) and 14 g. of a silver nitrate solution (4 g. of silver nitrate, 4 g. of water, 6 g. of concentrated ammonium hydroxide solution) yield a white silver salt.[8] The salt is quickly centrifuged and repeatedly washed with water. The free benzimidazole is obtained by treating a suspension of the salt in alcohol–water mixture with hydrogen sulfide, decolorizing with a *small* quantity of Norit A and concentrating the filtrate until dry. Toward the end of the concentration, 1 ml. of ammonium hydroxide solution is added. White needles (750 mg.) are obtained, m.p. 174–176° (cor.). Purification of the compound is effected either by recrystallization from dilute ammonium hydroxide solution or by vacuum sublimation at 130–145° and 10^{-5} mm. pressure. The purified product melts at 175.5–176.5°.

When micro quantities are used, the condensation is carried out as described and the benzaldehyde treatments are performed in centrifuge tubes utilizing ether rather than chloroform for the extractions. From 5.3 mg. of acetic acid, 10.0 mg. of crude 2-methylbenzimidazole (m.p. 174–176°) was obtained.[9]

Conversion of DL-Lactic Acid to Racemic 2-(α-Hydroxyethyl)-benzimidazole (V).—The procedure employed is identical with that described for acetic acid except that the 2-hour heating period in a sealed tube is omitted, the open reaction tube being inserted directly into the oil-bath. The benzimidazole can be obtained as a silver salt as described, or at the same point in the procedure it can be extracted from the neutralized aqueous solution with ether. From 0.40 g. of lactic acid, 0.40 g. of the benzimidazole (m.p. 179–180°) was obtained. Purification can be effected either by recrystallization from dibutyl ether or by sublimation *in vacuo*; m.p. 180–181°.[10]

The average yields obtained from 10 to 20-mg. samples of lactic acid were the same as indicated above.

Degradation of 2-Methylbenzimidazole.—The derivative II is obtained by heating I at 190–200° with threefold its weight of benzaldehyde in a sealed tube. After 2 hours, the oil is dissolved in an acetone–ether mixture (1:1), and an excess of concentrated sulfuric acid is added with vigorous stirring. The white sulfate salt is quickly centrifuged, washed with acetone–ether mixture, dried, and it is then heated with 4 volumes of 0.4 *N* sulfuric acid in a boiling water-bath. The mixture is allowed to cool in ice for several hours, centrifuged and washed with ice-water. The crystals are then dissolved in the minimum quantity of hot ethanol containing an excess of concentrated ammonium hydroxide solution. The addition of 3 to 4 volumes of hot water yields a colorless oil which crystallizes in the refrigerator. The compound melts at 200–201°.[11] Typical yields: from 200, 60 and 11 mg. of I—295, 65 and 13 mg., respectively of II are obtained.

To a cold solution of 60 mg. of II in 5 ml. of pyridine is added 10 mg. of potassium carbonate followed by 5 ml. of potassium permanganate solution (containing 10% excess of permanganate over that necessary for the conversion of II to III). The mixture is maintained at 0° for 2 hours and the pyridine is then removed by steam distillation. A few drops of ethanol are added and the mixture is heated to boiling and filtered with the aid of Celite. After adjusting the filtrate to *p*H 6 with acetic acid, the solution is maintained at 4° for 2 days. The desired 2-benzimidazolecarboxylic acid (III) is obtained as long, colorless needles and the yield is about one half the weight of II used in the oxidation. Additional quantities can be isolated from the mother liquors—a necessary step when the oxidation is carried out on a 10-mg. scale. The compound decomposes at 174° and is dried at room temperature for analysis as it

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[6] A number of procedures have been published for the degradation of acetic and lactic acids; M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert and P. F. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949; "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 307; J. Kleinberg, *Chem. Revs.*, **40**, 381 (1947); E. F. Phares, *Arch. Biochem.*, **33**, 173 (1951).

[7] S. Moore and K. P. Link, *J. Org. Chem.*, **5**, 637 (1940); *J. Biol. Chem.*, **133**, 293 (1940).

[8] If the excess reagent and its degradation products have not been completely removed by the benzaldehyde treatments, the silver salt will precipitate white but will darken rapidly. The usual precautions are observed in working with the silver nitrate–ammonium hydroxide solution.

[9] The analyses were performed by Mr. William Saschek, Department of Chemistry, University of Chicago.

[10] R. J. Dimler and K. P. Link, *J. Biol. Chem.*, **143**, 557 (1952); S. Moore, R. J. Dimler and K. P. Link, *Ind. Eng. Chem.*, *Anal. Ed.*, **13**, 160 (1941).

[11] This substance has been obtained previously by another method: R. Weidenhagen, *Ber.*, **69**, 2270 (1936).

contains water of crystallization which is lost on more vigorous treatment.[12] Recrystallization of this compound must be performed with care.[13]

Anal. Calcd. for $C_8H_6O_2N_2 + 2H_2O$: C, 48.50; H, 5.01; N, 14.14. Found: C, 48.70; H, 5.32; N, 14.01.

For isotope experiments, III is heated to its m.p. and yields carbon dioxide and benzimidazole.[14] The carbon dioxide originates from the methyl carbon atom of the acetic acid molecule while the benzimidazole nucleus contains the carboxyl carbon atom.[15] It has been possible to perform the entire degradation starting with 11 mg. of 2-methylbenzimidazole, although in this case difficulty was experienced in isolating the pure benzimidazole.

Degradation of 2-(α-Hydroxyethyl)-benzimidazole (V).—The lactobenzimidazole isolated as described above is oxidized with potassium permanganate to III. A solution of 2.90 g. of potassium permanganate in 100 ml. of boiling water is added *all at once* to a boiling solution of 810 mg. of V and 200 mg. of sodium carbonate in 50 ml. of water. The mixture is boiled for 3 minutes and is placed on the steam-bath for 30 minutes. After the addition of small amounts of ethanol and Norit A, filtration, and adjustment to *p*H 6 with acetic acid, the colorless solution is placed in the refrigerator. After 2 days, 675 mg. of colorless needles is deposited, m.p. 174°. In other experiments, oxidation of 102 mg. and 41 mg. of V yielded 72 and 25 mg. of III, respectively. Decomposition of III as described above yields carbon dioxide (C-2 of lactic acid) and benzimidazole (contains C-1 of lactic acid).

The methyl carbon atom of lactic acid is obtained by treating V with sodium hypoiodite under the standard conditions[16] used for hydroxyethyl groups. The reaction is performed at 60° for 30 minutes and 54 mg. of V yields 22 mg. of iodoform, m.p. 117–119°. The iodoform is purified before combustion.

Isotope Experiments.—The validity of the degradation procedures was tested by degradation of benzimidazole derivatives of isotopic acetic and lactic acids. Standard techniques[6] were used to prepare 1-C^{14}-acetic acid. Group A streptococcus grown[1] in the presence of 1-C^{14}-glucose was used to produce 2-C^{14}-acetic acid and 3-C^{14}-lactic acid.[17] It is clear that in the case of the biosynthetic acids, it is possible that carbon atoms other than those indicated may contain isotope. Under these conditions, radioactivity will be obtained during the course of the degradation procedure where none is predicted. It is to be noted, however, that interpretation is always made that such results are due to the errors of the method (mixing of carbon atoms, etc.) rather than to isotope impurity of the starting material. The error of the method, as determined by these techniques, must therefore be considered the maximum error. All samples were plated as barium carbonate after combustion according to an accepted technique.[18] The activities reported have all been corrected to "infinite thickness" and are reported as counts per minute. Counting was performed using a windowless counter and "Q" gas. Table I gives the results obtained with isotopic acetic acid and Table II—with lactic acid.

The results obtained indicate that the *maximum* possible contamination of the methyl carbon atom by the carboxyl carbon atom in the case of the synthetic acetic acid is less than 0.02%, on the assumption that 1 count per minute above background is detectable. When biosynthetic acetic acid is used, and the assumption made that all of the isotope in the acid is present in the methyl carbon atom, it is possible to set an upper limit for mixing of carbon atoms during the degradation procedure at 0.37%. Calculations of this type (Table II) for the lactic acid derivatives indicate that the possible errors are of the same order of magnitude as those obtained with acetic acid. Within this range, therefore, the degradation procedure is considered valid.

Table I

Degradation of Isotopic 2-Methylbenzimidazole

Starting material		$CH_3C^{14}O_2H^a$	$C^{14}H_3C^?O_2H^b$
Benzimidazole (C-1 of acetic acid)	c.p.m.	601	5
	× 7[c]	4207	35
CO_2 (C-2 of acetic acid), c.p.m.		0	9485
Max. possible contamination of			
C-2 by C-1	c.p.m. ratio	0–1/4207	
	%	0.02	
C-1 by C-2	c.p.m. ratio		35/9485
	%		0.37

[a] Synthetic acetate; the isolated 2-methylbenzimidazole activity was 551. [b] Bacterial product[1] after metabolism of 1-C^{14}-glucose. The isolated 2-methylbenzimidazole activity was 1,280 (× 8 = 10,240). [c] The benzimidazole activity is multiplied by 7 to correct for the dilution of C-1 of acetic acid by the carbon atoms in the benzene ring. The value 4207 compares satisfactorily with 4408 (551 × 8)—the corrected activity of the synthetic 2-methylbenzimidazole.

Table II

Degradation of Isotopic 2-(α-Hydroxyethyl)-benzimidazole

Starting material		$CH_3C^{14}HOHCO_2H^a$	$C^{14}H_3C^?HOHC^?O_2H^b$
Benzimidazole			
(C-1 of lactic acid)	c.p.m.	0	2
	× 7[c]	0	14
CO_2 (C-2 of lactic acid), c.p.m.		339	9
CHI_3 (C-3 of lactic acid), c.p.m.		0	13,200
Max. possible contamination of			
C-3 or C-1 by C-2	c.p.m. ratio	0–1/339	
	%	0.3	
C-1 or C-2 by C-3	c.p.m. ratio		14/13,200
	%		0.11

[a] Synthetic lactic acid. The activity of the lactobenzimidazole was 38 c.p.m. [b] Bacterial product[1] obtained after metabolism of 1-C^{14}-glucose. The isolated lactobenzimidazole activity was 1,437 c.p.m. (× 9 = 12,930). [c] The benzimidazole activity is multiplied by 7 to correct for dilution of C-1 of lactic acid by the carbon atoms in the benzene ring. The activity of C-2 of the synthetic lacto-benzimidazole (339) compares satisfactorily with the corrected activity of the whole molecule, 342 (38 × 9).

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Department of Pediatrics and Biochemistry
The University of Chicago
Chicago, Illinois

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[12] A. Bistrzycki and G. Przeworski, *Ber.*, **45**, 3483 (1912).

[13] R. A. B. Copeland and A. R. Day, This Journal, **65**, 1072 (1943).

[14] C. F. Huebner, T. Lohmar, R. T. Dimler, S. Moore and K. P. Link, *J. Biol. Chem.*, **159**, 503 (1945).

[15] It has been reported that the carboxyl carbon atom can be obtained as formic acid by opening the imidazole ring: E. Bamberger and B. Berlé, *Ann.*, **273**, 342 (1893).

[16] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 2nd edition, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 53.

[17] Dr. Herbert S. Anker, Dept. of Biochemistry, University of Chicago, kindly supplied the 2-C^{14}-lactic acid (synthetic).

[18] J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Analysis," 2nd edition, John Wiley and Sons, Inc., New York, N. Y., 1942.

Activities of Aqueous Magnesium and Barium Acetate Solutions at 25°

By R. H. Stokes

Received March 19, 1953

The measurements reported here were made in 1947 as part of a proposed study (since abandoned from lack of time) of a number of bivalent metal acetates in aqueous solution.

Experimental

Barium acetate of analytical reagent quality was made into a stock solution which was analyzed by evaporating suitable portions with excess sulfuric acid and weighing the dry barium sulfate. Magnesium acetate was prepared by dissolving the calculated amount of pure MgO (calcined at 900°) in an acetic acid solution of known concentration. These solutions were equilibrated against sodium chloride solutions in an isopiestic vapor pressure apparatus of the usual pattern.[1] The molalities of the pairs of isopiestic solutions are given in Table I. Table II gives the molal-scale osmotic coefficients $\phi = -55.51/3m \ln (p/p_0)$ and activity coefficients γ. There is some difficulty in estimating the value to be assigned to γ at 0.1 m owing to the form of the osmotic coefficient curves; ϕ evidently has a minimum somewhere below the experimental range and then turns sharply upward to reach the value unity at zero concentration. The value $\gamma_{0.1m} = 0.450$ has been rather arbitrarily assigned to both salts from a comparison with some other 2:1 electrolytes; the remaining values are correct relative to these, but the absolute values could well be as much as 5% different.

TABLE I

MOLALITIES OF ISOPIESTIC SOLUTIONS AT 25°

m_1 = molality of acetate solution, m_2 = molality of sodium chloride solution

m_1	m_2	m_1	m_2	m_1	m_2
		Barium acetate			
0.1073	0.1384	0.6496	0.8926	1.870	2.454
.1510	.1964	1.087	1.493	2.062	2.649
.1902	.2500	1.283	1.755	2.822	3.332
.2593	.3434	1.464	1.973	3.474	3.812
.5045	.6880	1.667	2.220		
		Magnesium acetate			
0.1431	0.1847	0.8053	1.337	2.205	3.173
.2013	.2597	.9605	1.355	2.748	3.994
.2503	.3245	1.053	1.443	3.300	4.794
.3799	.4930	1.259	1.740	4.149	5.984
.4286	.5588	1.728	2.439		

TABLE II

OSMOTIC AND ACTIVITY COEFFICIENTS OF BARIUM AND MAGNESIUM ACETATES AT 25°

	$Ba\overline{Ac}_2$		$Mg\overline{Ac}_2$	
m	ϕ	γ	ϕ	γ
0.1	0.800	(0.450)	(0.797)	(0.450)
.2	.807	.395	.793	.389
.3	.817	.370	.795	.359
.5	.841	.347	.807	.328
.7	.857	.335	.826	.314
1.0	.873	.325	.861	.307
1.2	.881	.320	.886	.308
1.4	.884	.315	.910	.310
1.6	.885	.311	.935	.315
1.8	.884	.306	.961	.321
2.0	.878	.301	.987	.329
2.5	.856	.286	1.049	.351
3.0	.832	.271	1.109	.378
3.5	.804	.256	1.159	.406
4.0			1.207	.436

The relative positions of the osmotic coefficient curves are noteworthy. At low concentrations that for barium acetate is slightly the higher, in contrast to the nitrates and halides where the magnesium salts have the higher osmotic coefficients. A similar reversal has been remarked with the alkali metal acetates.[2] Potassium acetate for example, has a higher osmotic coefficient than lithium acetate, though that of potassium chloride is lower than that of lithium chloride. This effect has been tentatively explained by Robinson and Harned[2] in terms of a "localized hydrolysis" resulting from interaction of a proton from the hydration sheath of the Li^+ ion with the acetate ion, the effect being most marked with the most strongly hydrated cation. A similar effect would appear to be operating in the present case. Above 1 M however the position is different; the osmotic coefficient of magnesium acetate continues to rise, while that of barium acetate passes through a maximum. It seems likely that here we have the effect of Bjerrum ion association dominating the osmotic coefficients; the heavily hydrated magnesium ion is larger than the less hydrated barium ion, and hence shows less tendency to form ion pairs. The behavior of these two salts thus provides a striking example of the complexities which may be encountered in moderately concentrated electrolytes, and which can be qualitatively explained by considerations of ion–ion and ion–solvent interactions.

CHEMISTRY DEPARTMENT
UNIVERSITY OF WESTERN AUSTRALIA
NEDLANDS, WESTERN AUSTRALIA

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[1] R. A. Robinson and D. A. Sinclair, THIS JOURNAL, **56**, 1830 (1934).

[2] R. A. Robinson and H. S. Harned, *Chem. Revs.*, **28**, 454 (1941).

The Configurations of the 3-Bromocyclohexanecarboxylic Acids[1]

BY SAMUEL SIEGEL[2] AND JEROME G. MORSE

RECEIVED DECEMBER 3, 1952

The configurations of the 3-bromocyclohexanecarboxylic acids were originally assigned by Perkin[3] on the basis of their mode of formation. The reaction of the lactone I with aqueous hydrobromic acid at room temperature yields a bromo acid, m.p. 65°, which was named *cis*-3-bromocyclohexanecarboxylic acid. Either *cis*- or *trans*-3-hydroxycyclohexanecarboxylic acid (III and IV) reacts with aqueous hydrobromic acid at 100° to yield a mixture from which a higher melting acid, m.p. 167–168°, is isolated and is labeled *trans*.[3] However, current theory suggests that these conversions are displacement reactions which proceed with the inversion of the configuration of the carbon atom under attack, although inversion may be accompanied by varying degrees of racemization.[4] Consequently the designated configurations of the 3-bromo acids are probably inverted. The more probable configurational relationships are diagrammed below.

Furthermore, a neutralized alcoholic solution of the bromo acid, m.p. 67–68°, decomposes in a few minutes at the reflux temperature to yield the lactone I, whereas the higher melting acid is stable under the same conditions.[5] Only the latter acid forms a stable benzylammonium salt. These phenomena clearly demonstrate the participation of the carboxylate group in the decomposition of the salt of the lower melting bromo acid and therefore, in this acid, the carboxylate group must be *trans* to the bromo group, a configuration which permits the carboxylate group to displace the latter in a

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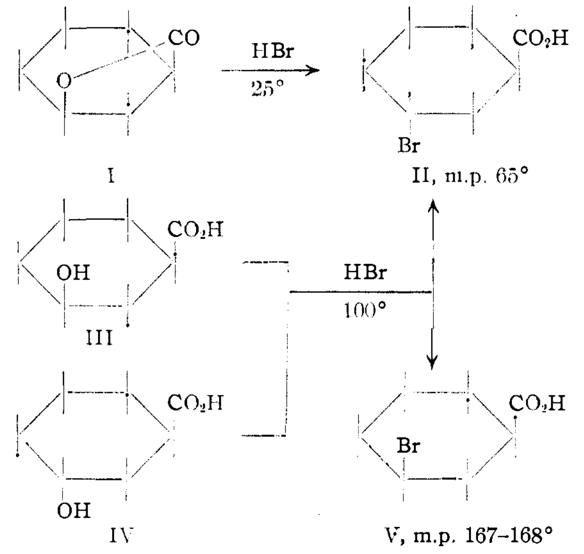
[1] Presented at the Southwestern Regional Meeting of the American Chemical Society, December, 1951.

[2] University of Arkansas, Fayetteville, Arkansas.

[3] W. H. Perkin, Jr., and G. Tattersall, *J. Chem. Soc.*, 482 (1907).

[4] W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *J. Chem. Soc.*, 1252 (1937).

[5] E. J. Boorman and R. P. Linstead, *ibid.*, 258 (1935).



one-stage process.[6] A comparison of the acidic dissociation constants of the bromo acids with the constants of the related hydroxy acids and the cyclohexanedicarboxylic acids provide further evidence of configuration. Clearly, dissociation constants reflect the relative orientation of the polar groups and the distance which separates them in a molecule.[7] Since the polarity of the bromo, the hydroxyl and the carboxylic acid groups is in the same direction (electron withdrawal from carbon) the relative acidities of *cis* and *trans* isomers should be in the same order.

The relative acidities (compared with cyclohexanecarboxylic acid) of the 3- and 4-substituted cyclohexanecarboxylic acids are given in Table I.[8] The configuration of the hydroxyacids[5,9] and the dicarboxylic[10,11] acids are well established. Apparently a *trans* 4-substituted acid is stronger than its isomer, a *cis* 4-substituted acid, whereas in the 3-series the *cis* acid is the stronger.

TABLE I

RATIO OF THE DISSOCIATION CONSTANTS ($K_{A_xB_0}$) OF SUBSTITUTED CYCLOHEXANECARBOXYLIC ACIDS

Substituent	Solvent	$K_{A_xB_0}$			
		cis-1,3	*trans*-1,3	*cis*-1,4	*trans*-1,4
CO_2H[a]	Water	4.3	2.8	2.4	3.6
OH[b]	Water	2.00	1.22	1.17	1.68
	Methanol	1.84	0.89	0.83	1.63
	Ethanol	1.82	0.92	0.87	1.44
Br	Methanol	2.47	<1.8	...	...
	Ethanol	2.71	<2.5	...	...

[a] R. Kuhn and H. Wasserman (*Helv. Chim. Acta*, 11, 50 (1928)) reports the dissociation constants of the acids. $K_{A_xB_0}$ was obtained by dividing them by 1.96×10^{-5}, K for cyclohexanecarboxylic acid in water at 25°, at an ionic strength of 0.1 (mainly sodium chloride). [b] Measurements to be reported by M. Kilpatrick and J. G. Morse.

This result is understandable in terms of current concepts of the stereochemistry of substituted cyclohexanes.[12,13] Thus the stronger acid for each pair is that isomer which can have both groups in the "equatorial" positions, *e.g.*, the 1,3-*cis* and 1,4-*trans*. And although the center of the dipole of a "polar" substituent is closer than that of an "equatorial" substituent to the ionizable proton of an "equatorially" placed carboxylic acid group, the orientation of the "polar" dipole is less favorable for the detachment of the proton. And the orientation factor is dominant here.

The substituted cyclohexanecarboxylic acids under consideration are stronger acids than cyclohexanecarboxylic acid. The acidity of the higher melting 3-bromo acid (m.p. 167–168°) is greater by a factor of 2.47 in methanol. Because of the instability of the lower melting acid in hydroxylic solvents, only an upper limit (< 1.8 in methanol) can be placed upon its relative acidity but it is unquestionably a weaker acid than the higher melting bromo acid. These data are again consistent with the assignment of the *cis* configuration to the bromo acid, m.p. 167–168°, and the *trans* configuration to the lower melting isomer.

Experimental

Preparation of the Higher Melting Acid (m.p. 167–168°).—The isomeric 3-bromocyclohexanecarboxylic acids were prepared in the manner described by Boorman and Linstead.[5] After it was recrystallized from benzene it had the properties: m.p. 167–168°; neutralization equivalent weight, 207.1 (calcd. 207.1).

Preparation of the Lower Melting Isomer (m.p. 65°).[6]—The lower melting isomer, m.p. 65°, was obtained from the reaction, at room temperature, of the lactone of 3-hydroxycyclohexanecarboxylic acid with hydrogen bromide in an aqueous solution saturated at 0°. It was purified by recrystallization from petroleum ether, b.p. 60–80°; neutralization equivalent weight, 206.6 (calcd. 207.1).

The acid (90 mg.) decomposed when it was stirred with water (15 ml.) for three hours at room temperature. An analysis of the solution showed 0.44 milliequivalent of acid and 0.42 milliequivalent of halogen. This indicates that the decomposition products are largely the lactone and hydrogen bromide.

Benzylammonium Salt of *cis* 3-Bromocyclohexanecarboxylic Acid.—This salt was prepared by combining a solution of the bromo acid in anhydrous ether with an equivalent quantity of benzylamine also dissolved in ether. It was recrystallized from ethyl acetate and was obtained in the form of white needles, m.p. 125–126°. The bromo acid, m.p. 167–168°, was regenerated from the salt in an acidified aqueous solution. *Anal.*[14] Calcd. for $C_{14}H_{20}O_2NBr$: N, 4.46; Br, 25.4. Found: N, 4.28; Br, 25.7.

Dissociation Constants.—The dissociation constants of the bromo acids were measured by an e.m.f. method which has been described previously.[15] The acids were not measured in water because of the limited solubility in that solvent. However, anhydrous methanol and ethanol were satisfactory media. The dissociation constant of the higher melting isomer was measured accurately but the dissociation constant of the lower melting isomer is approximate because its ready solvolysis caused an apparent increase of acidity with time. Nevertheless, an upper limit for its acidity can be stated with confidence and an approximation of its true value was obtained by an extrapolation of the acidity of the solution to the zero time of mixing. The ionization con-

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[6] (a) P. D. Bartlett and P. N. Rylander, THIS JOURNAL, **73**, 4275 (1951); (b) D. W. Wujciak, R. L. Feller and J. F. Lane, *ibid.*, **73**, 2392 (1951).

[7] J. G. Kirkwood and F. A. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938).

[8] The 2-substituted acids are not included because of the probable occurrence of proximity effects.

[9] N. R. Campbell and J. H. Hunt, *J. Chem. Soc.*, 1379 (1950).

[10] S. Boeseken and A. E. J. Peek, *Rec. trav. chim.*, **44**, 841 (1925).

[11] W. H. Mills and G. H. Keats, *J. Chem. Soc.*, **147**, 1373 (1935).

[12] C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

[13] H. A. Smith and F. P. Byrne, *ibid.*, **72**, 4406 (1950).

[14] Elementary analysis was performed by the Micro-Tech Laboratory, Skokie, Illinois.

[15] J. H. Elliott and M. Kilpatrick, *J. Phys. Chem.*, **45**, 454 (1941).

stants relative to cyclohexanecarboxylic acid are given in Table I.

DEPARTMENT OF CHEMISTRY
ILLINOIS INSTITUTE OF TECHNOLOGY
CHICAGO, ILLINOIS

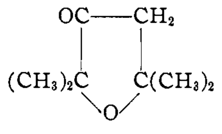
The Dehydration of 4-Hydroxy-2,2,4,5,5-pentamethyltetrahydrofuran (Acetylene Studies, Part VI)[1]

BY MAX SULZBACHER AND ERNST D. BERGMANN

RECEIVED JANUARY 26, 1953

When II, the product of the reaction between 4-keto-2,2,5,5-tetramethyltetrahydrofuran (I) and methylmagnesium iodide, is dehydrated, a compound of the expected composition $C_9H_{16}O$ is obtained. Apart from the normal formulas, III, IV, the structure V is possible for this compound. Indeed, V has been proposed by Bouveault and Locquin,[2] as the same substance is also formed by acid dehydration of 2,3,5-trimethylhexane-2,3,5-triol (VI).

The infrared spectrum of the dehydration product is compatible only with formula V. Whilst it does not show any sign of double bond absorption in the 1620–1700 cm.$^{-1}$ region, the following bands were observed: 980 cm.$^{-1}$ (optical density d = 0.6) cyclobutane[3]; 1099 cm.$^{-1}$ (d = 0.3) isopropyl; 1175 cm.$^{-1}$ (d = 0.8) superposition of the isopropyl and the tetrahydrofuran absorption.[4] The chemical properties of the compound $C_9H_{16}O$ are in accord with formula V. It could not be hydrogenated catalytically to 2,2,4,5,5-pentamethyltetrahydrofuran at ordinary temperature and pressure, and did not decolorize bromine in carbon tetrachloride.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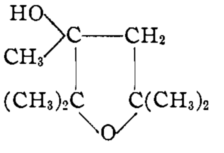
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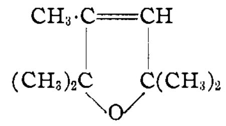
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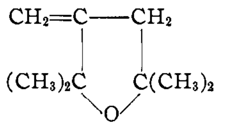
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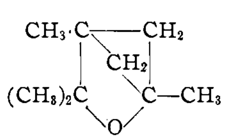
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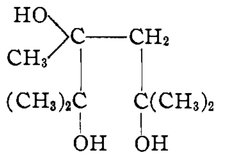
VI

Experimental

I was prepared in quantitative yield from 1,1,4,4-tetramethyl-2-butyne-1,4-diol and aqueous mercuric sulfate,[5–7] b.p. 150° (760 mm.).

4-Hydroxy-2,2,4,5,5-pentamethyltetrahydrofuran (II).—The reaction of I with 2 moles of methylmagnesium iodide[6] gave II in 63% yield; from diisopropyl ether, m.p. 77°.[8]

Dehydration to V.—The mixture of 80 g. of II and 100 g. of freshly fused and finely ground potassium hydrogen sulfate was heated for six hours at 120°. The liquid product was distilled directly, dried and fractionated; b.p. 132°, yield 68 g. (96%), $d^{27.5}_4$ 0.820 (literature 0.826).

Anal. Calcd. for $C_9H_{16}O$: C, 77.1; H, 11.4. Found: C, 77.0; H, 11.5.

The infrared spectrum was measured in the 950–1200 cm.$^{-1}$ region in carbon disulfide solution (0.015 g. plus 1 cc. of solvent), in the 1600–1700 cm.$^{-1}$ region in carbon tetrachloride (0.016 g. plus 1 cc. of solvent); cell thickness 0.5 mm.[9]

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[1] Part I: THIS JOURNAL, **73**, 4013 (1951); Part II–V, *J. Applied Chem.*, **3**, 39, 42, 97, 145 (1953).

[2] L. Bouveault and R. Locquin, *Ann. chim,.* [8] **21**, 414 (1910).

[3] L. W. Marrison, *J. Chem. Soc.*, 1614 (1951).

[4] H. Tschamler and H. Voetter, *Monatsh.*, **83**, 302 (1952). See also G. M. Barrow and S. Searles, THIS JOURNAL, **75**, 1175 (1953).

[5] G. Dupont, *Compt. rend.*, **152**, 1486 (1911).

[6] G. Dupont, *Ann. chim.*, [8] **30**, 536 (1913).

[7] H. Richet, *ibid.*, [12] **3**, 317 (1948).

[8] G. Dupont, *Compt. rend.*, **154**, 601 (1912).

[9] We are greatly indebted to Dr. S. Pinchas, Optics Department, Weizmann Institute of Science, Rehovoth, for the determination of the spectrum.

GROSVENOR LABORATORY
LONDON, S.W. 1, ENGLAND

LABORATORIES OF THE SCIENTIFIC DEPARTMENT
MINISTRY OF DEFENCE
TEL-AVIV, ISRAEL

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cis- and *trans*-Tropine (Tropanol)[1]

BY PIERRE F. SMITH[2] AND WALTER H. HARTUNG[3]

RECEIVED MARCH 5, 1953

Recent papers establish the stereochemical structure of the tropine (tropanol) isomers,[4–6] namely, that in tropine the hydroxyl group and N-methyl bridge are *trans* and that in ψ-tropine they are *cis*. We now submit additional experimental evidence confirming these conclusions.

A study of models suggested that the structure with the –OH and $>NCH_3$ groups in close proximity might be expected, owing perhaps to hydrogen bonding, to exhibit greater pK values in aqueous solution and less change in pH upon titration. Our results, obtained from the titration of 20.00-ml. portions of 0.050 N solutions of the isomeric tropines (purified by sublimation *in vacuo*) with 0.0613 N hydrochloric acid, are summarized in Fig. 1. The pK values at 25°, as estimated from the half neutralization points, are 2.98 for tropine and 3.67 for ψ-tropine. The greater value for ψ-tropine is suggestive of intramolecular hydrogen bonding and therefore a configuration of the –OH *cis* to the $>NCH_3$ group.

Tropine, refluxed for ten minutes with benzoyl chloride in a 1:8 molar ratio, yielded 84.5% of tropine benzoate hydrochloride. ψ-Tropine, identically treated, yielded 79.2% of ψ-tropine benzoate hydrochloride. Regrettably limited amounts of materials did not permit further study of the reactivity of the –OH groups in the isomeric alcohols.

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[1] Experimental work performed at the University of Maryland.

[2] Rutgers University, Newark, N. J.

[3] University of North Carolina, Chapel Hill, N. C.

[4] G. Fodor and K. Nador, *Nature*, **169**, 462 (1952).

[5] B. L. Zenitz, C. M. Martini, M. Priznar and F. C. Nachod, THIS JOURNAL, **74**, 5564 (1952).

[6] A. Nickon and L. F. Fieser, *ibid.*, **74**, 5566 (1952).

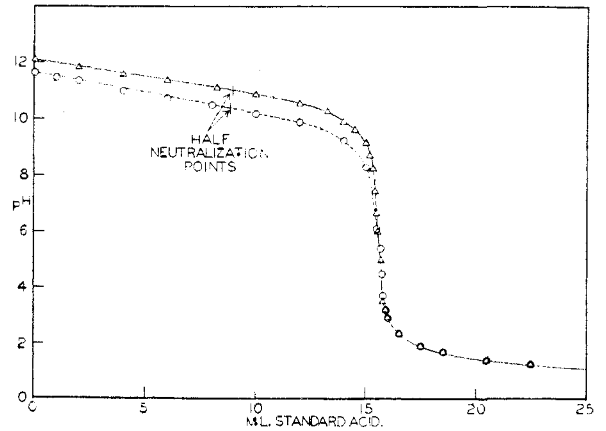
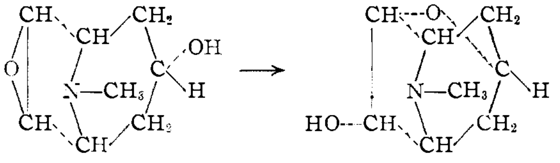


Fig. 1.—Titration curves of tropanol (Δ and solid line) and pseudotropanol (O and dashed line).

It was hoped that the rule of v. Auwers[7] might be applied, although tridimensional models of the molecules reveal that the reference point for *cis–trans* definition is not clear. The densities obtained for liquid tropine and ψ-tropine are $d^{116}{}_{20}$ 1.001 and $d^{116}{}_{20}$ 0.998.

In this connection it may be pointed out that in scopine, I, the basic moiety of hyoscine (scopolamine), the -OH group at position 3 is most probably *trans* to the $\rangle NCH_3$ bridge, since that configuration best explains the easy rearrangement to scopoline, II. Hyoscine frequently occurs together with atropine in various *Atropa* and *Datura* species,[8] suggesting similar stereo-biochemical genesis for the two alkaloids.



I Scopine

II Scopoline

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(7) K. v. Auwers, *Ann.*, **410**, 287 (1915); **420**, 84 (1920).

(8) T. A. Henry, "The Plant Alkaloids," The Blakiston Co., Philadelphia, Pa., 1949, p. 65.

RUTGERS UNIVERSITY
NEWARK, NEW JERSEY

UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, NORTH CAROLINA

Simultaneous Dissociation of Two Protons. The Acid–Base Equilibria of Porphyrins[1]

BY ROBERT IRVING WALTER[2]

RECEIVED FEBRUARY 19, 1953

The four nitrogen atoms of the porphyrin ring system can participate in a series of acid–base equilibria which can be written (PH_2 is the neutral porphyrin molecule)

$$PH_4^{++} \rightleftarrows PH_3^+ + H^+ \tag{1}$$

$$PH_3^+ \rightleftarrows PH_2 + H^+ \tag{2}$$

$$PH_2 \rightleftarrows PH^- + H^+ \tag{3}$$

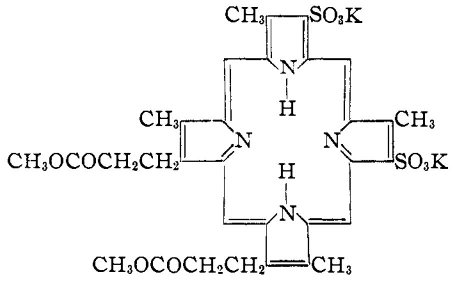
$$PH^- \rightleftarrows P^= + H^+ \tag{4}$$

A potentiometric study of equilibria (1) and (2) was reported by Conant, *et al.*,[3] who observed only a single inflection in the titration curve for the addition of two equivalents of acid to PH_2. They assumed $pK_1 = pK_2$, and reported values averaging 2.5 for five porphyrins in glacial acetic acid. A colorimetric study of equilibria (1) and (2) was reported by Aronoff and co-workers,[4] who found only one absorption curve for each of three porphyrins in various sulfuric acid–pyridine mixtures. From the absence of a spectrum intermediate between those of PH_4^{++} and PH_2, they concluded that PH_3^+ could exist over only a limited *p*H range, and assumed that K_1 and K_2 were very nearly equal.

Equilibria (3) and (4) have been studied colorimetrically by McEwen,[5] who found that no difference in acid strength could be detected for the first and second ionization steps of PH_2. He assigned $pK_3 = pK_4 = 16$ for both steps of the ionization of etioporphyrin in methanol.

The authors quoted[3-5] apparently intended to express the conclusions that reactions (1) and (2) occur with equal ease and, similarly, that reactions (3) and (4) occur with equal ease. If this is the case, it is *not* true that $K_1 = K_2$ and $K_3 = K_4$. Instead, due to statistical factors arising in the conventional definition of the dissociation constants, $K_1 = 4K_2$ and $K_3 = 4K_4$[6] (if PH_4^{++} and PH_2 be assumed to dissociate as independent dibasic acids). In such a reaction, the intermediate (PH_3^+ or PH^-) would attain a maximum concentration, when the reaction was half completed, equal to half that of the total porphyrin present.

These results on a number of different porphyrins in a variety of solvents are not strictly comparable, but they suggest an unusual situation in which a tetrabasic acid loses two protons more or less simultaneously in each of two widely separated stages on the *pK* scale. Accordingly, equilibria (1) and (2) have been investigated in an effort to detect the presence of PH_3^+. The water soluble porphyrin chosen for study was the dipotassium salt of 1,3,5,8-tetramethylporphyrin-6,7-dipropionic acid methyl ester-2,4-disulfonic acid



The formula given is thus the species PH_2.

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[1] This material was presented before the Organic Section at the 119th meeting of the American Chemical Society, Cleveland, April, 1951.

[2] School of Chemistry, Rutgers University, New Brunswick, New Jersey.

(3) J. B. Conant, B. F. Chow and E. M. Dietz, THIS JOURNAL, **56**, 2185 (1934).

(4) (a) S. Aronoff and C. A. Weast, *J. Org. Chem.*, **6**, 550 (1941); (b) S. Aronoff and M. Calvin, *ibid.*, **8**, 205 (1943).

(5) W. K. McEwen, THIS JOURNAL, **58**, 1124 (1936).

(6) J. Greenspan, *Chem. Revs.*, **12**, 339 (1933).

Experimental

The porphyrin was prepared from ferriprotoporphyrin chloride and purified chromatographically by a method described elsewhere.[7] The substance actually recovered from the column was the dipotassium salt of the two strong sulfonic acid groups. Aliquots of a standard solution in methanol were air dried and made up in distilled water or aqueous buffers for study. The concentrations of all solutions thus were self-consistent, but involved a constant error estimated to be ±10% because the porphyrin was hygroscopic and only a small sample was weighed.

The buffer used was acetic acid–potassium acetate, with pH 4.75 and ionic strength 0.20. Acid solutions were prepared by diluting hydrochloric acid of known concentration.

Absorption of the various solutions was read in the visible region on a Beckman model DU spectrophotometer using 1-cm. corex cells.

Results

Figure 1 shows the absorption spectra of the porphyrin in neutral and acid aqueous solution. These curves differ sufficiently to permit application of the method of continuous variations of Vosburgh and Cooper[8] to the study of the equilibrium

$$PH_2 + nH^+ \rightleftarrows PH_{2+n}^{n+} \qquad (5)$$

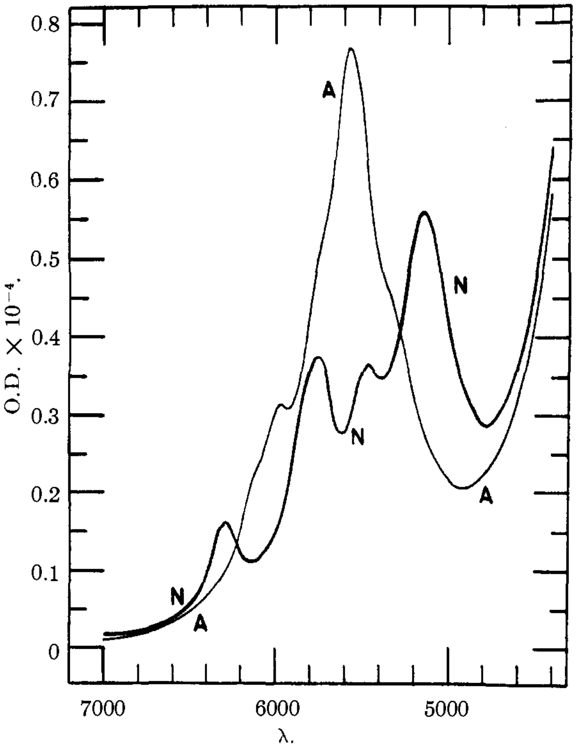

Fig. 1.—Optical densities *vs.* wave lengths in ångströms. The ordinates are calculated for 1 M concentration, and thus equal molar extinction coefficients within the estimated concentration error of ±10%: Curve N, absorption of neutral porphyrin, PH_2, in aqueous HOAc–NaOAc buffer, pH 4.75, ionic strength = 0.20; curve A, absorption of acid porphyrin, PH_4^{++}, in aqueous HCl, pH 0.70, ionic strength = 0.20.

Figure 2 gives the results, in a plot of the difference function Y against the volume fraction X, of acid solution in a mixture of 0.001 M aqueous solutions of porphyrin and hydrochloric acid. Y is defined as the optical density observed less the optical density calculated for the mixed solutions assuming no reaction between the solutes. For the nine wave lengths at which it was determined, the extreme value of Y occurs at X_{max} = 0.667 ± 0.004, and the value of n in equation (5) above, found from Vosburgh and Cooper's equation (5), is two. (Formation of the intermediate PH_3^+ would result in X_{max} = 0.50.) The transformation observed thus involves equilibria (1) and (2) simultaneously. Since the points in Fig. 2 were obtained both by dilution of porphyrin with acid solution, and by dilution of acid with porphyrin solution, the system is reversible. Furthermore, the sharpness of the maxima and the invariance of X_{max} for measurements at different wave lengths mean that no intermediate substance PH_3^+ is formed. Stated another way, the two protons add simultaneously to PH_2, within the limits of error of the method.

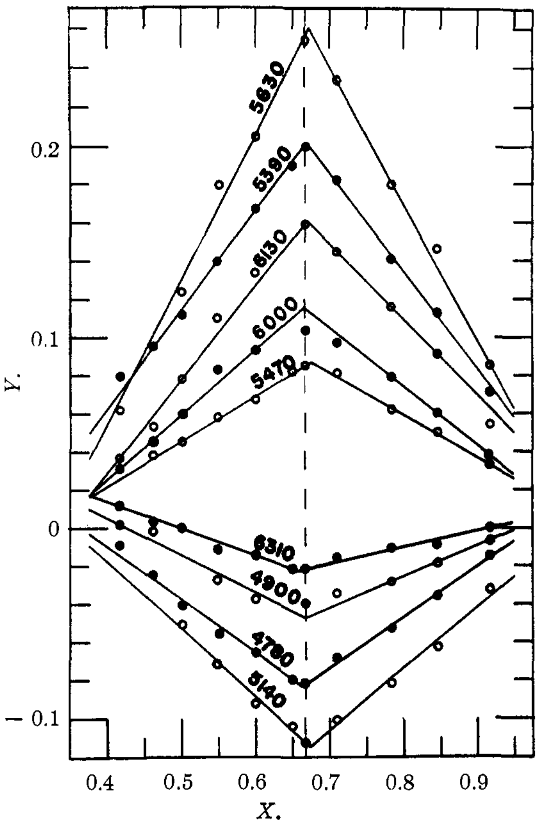

Fig. 2.—Application of the method of continuous variations: Y = observed optical density less that calculated for the porphyrin solution assuming no reaction with acid; X = volume fraction of acid in the mixture of porphyrin and acid solutions.

The Y values in Fig. 2 represent a small difference between two relatively large values of the optical density, so the scatter of the points, including those at the maxima, is within the experimental error of the measurements. Calculation of the minimum concentration at which PH_3^+ could be detected would require assignment of arbitrary values for the extinction coefficient of this substance in aqueous solution, and has not been attempted.

It would be desirable to confirm the result by analysis of the shape of the acid–base titration

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[7] R. I. Walter, *J. Biol. Chem.*, **196**, 151 (1952).

[8] W. C. Vosburgh and G. R. Cooper, THIS JOURNAL, **63**, 437 (1941).

curve for this substance, so attempts were made to determine the curve potentiometrically. However, the species PH_4^{++} is a sufficiently strong acid that the complete titration curve could not be observed in water, aqueous methanol, or aqueous dioxane. The anhydrous solvents could not be used because the LiCl required to maintain a constant high ionic strength for the accurate determination of curve shape was not sufficiently soluble in them.

Discussion

Although acid–base and oxidation–reduction systems have traditionally been considered from different viewpoints, the exact analogy in principle between the two classes has been discussed by various authors.[9,10] For both systems, the titration curves (potential or *p*H plotted against per cent. reaction) form a family in which the individual members can be identified by their midpoint slopes. Michaelis demonstrated the existence of this family of curves both experimentally and theoretically in his studies of the semiquinones.[11] He showed that the titration curves of lowest midpoint slope, for reactions in which two electrons are transferred simultaneously, are replaced by curves whose midpoint slope increases as conditions are chosen which increase the stability of the semiquinone intermediate in the reaction. The extreme case is the two-step titration curve (with very steep midpoint slope) observed for very stable semiquinone systems.

In the case of the dibasic acids, successive stages of proton transfer almost always occur with increasing difficulty because of the accompanying ionic charge accumulation. As a result, the intermediate stage of ionization is stable and reaches a maximum concentration exceeding 50% that of the total acid–base system at the titration midpoint, and $K_1 >> K_2$. Only in the limiting case of dibasic acids in which the functional groups are separated by long carbon chains do the protons dissociate independently. The intermediate then has the same stability as the completely ionized or completely un-ionized forms, and reaches a maximum concentration of 50% that of the total acid–base system at the midpoint of the titration.[6,10] The acid–base reactions given by equations (1) and (2) *cannot* be of this type, with $K_1 = 4K_2$, since the concentration of intermediate has been shown to be too small to detect, and certainly less than the 50% maximum expected in such a reaction. (If $K_1 = K_2$, as has been assumed previously for the porphyrins, the concentration of PH_3^+ would still reach a maximum equal to 33% that of the total acid–base system.) Thus the intermediate PH_3^+ is less stable than PH_4^{++} or PH_2, and in consequence the second proton is transferred more readily than the first. (The transfer is simultaneous if the concentration of PH_3^+ is zero.) In this case, $K_1 << K_2$, and the individual constants have little meaning. The significant constant is that for the overall reaction, equation (5), given by $K = K_1K_2$.

One previous example has been reported of proton transfer leading to an intermediate of lower stability, so that the second proton is transferred more readily than the first. Schwarzenbach[10] described a dibasic acid in which the maximum concentration of intermediate was only 22% at the titration midpoint, but his system was too unstable for complete reversibility.

Consideration of the oxidation–reduction analogy has led to the expectation that the intermediate PH_3^+ will be less stable than either PH_4^{++} or PH_2. This is confirmed by consideration of the structures which might reasonably contribute to resonance in the porphyrin system. Assuming fixed N–H bonds, two uncharged and four separated charge structures have been proposed for PH_2, and twelve with no charge separation for PH_4^{++}.[12] The number of such structures depends upon the twofold axis of symmetry in PH_2, and the fourfold axis in PH_4^{++}. Loss of these symmetry elements in PH_3^+ reduces the number of structures contributing to its resonance, and results in its relatively lower stability.

The argument can be repeated for the ionization of PH_2 to give $P^=$, and one would expect in this case also a smaller stability for PH^- than for the other species. (The very close similarity of the absorption spectra of PH_4^{++} and $P^=$ in the case of etioporphyrin[12] indicates that they must be similar electronically.) The ionization of PH_2 could not, however, be studied conveniently by the method of continuous variations, because the *pK* value reported by McEwen[5] would require that the solutions of both porphyrin and hydrogen ion be of the order of 10^{-16} *M* concentration, too low for spectrophotometric work.

Although variation of substituents on the porphyrin ring will alter the magnitude of the acid dissociation constants, their distribution would not be greatly changed. It thus seems probable that the simultaneous dissociation reported here is general for the porphyrin ring system (but not necessarily for reduced ring systems such as the chlorins).

[12] J. G. Erdman and A. H. Corwin, THIS JOURNAL, **68**, 1885 (1946).

CHEMISTRY DEPARTMENT
UNIVERSITY OF COLORADO
BOULDER, COLORADO

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[9] M. Schubert, *Ann. N. Y. Acad. Sci.*, **40**, 111 (1940).

[10] G. Schwarzenbach and R. Sulzberger, *Helv. Chim. Acta*, **26**, 453 (1943).

[11] L. Michaelis and M. P. Schubert, *Chem. Revs.*, **22**, 437 (1938).

Studies on Coördination Compounds. VIII. Some Factors Concerning the Effect of the Terminal Groups on the Chelating Abilities of β-Diketones

BY LEGRAND G. VAN UITERT[1] AND W. CONARD FERNELIUS

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The general relationships between the stability constants of the β-diketones and their terminal groups have been discussed in a previous paper.[2] Additional constants are given herein which enable a further clarification of the relationships involved to be made.

Experimental

The β-diketones, other than those mentioned previously,

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[1] Union Carbide and Carbon Corporation Fellow, 1951–1952; Bell Telephone Laboratories, Murray Hill, New Jersey.

[2] L. G. Van Uitert, W. C. Fernelius and B. E. Douglas, THIS JOURNAL, **75**, 457 (1953).

were prepared in this Laboratory by Mrs. Lillian Berg. The $NiCl_2$ and $Ce(ClO_4)_3$ employed were reagent grade.

The experimental procedures were those previously employed with the exception that the chelate compound formation constants for cerium were measured using 1×10^{-4} mole of $Ce(ClO_4)_3$ and 6×10^{-4} mole of chelating agent in 100 ml. of solution. Measurements were made in 75 volume per cent. dioxane–25 volume per cent. water (mole fraction of dioxane, n_2, = 0.380) at 30°.

Discussion

Previously it has been observed[2] that within certain groups of β-diketones there exists a linear relationship between the negative logarithms of the acid dissociation constants (pK_D values) of the β-diketones and their formation constants (log K_f values) with a given metal ion. These principal groups consist of a series of β-diketones with aromatic rings as terminal groups (containing combinations of the groups: 2-thienyl, 2-furyl and phenyl) and a series having one methyl group. The values plotted in Figs. 1 and 2 for Ni^{++} and Ce^{+++}, respectively, show that each of these groups may be subdivided.

The chelation constants for the β-diketones containing methyl groups with nickel(II), as shown in Fig. 1 (refer Table I), resolve into two subgroups; one consisting of those having one aromatic group and the other having the terminal group series: CH_3, C_2H_5, $CH(CH_3)_2$, $CH_2CH_2Si(CH_3)_3$ and $C(CH_3)_3$ where log $K_{f_{av}}$ and pK_D increase in that order. 2-Methyl-3,5-heptanedione falls on the latter line. Within the limits that the above series of β-diketones have equivalent keto–enol ratios (50% enol or better),[3] the observed inductive effects are in the order to be expected from the group electronegativities.[4]

TABLE I

CHELATION DATA FOR NICKEL(II) EMPLOYING 0.01 *M* $NiCl_2$ SOLUTION

Symbol in Fig. 1	Chelating agent	pK_D	log K_{f_1}	log K_{f_2}
⦶	2,4-Pentanedione	12.70	9.37	8.03
⊖	2,4-Hexanedione	13.20	9.60	8.30
⦸	2-Methyl-3,5-hexanedione	13.40	9.55	8.60
⊘	2,2-Dimethyl-2-sila-5,7-octanedione	13.50	9.65	8.70
●	2-Methyl-3,5-heptanedione	13.95	9.86	9.03
⊕	2,2-Dimethyl-3,5-hexanedione	14.20	9.94	9.19

◔2, ⊙3, ◒4, ◕6, ◓7, ◑8, ◐9 (see Table II).

TABLE II

CHELATION DATA FOR CERIUM(III) EMPLOYING 0.001 *M* $Ce(ClO_4)_3$ SOLUTION

No. in Fig. 2		pK_D	log K_{f_1}	log K_{f_2}	log K_{f_3}
1	Di-2-furoylmethane	12.10	10.61	9.59	7.87
2	2-Thenoyl-2-furoylmethane	12.30	10.60	9.81	8.17
3	2-Thenoylacetone	12.35	10.05	9.40	7.74
4	Di-2-thenoylmethane	12.63	10.65	10.20	8.87
5	2,4-Pentanedione	12.70	9.86	8.53	6.91
6	Benzoylacetone	12.85	10.09	9.33	7.62
7	2-Furoylbenzoylmethane	12.95	10.82	10.21	8.40
8	2-Thenoylbenzoylmethane	13.30	11.02	10.57	9.07
9	Dibenzoylmethane	13.75	10.99	10.54	8.85
10	2,2-Dimethyl-3,5-hexanedione	14.20	10.60	10.20	8.50

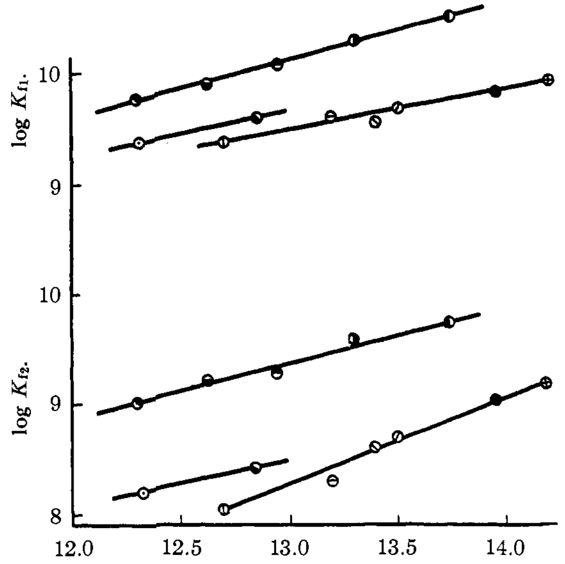

Fig. 1.—Nickel(II) chelation constants *vs.* β-diketone pK_d values. (See Table I).

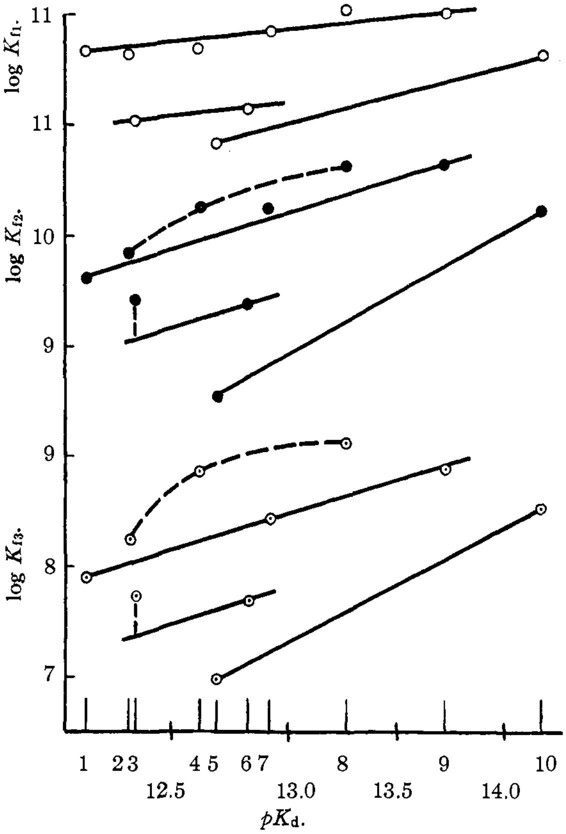

Fig. 2.—Cerium(III) chelation constants *vs.* β-diketone pK_d values. Numbers refer to compounds listed in Table II: O, first constant; ●, second constant; ⊙, third constant.

Data for the points in Fig. 1 that are not given in Table I have been given previously.[2] However,

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[3] L. G. Van Uitert, with C. G. Haas, Jr., W. C. Fernelius and B. E. Douglas, THIS JOURNAL, **75**, 455 (1953).

[4] D. Walsh, *J. Chem. Soc.*, 401 (1948).

the β-diketones employed in obtaining the previous data have been used again in obtaining the data for Ce(III) given in Table II. So, for convenience of comparison of the points in Fig. 1, the symbols for the points representing the previously reported data are given at the bottom of Table I along with the Table II guide numbers for the β-diketones involved.

In Fig. 2, it is seen that there is essentially a linear relationship between pK_{D} and log K_{f_1}, the first chelate compound formation constant, for the series of β-diketones containing two aromatic rings with cerium(III). However, upon the addition of a second chelating group to cerium(III), those β-diketones which contain a thienyl group have slightly higher stability constants than would be expected from the positions of the other β-diketones. The same relationship, but of greater magnitude, is noted for the third constants. Since the effect is most pronounced for the third constants, in which case the cerium is probably surrounded by the six oxygen atoms of the three attached β-diketones in an octahedral fashion, it would appear that the close proximity of the bulky sulfur atoms to the central metal ion aids in shielding the coördination centers from interaction with the solvent.

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THE SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNSYLVANIA

COMMUNICATIONS TO THE EDITOR

ACHROMYCIN.[1] SYNTHETIC STUDIES. III. SYNTHESIS OF 3-AMINO-D-RIBOSE, A HYDROLYTIC PRODUCT

Sir:

One of the hydrolysis products of Achromycin is a 3-aminopentose, either 3-aminoribose or 3-aminoxylose. This is the first known 3-amino sugar and first known aminopentose to exist in a natural source.[2] The structure has now been proven to be 3-amino-D-ribose by synthesis from L-arabinose via β-methyl 2,3-anhydro-L-ribopyranoside (I).[3]

Treatment of I with ammonium hydroxide at 100° under pressure afforded a 65% yield of β-methyl-3-amino-L-xylopyranoside, m.p. 191–192° dec., $[\alpha]^{34}\mathrm{D}$ +61.4° (1% in H_2O). *Anal.* Calcd. for $C_6H_{13}NO_4$: C, 44.2; H, 8.03; N, 8.60. Found: C, 44.2; H, 8.07; N, 8.93. Acetylation with aqueous acetic anhydride formed 98% of β-methyl 3-acetamino-L-xylopyranoside (II), m.p. 194–195°, $[\alpha]^{24}\mathrm{D}$ +64.4° (2% in H_2O). *Anal.* Calcd. for $C_8H_{15}NO_5$: C, 46.8; H, 7.36; N, 6.83. Found: C, 46.4; H, 7.53; N, 6.74. Since II failed to consume periodate, the alternate structure, β-methyl-2-amino-L-arabinopyranoside, which could be formed on ring opening of I, was eliminated.[4]

When II was treated with methanesulfonyl chloride in pyridine, an 83% yield of β-methyl-2,5-dimesyl-3-acetamino-L-xylopyranoside (III), m.p. 150°, $[\alpha]^{24}\mathrm{D}$ +18.8° (2% in pyridine), was obtained. *Anal.* Calcd. for $C_{10}H_{19}NO_9S_2$: C, 33.2; H, 5.30; N, 3.88. Found: C, 33.7; H, 5.43; N, 4.06. Reaction of III with sodium acetate in boiling 95% alcohol caused elimination of one mesyl group with inversion via an oxazoline.[5] Work-up by acetylation gave a 66% yield of β-methyl 2-acetyl-3-acetamino-4-mesyl-L-lyxopyranoside, m.p. 171–172°, $[\alpha]^{24}\mathrm{D}$ −11.0° (1.4% in pyridine). *Anal.* Calcd. for $C_{11}H_{19}NO_8S$: C, 40.6; H, 5.89; N, 4.31. Found: C, 40.9; H, 5.78; N, 4.22. Further treatment with sodium acetate in 95% boiling Methyl Cellosolve eliminated the second mesyl group with inversion to an all *cis*-configuration. Acetylation then afforded 70% of α-methyl-2,4-diacetyl-3-acetamino-D-ribopyranoside, IV, m.p. 116–117°, $[\alpha]^{24}\mathrm{D}$ +93.7° (1.6% in $CHCl_3$). *Anal.* Calcd. for $C_{12}H_{19}NO_7$: C, 49.8; H, 6.62; N, 4.85. Found: C, 49.8; H, 6.84; N, 4.73. Direct treatment of III with sodium acetate in 95% Methyl Cellosolve caused elimination of both mesyl groups with inversion. Acetylation afforded 70% yield of IV. Hydrolysis of IV with boiling 1% hydrochloric acid gave 83% of 3-amino-D-ribose hydrochloride, m.p. 160° dec., $[\alpha]\mathrm{D}$ −25.0° (2% in H_2O). *Anal.* Calcd. for $C_5H_{11}NO_4\cdot HCl$: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.6; H, 6.82; N, 7.79. Comparative I.R. spectra showed this compound to be identical with the 3-aminopentose obtained on hydrolysis of Achromycin.[2]

It is interesting to note that this synthesis proceeds through all four pentose configurations. Derivatives of 3-amino-D-allose also have been

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(1) Achromycin is the American Cyanamid Co. trademark for the antibiotic, Puromycin.

(2) C. W. Waller, P. W. Fryth, B. L. Hutchings and J. H. Williams, THIS JOURNAL, **75**, 2025 (1953).

(3) S. Mukherjee and A. R. Todd, *J. Chem. Soc.*, 971 (1947).

(4) It should be noted that a *trans* configuration of amine and hydroxyl is obtained by Walden inversion. Opening of the oxide ring of α-methyl-2,3-anhydro-4,6-benzylidene-D-mannopyranoside with ammonia has been shown by W. H. Myers and G. J. Robertson [THIS JOURNAL, **65**, 8 (1943)] to give α-methyl-3-amino-4,6-benzylidene-D-altropyranoside and α-methyl-2-amino-4,6-benzylidene-D-glucopyranoside.

(5) Although this is the first known example of this reaction in the carbohydrate field, the reaction has been described with *trans*-acetaminocyclohexanol-2-tosylate by G. E. McCasland, R. K. Clark and H. E. Carter in THIS JOURNAL, **71**, 641 (1949).