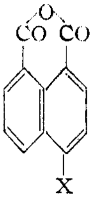
NOTES

A New Synthesis of Acenaphthene

By Ernst D. Bergmann and Jacob Szmuszkovicz

Received December 15, 1952

Reaction of bis-(2,2'-bromomethyl)-biphenyl with lithium phenyl gives 9,10-dihydrophenanthrene.[1] It seemed interesting to investigate whether, analogously, a five-membered ring could be fused to the naphthalene system by the reaction of 1,8-bis-(bromomethyl)-naphthalene (III, X = H) with lithium phenyl. This paper describes the synthesis of acenaphthene (IV, X = H) and 5-bromoacenaphthene (IV, X = Br) by this method.



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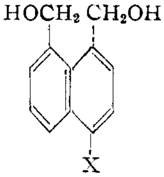

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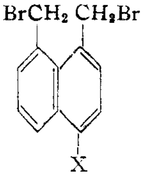
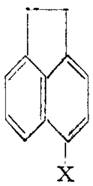


III



IV

Dimethyl naphthalate, prepared from naphthalic anhydride (I, X = H), was reduced to (II, X = H) by means of lithium aluminum hydride (yield, 98%) and the dialcohol (II, X = H) converted into the corresponding dibromide (III, X = H). Reaction with lithium phenyl gave acenaphthene (IV, X = H) in an over-all yield of 53% (calculated on dimethyl naphthalate). The hydrocarbon was identified by mixed m.p. and by its picrate. The dialcohol has recently[2] been obtained analogously from naphthalic anhydride, but only in 61% yield.

The same sequence of reactions was applied to 4-bromonaphthalic anhydride (I, X = Br), which is obtained by bromination of I (X = H).[3] The over-all yield of (IV, X = Br) was 41% (calculated on dimethyl 4-bromonaphthalate).

This synthesis of the acenaphthene system from an 1,8-disubstituted naphthalene recalls the preparation of the hydrocarbon from 1,8-malonylnaphthalene by successive treatment with alkaline permanganate and phosphorus and hydriodic acid[4] and from naphthalene with the phenylimidochloride of oxalic acid in the presence of aluminum chloride.[5]

Experimental

Dimethyl Naphthalate.—Naphthalic anhydride was dissolved in hot alkali, the solution filtered and acidified. The resulting acid was dried in air and esterified with diazomethane. The dimethyl ester was purified by recrystallization from methanol, m.p. 100°.[6]

1,8-Bis-(hydroxymethyl)-naphthalene (II, X = H).—The above dimethyl ester (2.6 g.) dissolved in a mixture of 100 ml. of ether and 50 ml. of benzene was added to a solution of 2 g. of lithium aluminum hydride in 200 ml. of ether. The mixture was refluxed for 1.5 hours, then decomposed with ice and dilute sulfuric acid. Part of the product crystallized spontaneously; the balance was obtained by evaporation of the organic solvent. Recrystallization from water afforded elongated needles, m.p. 153.5–155.5° (lit.[2] 158°), yield 1.9 g. (95%).

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.6; H, 6.4. Found: C, 76.8; H, 6.6.

1,8-Bis-(bromomethyl)-naphthalene (III, X = H).—The dialcohol (1.6 g.) was dissolved in 300 ml. of boiling benzene, which contained a few drops of pyridine. The solution was cooled to about 70°, treated dropwise with 4.8 g. of phosphorus tribromide, and then kept at 55° for 2 hours. After cooling, it was washed with water, bicarbonate solution and water and dried over anhydrous sodium sulfate. Evaporation of the solvent and recrystallization of the residue from benzene–petroleum ether afforded prisms, m.p. 129–131° (2.2 g., 81.4%). Further recrystallization from the same solvent mixture raised the m.p. to 130–131.5°.

Anal. Calcd. for $C_{12}H_{10}Br_2$: Br, 51.0. Found: Br, 50.8, 51.2.

Acenaphthene (IV, X = H).—Eleven ml. of a solution of lithium phenyl prepared as described previously[1e] was added dropwise during ten minutes in an atmosphere of nitrogen and at room temperature to a solution of 1.9 g. of (III, X = H) in 25 ml. of benzene. The product was stirred for one-half hour at room temperature, refluxed for one hour, and worked up as usual. The residue, upon recrystallization from a small amount of benzene, formed elongated needles, m.p. 92–93°. The benzene filtrate was diluted with petroleum ether, filtered from some amorphous impurity and evaporated, and the residue recrystallized from ethanol, m.p. 92–93°; total yield 0.65 g. (69%), mixed m.p. with pure acenaphthene (m.p. 93.4°) 92–94°. **The picrate** of the above product melted at 160–161.5°; its mixed m.p. with an authentic sample of acenaphthene picrate (m.p. 161–162.5°) showed no depression.

Dimethyl 4-Bromonaphthalate.—Naphthalic anhydride was brominated according to Rule and Thompson.[3] The 4-bromo derivative (I, X = Br) melted at 214–216° after recrystallization from nitrobenzene, acetic anhydride and again nitrobenzene; it was dissolved in dilute alkali, filtered, precipitated with acid in the cold and dried in air. Esterification of the methanolic suspension of the acid thus obtained with an excess of ethereal diazomethane afforded the dimethyl ester, which was recrystallized twice from methanol (charcoal) and melted at 109.5–110.5°.

Anal. Calcd. for $C_{14}H_{11}O_4Br$: C, 52.0; H, 3.4. Found: C, 52.0; H, 3.4.

4-Bromo-1,8-bis-(hydroxymethyl)-naphthalene (II, X = Br).—A solution of 2.43 g. of the dimethyl ester in a mixture of 25 cc. of benzene and 25 cc. of ether was added to 2 g. of lithium aluminum hydride dissolved in 120 cc. of ether. The product was refluxed for one hour, kept overnight at room temperature and decomposed with 100 cc. of 25% sulfuric acid. Part of the dialcohol separated spontaneously, the remainder was obtained by evaporation of the organic layer. Recrystallization from dilute methyl alcohol gave material melting at 145–150°. One further recrystallization raised the melting point to 162–163.5° which remained unchanged on further treatment.

Anal. Calcd. for $C_{12}H_{11}O_2Br$: C, 54.0; H, 4.2. Found: C, 53.9; H, 4.4.

4-Bromo-1,8-bis-(bromomethyl)-naphthalene (III, X = Br).—The dialcohol (2 g.) was dissolved in 200 ml. of boiling benzene, and the solution treated at about 70° dropwise with 4.5 g. of phosphorus tribromide. The solution was heated at 55° for two hours, cooled to room temperature, washed with water, bicarbonate solution and water, and evaporated. The residue (m.p. 113–115.5°) was recrys-

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[1] (a) D. M. Hall and E. E. Turner, *Nature*, **163**, 537 (1949); (b) D. M. Hall, M. S. Lesslie and E. E. Turner, *J. Chem. Soc.*, 711 (1950); (c) D. M. Hall and E. E. Turner, *ibid.*, 3072 (1951); *cf.* (d) E. D. Bergmann and Z. Pelchovitz, This Journal, **75**, 2663 (1953); (e) E. D. Bergmann and J. Szmuszkovicz, *ibid.*, **73**, 5153 (1951).

[2] R. E. Beyler and L. H. Sarett, *ibid.*, **74**, 1406 (1952).

[3] H. G. Rule and S. B. Thompson, *J. Chem. Soc.*, 1764 (1937).

[4] G. Errera and A. Cuffaro, *Gazz. chim. ital.*, **41**, II, 807 (1911); G. Errera and G. Ajon, *ibid.*, **44**, II, 92 (1914).

[5] H. Staudinger, H. Goldstein and E. Schlenker, *Helv. Chim. Acta*, **4**, 342 (1921).

[6] *Cf.* F. A. Mason, *J. Chem. Soc.*, **125**, 2116 (1924).

tallized twice from benzene–petroleum ether, and once from petroleum ether alone, m.p. 117.5–119° (yield 75%).

Anal. Calcd. for $C_{12}H_9Br_3$: Br, 61.1. Found: Br, 60.1.

5-Bromoacenaphthene (**IV**, **X** = **Br**).—The cyclization of the dibromide (III, X = Br) was carried out as before, and the crude product dissolved in a mixture of methanol and ethanol. On scratching, a small amount of material, m.p. 90–102°, was obtained which was not investigated any further. The filtrate, upon concentration, left an oil which gave a very soluble picrate,[7] but afforded a very well-crystallized **trinitrobenzene complex**, m.p. 141–144° and after recrystallization from alcohol (elongated yellow rods) 144–146° (yield 55%).

Anal. Calcd. for $C_{18}H_{12}N_3O_6Br$: N, 9.4. Found: N, 9.3.

The TNB complex was decomposed by adsorption of its benzene solution on alumina and elution with ethanol. Evaporation and recrystallization from methanol gave 5-bromoacenaphthene in plates, m.p. 53–54° (literature[8] 52–53°).

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(7) The picrate, m.p. 114°, has been described by H. Crompton and M. Walker, *J. Chem. Soc.*, **101**, 958 (1912).

(8) M. Blumenthal, *Ber.*, **7**, 1092 (1874).

SCIENTIFIC DEPARTMENT
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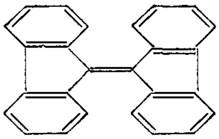
Highly Polarizable C═C Double Bonds (Fulvenes and Thermochromic Ethylenes. Part 28)[1]

BY ERNST D. BERGMANN

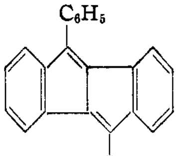
RECEIVED JANUARY 7, 1953

Whilst the addition reactions of fulvenes with reagents typical for polar double bonds (metal-organic compounds,[2,3] lithium aluminum hydride,[4] donors in the Michael reaction,[5] can be explained by the polar character of the semicyclic double bond,[6,7] the analogous behavior of so symmetrical a substance as dibiphenylenethylene (I),[7,8] is very surprising. Bergmann, Fischer and Jaffe[9] and Lavie and Bergmann[1] have suggested that the "polar reactions" of I are due to the high *polarizability* of the central double bond. Indeed, the molecular refraction of I, which is a measure of the polarizability of the molecule, is unusually large, even in the infrared.[10,11] If this hypothesis is correct, other hydrocarbons which show the same phenomenon of an abnormally large molecular refraction, should be capable of reactions similar to I. This has been found to be true for tetraphenyl-*p*-quinodimethane (II) (*MR*, calcd., 138; *MR* found, 182 ± 4[12]), and diphenyldiphensuccindadiene (III) (for the corresponding dimethyl compound: *MR*, calcd., 75.5; *MR*, found, 86.5 ± 0.8[9,13]). *Both hydrocarbons add lithium aluminum hydride.* With this reagent, II gives in N-methylmorpholine as solvent a colored addition product, which, by hydrolysis, is converted into *p*-dibenzhydrylbenzene (IV). Analogously, III is transformed into diphenylsuccindene (V).

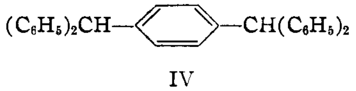


I

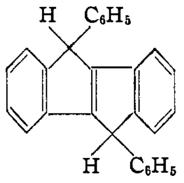
II



III



IV



V

The spectrum of V (Fig. 1) shows a maximum (3225 Å., log ε 4.20) similar to that of the unsubstituted diphensuccindene (3100 Å., log ε 4.56[14]); a second maximum lies at 2400 Å. (log ε 4.25).

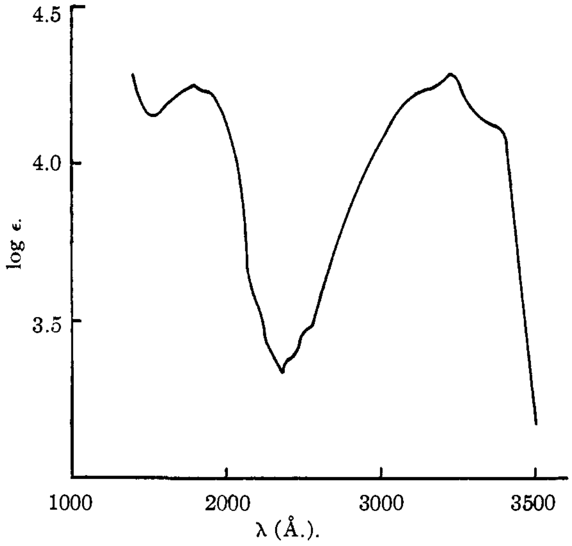


Fig. 1.—Diphenylsuccindene (V) in alcohol.

Experimental

Tetraphenyl-*p*-quinodimethane (**II**) was prepared according to Staudinger[15] (from xylene, m.p. 268°), **diphenyldiphensuccindadiene** (III) according to Brand[16] (from amyl alcohol, m.p. 260°).

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(1) Part 27, D. Lavie and E. Bergmann, *J. Org. Chem.*, **18**, in press (1953).

(2) K. Ziegler and W. Schaefer, *Ann.*, **511**, 101 (1934).

(3) R. C. Fuson and H. D. Porter, THIS JOURNAL, **70**, 895 (1948).

(4) D. Lavie and E. Bergmann, *Bull. soc. chim. France*, **18**, 250 (1951).

(5) L. A. Pinck and G. E. Hilbert, THIS JOURNAL, **68**, 2014, 2739 (1946).

(6) A. Pullman, G. Berthier and B. Pullman, *Bull. soc. chim. France*, **17**, 1097 (1950).

(7) B. Pullman and A. Pullman, "Les Theories Electroniques de la Chimie Organique," Masson et Cie, Paris, 1952, p. 333 ff.

(8) E. Bergmann, G. Berthier, A. Pullman and B. Pullman, *Bull. soc. chim. France*, **17**, 1079 (1950).

(9) E. Bergmann, E. Fischer and J. Jaffe, THIS JOURNAL, **75**, in press (1953).

(10) E. Bergmann and E. Fischer, *Bull. Israeli Research Council*, **1**, No. 4, 84 (1952).

(11) E. Bergmann and E. Fischer, *Bull. soc. chim. France*, **19**, 712 (1952).

(12) B. Pullman, A. Pullman, E. Bergmann, G. Berthier, E. Fischer, D. Ginsburg and Y. Hirshberg, *ibid.*, **18**, 707 (1951).

(13) B. Pullman, A. Pullman, E. Bergmann, G. Berthier, E. Fischer, Y. Hirshberg and J. Pontis, *J. chim. phys.*, **49**, 24 (1952).

(14) L. F. Fieser and M. U. Pechet, THIS JOURNAL, **68**, 2577 (1946).

(15) H. Staudinger, *Ber.*, **41**, 1355 (1908); H. Staudinger and S. Bereza, *Ann.*, **380**, 276 (1911).

(16) K. Brand, *Ber.*, **45**, 3071 (1912).

p-**Dibenzhydrylbenzene (IV).**—Finely powdered II (0.8 g.) was added to a solution of lithium aluminum hydride (1.0 g.) in N-methylmorpholine (50 ml.),[17] and the mixture refluxed for one hour. It was then poured into ice-cold dilute sulfuric acid and the reaction product extracted with ether. The crystalline residue of the extract was recrystallized from glacial acetic acid and formed needles of m.p. 171° (literature[18] 172°).

Anal. Calcd. for $C_{32}H_{26}$: C, 93.7; H, 6.3; mol. wt., 410. Found: C, 93.3; H, 6.3; mol. wt., 423.

Diphenyldiphensuccindene (V).—In the manner described, 0.8 g. of III was reduced with 1 g. of lithium aluminum hydride in 50 ml. of N-methylmorpholine and the reaction product isolated as above. It crystallized from methyl isobutyl ketone in prisms of m.p. 286° (literature[19] 285–286°). The same product is obtained when III is reduced with zinc dust and acetic acid.[19]

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(17) For the use of N-alkylmorpholines in reactions of this type, see F. A. Hochstein, THIS JOURNAL, **71**, 305 (1949).

(18) F. Ullmann and C. Schlaepfer, *Ber.*, **37**, 2001 (1904).

(19) K. Brand and W. Muehl, *J. prakt. Chem.*, [2] **110**, 1 (1925).

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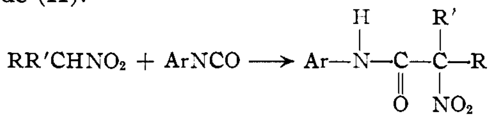
The Reactions of Aliphatic Nitro Compounds: Condensations with Isocyanates[1]

BY ROBERT NEILSON BOYD AND RICHARD LESHIN[2]

RECEIVED FEBRUARY 11, 1953

The reaction between the sodium salt of nitromethane and phenyl isocyanate has been found[3,4] to give ω(or α-)-nitroacetanilide (I) and nitromalonanilide (II).



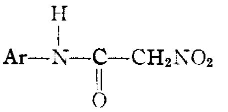
$$RR'CHNO_2 + ArNCO \longrightarrow Ar{-}N(H){-}C(=O){-}C(R')(NO_2){-}R$$

I, Ar = C_6H_5, R = H, R' = H
II, Ar = C_6H_5, R = H, R' = C_6H_5NHCO
III, Ar = C_6H_5, R = H, R' = COOEt
IV, Ar = *p*-$NO_2C_6H_4$, R = H, R' = COOEt

This reaction has now been extended to include the reaction of nitromethane and ethyl nitroacetate with 1-naphthyl, *o*-chlorophenyl and *o*-tolyl isocyanates to give a series of new N-substituted α-nitroacetamides and α-carbethoxy-α-nitroacetamides (Tables I and II).

TABLE I

N-ARYL α-NITROACETAMIDES



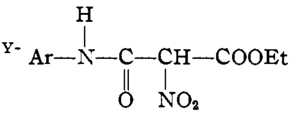
$$Ar{-}N(H){-}C(=O){-}CH_2NO_2$$

Aryl group	M.p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
Phenyl	138[a]	$C_8H_8O_3N_2$	15.55	15.28
1-Naphthyl[b]	159–160[c]	$C_{12}H_{10}O_3N_2$	12.17	11.58
o-Chlorophenyl	121–122[d]	$C_8H_7O_3N_2Cl$	13.06	12.83
o-Tolyl	133[e]	$C_9H_{10}O_3N_2$	14.43	14.28

[a] Found by Michael and Steinkopf (ref. 3, 4). [b] Calcd.: C, 62.60; H, 4.38. Found: C, 62.33; H, 4.58. [c] Recrystallized from water or toluene; white plates which retain static electricity. [d] Recrystallized from water; yellow crystals. [e] Recrystallized from benzene; white needles.

TABLE II

N-ARYL α-CARBETHOXY-α-NITROACETAMIDES



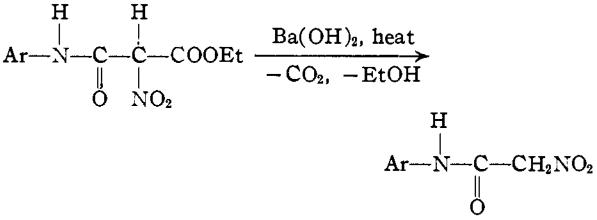
$$Ar{-}N(H){-}C(=O){-}CH(NO_2){-}COOEt$$

Aryl group	M.p., °C.	Yield, %	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
Phenyl[a]	100–101[b]	31	$C_{11}H_{12}O_5N_2$	11.11	11.37
1-Naphthyl[c]	124–125[d]	21	$C_{15}H_{14}O_5N_2$	9.27	9.42
o-Chlorophenyl	88[e]	55	$C_{11}H_{11}O_5N_2Cl$	9.77	10.11
o-Tolyl	86–88[f]	32	$C_{12}H_{14}O_5N_2$	10.52	10.63
p-Nitrophenyl	130–131.5[g]	12	$C_{11}H_{11}O_7N_3$	14.14	13.75

[a] Calcd.: C, 52.38; H, 4.80. Found: C, 52.68; H, 4.73. [b] Recrystallized from benzene–cyclohexane; white, curdy solid. [c] Calcd.: C, 59.60; H, 4.67. Found: C, 59.60; H, 4.45. [d] Recrystallized from benzene–cyclohexane; peach-colored needles. [e] Recrystallized from cyclohexane; white, curdy solid. [f] Recrystallized from benzene–cyclohexane; white, curdy solid. [g] Recrystallized from benzene; pale yellow needles.

It was not always found necessary to isolate the dangerously explosive sodium salt of nitromethane in order to effect a condensation; nitromethane could be condensed with phenyl and 1-naphthyl isocyanates in the presence of an equimolecular quantity of anhydrous potassium carbonate. The same base catalyzed all the condensations of ethyl nitroacetate.

Three compounds, III, V and VI were hydrolyzed and decarboxylated by hot barium hydroxide solution to give the corresponding N-substituted α-nitroacetamides (IIIa, Va, VIa).



$$Ar{-}N(H){-}C(=O){-}CH(NO_2){-}COOEt \xrightarrow[-CO_2,\ -EtOH]{Ba(OH)_2,\ heat} Ar{-}N(H){-}C(=O){-}CH_2NO_2$$

III, Ar = C_6H_5 IIIa, Ar = C_6H_5
V, Ar = *o*-ClC_6H_4 Va, Ar = *o*-ClC_6H_4
VI, Ar = *o*-$CH_3C_6H_4$ VIa, Ar = *o*-$CH_3C_6H_4$

Nitroethane,[3,4] 1- and 2-nitropropane, phenylnitromethane, ethyl nitromalonate, nitromalonamide and bromonitromethane could not be condensed with phenyl isocyanate, either in the presence of potassium carbonate or when used in the form of their salts.

Experimental

N-Substituted α-Carbethoxy-α-nitroacetamides.—A typical preparation is that of N-phenyl-α-carbethoxy-α-nitroacetamide (III).

A mixture of 4.4 g. (0.033 mole) of ethyl nitroacetate, 40 ml. of dry benzene, 4.6 g. (0.033 mole) of anhydrous potassium carbonate and 4.0 g. (0.033 mole) of phenyl isocyanate was refluxed for three hours (or allowed to stand at room temperature for 2 weeks), during which time it was protected from moisture by a calcium chloride tube. The reaction mixture was cooled, and the precipitated material was collected, and then thoroughly stirred with 200 ml. of ice-water. The water-insoluble carbanilide (m.p. 238°) was removed and the aqueous filtrate was chilled and acidified to congo red, with constant stirring. The solution became opaque and after a short while a yellow-white precipitate appeared. The precipitate was collected after stirring an additional half hour, and was washed with cold water and dried in air. One recrystallization from benzene-cyclohexane gave 2.6 g. (31% yield) of a curdy, colorless solid (m.p. 100–101°).

N-Substituted α-Nitroacetamides.—N-Phenyl-α-nitroacetamide (I, α-nitroacetanilide) and N-(1-naphthyl)-α-

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(1) Presented at the 121st Meeting of the American Chemical Society at Buffalo, N. Y., March 25, 1952.

(2) Based on a portion of the dissertation submitted by Richard Leshin to the Department of Chemistry, New York University, February, 1952, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) A. Michael, *Ber.*, **38**, 22, 39 (1905).

(4) W. Steinkopf and H. M. Daege, *ibid.*, **44**, 497 (1911).

nitroacetamide were prepared in the manner described above for the derivatives of ethyl nitroacetate. It was necessary, however, to use the sodium salt of nitromethane in the preparation of the other two compounds in Table I. A typical preparation is that of N-(*o*-chlorophenyl)-α-nitroacetamide (V).

To a solution of 2.2 g. (0.036 mole) of nitromethane in 35 ml. of dry benzene, protected from moisture by a calcium chloride tube, was added 0.7 g. (0.030 mole) of sodium wire. After all the sodium had reacted, the benzene was decanted from the precipitated salt, which was then washed with several portions of dry benzene, and finally suspended in 35 ml. of dry benzene. To this suspension was added 5.0 g. (0.032 mole) of *o*-chlorophenyl isocyanate. The mixture was refluxed (the condenser was protected by a calcium chloride tube) for 2 hours, after which the solid reaction product was filtered off and washed with benzene. The solid was then added, portionwise, to 200 g. of crushed ice; an insoluble residue of 2,2′-dichlorocarbanilide (m.p. 238°)[5] was filtered off, and the aqueous solution was acidified to congo red. A yellow precipitate appeared, and after stirring for an additional half hour the product was filtered off, recrystallized once from water, and obtained as a yellow solid, m.p. 121–122°, in less than 10% yield.

Hydrolysis and Decarboxylation.—About 0.5 g. of the compound obtained by the reaction of ethyl nitroacetate with an isocyanate (except *p*-nitrophenyl isocyanate) was suspended in a large excess of a filtered saturated solution of barium hydroxide, and the mixture was boiled for about 5 minutes. After cooling, the mixture was acidified to congo red, and the solid residue was filtered off and recrystallized from water. In each case, the m.p. of the product was found to be the same as that of the corresponding compound prepared directly from nitromethane; furthermore, no depression of the m.p. was observed in any case for a mixture of a hydrolyzed and decarboxylated product with the corresponding direct condensation product.

Acknowledgments.—The nitroalkanes were a gift of Commercial Solvents Corporation. The analyses were done in the Microchemical Laboratory of New York University by Dr. W. C. Woodland and Professor T. S. Ma who supervised the laboratory, and their assistants, Dr. H. J. Stolten, Dr. R. H. Hansen, Mr. J. D. McKinley, Jr., and Mr. Paul Pemsler.

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(5) C. Manuelli and B. Ricca-Rosellini, *Gazz. chim. ital.*, **29**, Part II, 128 (1899).

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Optical Dispersion of Perdeuterobenzene and Perdeuterocyclohexane

BY RAYMOND T. DAVIS, JR.,* AND ROBERT W. SCHIESSLER

RECEIVED JANUARY 28, 1953

In the course of some investigations being carried out in this Laboratory[1] on the physical properties of perdeuterobenzene and perdeuterocyclohexane the index of refraction of these compounds has been measured at three different wave lengths of light. It is the purpose of this note to record these index values and the various dispersion constants calculated from them.

The measurements were made with a Bausch and Lomb, Precision Abbe-type refractometer. The temperature of the prisms was maintained at 25.00 ± 0.02°. A sodium vapor light provided the light of wave length 5892.6 Å. (intensity-weighted mean of the doublet D_1,D_2). A mercury vapor lamp together with suitable filters provided the light of wave lengths 5460.7 and 4358.3 Å. The index of refraction of samples of N.B.S. Standard samples of 2,2,4-trimethylpentane and toluene, and of a purified sample of benzene, whose index had been previously checked against an NBS sample, was measured at each of the above wave lengths. Precautions were taken to ensure the purity of the samples, and in all cases the measurements were made on the samples immediately after their removal from sealed glass ampoules. From a comparison of the measured index values at each of the three wave lengths, with the certified values of their indices as reported by the National Bureau of Standards and tabulated by Forziati,[2] suitable instrument corrections were obtained. The instrument corrections were assumed to be a linear function of the refractive index reading, and did not appear to be a function of the wave length of the light used in the measurement. Correction values obtained on this basis were applied to the data reported here. The preparation of these deuterocarbons and their n_D values at 20° and 30° have been reported by Dixon and Schiessler.[3] Linear interpolations at 25° from their reported values are in excellent agreement with the values reported here. Table I lists the data for the deuterocarbons together with the data for the hydrocarbon isomers.

TABLE I

Wave length, Å.	Index of refraction at 25° C_6H_6[3]	C_6D_6[a]	C_6H_{12}	C_6D_{12}[b]
5892.6	1.49792	1.49597	1.42361	1.41909
5460.7	1.50197	1.49998	1.42544	1.42082
4358.3	1.51964	1.51798	1.43304	1.42802

[a] The purity of the C_6D_6 sample was equal to 99.3% replacement of protium with deuterium. Linear extrapolation of the measured value to 100.0% deuteration decreases the measured index by about 0.00001 which is less than the estimated uncertainty in the measurement. [b] The purity of the C_6D_{12} sample was equal to 98.8% deuteration. Linear extrapolation of the measured values to 100.0% purity decreases the measured index by about 0.00005 which is about the same as the estimated uncertainty in the measurement.

Forziati[2] has shown that the optical dispersion of organic compounds can be represented accurately by the modified Hartmann dispersion formula

$$n_\lambda = n_\infty + \frac{C}{(\lambda - \lambda^*)^{1.6}} \qquad (1)$$

where n_λ is the refractive index at light of wave length λ, and C, λ^*, and n_∞ are constants. The constants of this equation have been evaluated (after the construction of suitable tables for the wave lengths involved) by the method described by Forziati,[2] and are tabulated in Table II. Since the characteristic frequency ν_0 in the simplified Sellmeier–Drude[4–6] dispersion equation

$$n^2 - 1 = C/(\nu_0^2 - \nu_1^2) \qquad (2)$$

may be useful in the evaluation of the "London Dispersion Forces,"[7] the constants of this equation have been evaluated by the method of least squares and also are tabulated in Table II.

From equation 2 a value of the refractive index at infinite wave length may be calculated and this is also listed in Table II for comparison with the η_∞ calculated from the Hartmann equation.

Values of the Hartmann equation dispersion constants reported here for benzene are in good agree-

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* Department of Chemistry, Juniata College, Huntingdon, Pa.

(1) American Petroleum Institute Project 42. Advisory Committee: H. Sutherland, Chairman, E. M. Barber, J. R. Bates, L. C. Beard, Jr., G. H. Denison, L. M. Henderson, R. F. Marschner, L. A. Mikeska and J. H. Ramser.

(2) A. F. Forziati, *J. Research Natl. Bur. Standards*, **44**, 373 (1950).

(3) J. A. Dixon and R. W. Schiessler, THIS JOURNAL, **75**, in press (1953).

(4) W. Sellmeier, *Pogg. Ann.*, **143**, 272 (1871); **145**, 399, 520 (1872); **147**, 389 (1872).

(5) P. Drude, *Ann. Phys.*, **14**, 677 (1904).

(6) S. S. Kurtz and A. L. Ward, *J. Franklin Inst.*, **222**, 563 (1936); **224**, 583, 697 (1937).

(7) F. London, *Z. physik. Chem.*, **B11**, 222 (1930).

TABLE II

DISPERSION EQUATION CONSTANTS AT 25°

		C_6H_6	C_6D_6	C_6H_{12}	C_6D_{12}
Eq. 1	λ^*, μ	0.12929	0.14981	0.09418	0.09594
	$C \times 10^{+3}$	6.858	5.978	3.779	3.538
	n_∞	1.47417	1.47369	1.41197	1.40813
	$\nu_0 + 10^{-15}$	2.18632	2.10355	2.91743	2.97928
Eq. 2	$C \times 10^{-30}$	5.629058	5.155144	8.471202	8.733591
	η_∞	1.47568	1.47140	1.41254	1.40853

ment with the values given by Forziati[2] even though the values calculated in this research are from measurements made at a combination of wave lengths which are different than those used in the calculations by Forziati. The Hartmann equation reproduces the data with an error of about ±0.00002 refractive index unit. The Sellmeier–Drude equation reproduces the data with an error of about ±0.0004 refractive unit.

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Cellulose Sheets as Chromatographic Supports[1,2]

BY L. S. CUENDET, R. MONTGOMERY AND F. SMITH

RECEIVED FEBRUARY 11, 1953

During our studies of the various techniques of partition chromatographic analysis[3-7] we have made extensive use of filter papers (*e.g.*, Whatman No. 3)[8] for the separation of relatively large amounts of mixtures of sugars containing mono-, di-, tri- and tetrasaccharides but they have a limited loading capacity.[9,10]

In an extension of this work it has been found that limited use can be made of cellulose sheets,[11] approximately one-eighth of an inch thick, as chromatographic supports for bringing about the separation of a relatively large amount of a mixture of sugars. Due to the poor wet strength of this type of support, which is made from cellulose of short fiber length, it was necessary to carry out the development of the chromatograms in a horizontal direction. For these preliminary experiments a horizontal glass tube, 100 mm. diameter and closed at each end with a rubber stopper covered with aluminum foil, served as the chromatographic chamber and glass T-pieces, inserted across the inside of the tube, formed a horizontal support for the cellulose strip. The developing solvent, contained in a cylindrical dish at one end of the glass tube, was led onto the cellulose strip by means of an adsorbent cotton bridge. This apparatus can also be used for carrying out horizontal partition chromatographic analysis with the usual Whatman No. 1 papers. Methylated sugars show the same R_f value as those determined by either the ascending or descending techniques.

The thick cellulose sheets have been found to have a high loading capacity, *e.g.*, D-xylose in concentrations of 20 mg./cm. moved as a discrete band.

TABLE I

SEPARATION OF SUGARS IN CELLULOSE SHEETS[a]

No.	Sugars	Solvent	Distance moved by solvent front (cm.)	Width of sugar bands (cm.)	R_f values: Cellulose sheet	R_f values: Whatman No. 1 paper
1	D-Glucose (15 mg.)	Phenol–water	26.0	4.1	0.40	0.38
	L-Rhamnose (17 mg.)			4.6	.64	.63
2[b]	2,3-Dimethyl-D-glucose (14.2 mg.)	Methyl ethyl ketone–	34.5	5.5	.28	.28
	2,3,4,6-Tetramethyl-D-glucose (8.6 mg.)	water azeotrope		3.2	.94	.82
3[c]	L-Arabinose (2 mg.)	1-Butanol–ethanol–water	24.8	4.1	.27	.14
4	D-Xylose (100 mg.)	1-Butanol–ethanol–water	26.5	4.3	.24	.15
5[c]	D-Glucose (2 mg.)	1-Butanol–ethanol–water	24.8	4.0	.20	.09
6	D-Glucose (14 mg.)	1-Butanol–ethanol–water	..[d]	4.5	1.00[d]	..
	L-Rhamnose (14 mg.)			4.0	1.63[d]	

[a] A cellulose strip 5 cm. in width was used in each experiment. [b] The methylated sugars could not be detected by the usual spray reagents (ammoniacal silver nitrate, *p*-aminodimethylaniline) due to the fact that aqueous solutions wash enough of the sugars into the inside of the sheet to make the level of sugar on the surface too low for detection by these reagents. They were detected, however, by spraying with a 3% solution of ethylleucine hydrochloride in 1-butanol and heating to 130° for about 10 minutes. The sugar bands fluoresced yellow in ultraviolet light. [c] These experiments were carried out in order to determine the R_f values of these sugars on the thick cellulose sheets. Each sugar was put onto the cellulose strip in the form of a spot. [d] The solvent was induced to flow off the end of the paper and the R_f value is quoted in reference to the movement of the glucose.

Moreover, successful separations of D-glucose and L-rhamnose, D-glucose and D-fructose, and 2,3-dimethyl- and 2,3:4,6-tetramethyl-D-glucose have been made using phenol–water, 1-butanol–ethanol–water and methyl ethyl ketone–water azeotrope, respectively. By lap-jointing two or three strips to-

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(1) Paper No. 2849, Scientific Journal Series, Minnesota Agricultural Experiment Station.

(2) A report of work done partially under contract with the U. S. Department of Agriculture and authorized by the Research and Marketing Act of 1946. The contract is being supervised by the Northern Regional Research Laboratory of the Bureau of Agricultural and Industrial Chemistry.

(3) L. Hough, J. K. N. Jones and W. H. Wadman, *J. Chem. Soc.*, 2511 (1949).

(4) H. K. Mitchell and F. A. Haskins, *Science*, **110**, 278 (1949).

(5) H. K. Mitchell, H. Gordon and F. A. Haskins, *J. Biol. Chem.*, **180**, 1071 (1949).

(6) W. L. Porter, *Anal. Chem.*, **23**, 412 (1951).

(7) L. Zechmeister and L. Cholnoky, "Principles and Practice of Chromatography," John Wiley and Sons, Inc., New York, N. Y., 1941.

(8) P. C. Zamecnik, R. B. Loftfield, Mary L. Stephenson and Jean M. Steele, *Cancer Research*, **11**, 592 (1951).

(9) G. Yanofsky, E. Wasserman and D. M. Bonner, *Science*, **111**, 61 (1950).

(10) J. H. Mueller, *ibid.*, **112**, 405 (1950).

(11) The cellulose sheets from which Whatman ashless filter tablets are cut, were kindly furnished by H. Reeve Angel and Co., Inc.

gether it was possible to induce the solvent to flow two or three times the length of the first strip. It was somewhat surprising to find that the R_f values of sugars using 1-butanol–ethanol–water were higher with thick sheets than those obtained using Whatman No. 1 paper. The reason for this is not apparent.

Some examples of the application of the above technique are given in Table I.

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Triesters of Carboxymethylmercaptosuccinic Acid[1]

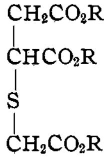
BY ROBERT FILLER AND RICHARD W. SNEED

RECEIVED DECEMBER 24, 1952

A number of esters of carboxymethylmercaptosuccinic acid have been described by Mulvaney, *et al.*[2] As part of a study on antioxidants, it was of interest to prepare several new trialkyl esters of this acid. These compounds and their physical properties are listed in Table I.

TABLE I

TRIALKYL ESTERS OF CARBOXYMETHYLMERCAPTOSUCCINIC ACID



$$\begin{array}{l} CH_2CO_2R \\ | \\ CHCO_2R \\ | \\ S \\ | \\ CH_2CO_2R \end{array}$$

R	B.p.[3] t. °C.	Mm.	n^{25}_D	d^{25}_4	MR Calcd.	MR Found	Sulfur analyses, % Calcd.	Sulfur analyses, % Found
Isobutyl	167–169	0.37	1.4583	1.042	98.0	98.6	8.54	8.65
n-Hexyl	200–203	.40	1.4644	1.013	125.7	125.6	6.96	7.32
2-Ethyl butyl	205–208	.40	1.4649	1.012	125.7	125.8	6.96	7.15
2-Ethyl hexyl	222–227	.37	1.4663	0.9801	153.4	153.6	5.88	5.92

Though somewhat unstable thermally, the esters may be distilled at the reduced pressures without appreciable decomposition. All of the esters are slowly hydrolyzed at room temperature by 5% aqueous potassium hydroxide. The tris-1,1-dihydroperfluorobutyl ester reacts rapidly with dilute potassium carbonate.[4] Esters of this fluoro alcohol which do not contain sulfur show no detectable hydrolysis under these conditions.[5]

Attempts to oxidize the triesters to sulfoxides or sulfones with chromic acid or potassium permanganate were unsuccessful. Hydrogen peroxide in acetic acid reacted with the tri-*n*-butyl ester,[6] but only a high yield of *n*-butyl acetate and a sulfur-containing residue, which may have been the original mercapto acid, were isolated. The formation of *n*-butyl acetate could result from oxidation or hydrolysis of the ester groups followed by esterification of the alcohol thus obtained by the acetic acid. Drastic oxidation with nitric or perchloric acids resulted in cleavage of the thioether linkages. In this manner, the sulfur could be determined quantitatively as sulfate. It is quite possible that the sulfones or the intermediate sulfoxides are formed but are unstable and react further.

Experimental

Preparation of Triesters of Carboxymethylmercaptosuccinic Acid.—The method used was similar to that described by Mulvaney,[2] except that sodium bisulfate was used as the catalyst, and is illustrated for the preparation of the triisobutyl ester. In a 300-ml. round-bottom flask fitted with a modified Dean and Stark apparatus used as a phase separator and to which was attached a reflux condenser, was placed 62.5 g. (0 3 mole) of carboxymethylmercaptosuccinic acid (Evans Chemetics, Inc.), 74 g. (1.0 mole) of isobutyl alcohol, 0.5 g. of sodium bisulfate and 50 ml. of benzene as a water entrainer. The mixture was heated under reflux for five hours, after which time the theoretical amount of water (16.4 ml.) had been collected. The reaction mixture was washed with three 50-ml. portions of a 10% sodium carbonate solution, then with water, and dried over anhydrous magnesium sulfate. The mixture was distilled and gave 90 g. (79.8%) of the triester, b.p. 167–169° (0.37 mm.). The other triesters, shown in Table I, were obtained in comparable yields.

Reaction of the Tri-*n*-butyl Ester with Hydrogen Peroxide in Acetic Acid.—In a 200-ml. round-bottom flask, fitted with a reflux condenser, was placed 22.6 g. (0.2 mole based on 100% H_2O_2) of 30% hydrogen peroxide and 50 ml. of glacial acetic acid. The mixture was heated with a Glas-Col mantle at 85° for one hour. The mixture was cooled to 25° and then 37.6 g. (0.1 mole) of the tri-*n*-butyl ester was added. The mixture was heated under reflux for two days. The upper, water-insoluble layer was separated and the lower acid layer was neutralized with a dilute solution of sodium bicarbonate and extracted with ether. The ether layer was combined with the original water-insoluble layer and dried over anhydrous sodium sulfate. The ether was removed by distillation and there was obtained 28.0 g. (80.5%) of *n*-butyl acetate, b.p. 121–124° and about 5 g. of a sulfur-containing residue, which decomposed on heating. This may have been carboxymethylmercaptosuccinic acid.

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(1) Opinions expressed are those of the authors and do not necessarily express the official opinions of the U. S. Air Force or the Wright Air Development Center.

(2) J. F. Mulvaney, J. G. Murphy and R. L. Evans, THIS JOURNAL, **70**, 2428 (1948).

(3) Boiling points uncorrected.

(4) M. Hauptschein, private communication.

(5) R. Filler, J. V. Fenner, C. S. Stokes, J. F. O'Brien and M. Hauptschein, THIS JOURNAL, **75**, 2693 (1953).

(6) Hardesty Chemical Co., Inc., New York City.

Preparation and Properties of Pentamethyleneketene Monomer and Dimer

BY CARL M. HILL AND MARY E. HILL

RECEIVED JANUARY 14, 1953

Recent studies[1,2] of mono- and disubstituted ketenes suggested investigation of the dehydrohalogenation products of hexahydrobenzoyl chloride.

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(1) C. M. Hill, H. I. Schofield, A. S. Spriggs and M. E. Hill, THIS JOURNAL, **73**, 1660 (1951).

(2) C. M. Hill and G. W. Senter, *ibid.*, **71**, 364 (1949).

Treatment of the acid chloride in dilute ether solution with triethylamine resulted in formation of pentamethyleneketene monomer and dimer in satisfactory yields. The relative yields of the monomer and dimer varied with the number of hours the reaction mixture was allowed to stand at room temperature; prolonged reaction time seemed to favor formation of the dimer.

The monomer was a slightly yellow colored liquid; the dimer a white solid which sublimed to form needle-like crystals. The monomer gave positive reaction with bromine in carbon tetrachloride and potassium permanganate, and reacted with aniline to form hexahydrobenzoanilide and with dilute alkali to yield hexahydrobenzoic acid.

The dimer reacted with hydroxylamine to form the monoxime and with hot dilute alkali to give dicyclohexyl ketone. Catalytic hydrogenation of the dimer at elevated temperature and high pressure produced a hydroxy ketone, which upon reaction with alkali formed dicyclohexyl ketone and formic acid.

Experimental[3]

Hexahydrobenzoyl Chloride.—The chloride was prepared from hexahydrobenzoic acid, m.p. 30–31°, by use of thionyl chloride. Boiling point of chloride was 65–65.5° (5 mm.) and 180–181° (750 mm.); reported b.p. 179° (760 mm.).[4] Observed m.p. of amide was 183–184°; reported m.p. 184°.[5]

Pentamethyleneketene Monomer and Dimer.—The monomer was prepared by treating 14.6 g. (0.10 mole) of hexahydrobenzoyl chloride dissolved in 300 ml. of diethyl ether with 11.4 g. (0.11 mole) of triethylamine. At the end of 16 hours, the hydrochloride was removed by inverted filtration. Removal of the ether by distillation left a dark colored residue which when distilled from a Claisen flask gave 3.6 g. (32%) of the monomer, b.p. 40–41° (3 mm.), d^{20}_4 1.0617, n^{20}_D 1.4680. *Anal.* Calcd. for $C_7H_{10}O$: mol. wt., 110. Found: mol. wt., 108.

The dimer was prepared by treating a solution of 36.6 g. (0.25 mole) of hexahydrobenzoyl chloride in 400 ml. of diethyl ether with 30.3 g. (0.30 mole) of triethylamine. The reaction mixture was allowed to stand for four days. At the end of this period, the precipitated triethylamine hydrochloride was separated by filtration. The filtrate was then concentrated by evaporation of the ether with a stream of dry, oxygen-free nitrogen. Prolonged chilling of the concentrated filtrate produced crystals of the dimer, which were removed by suction filtration. Repeated chilling of the filtrate caused additional crops of the dimer to separate. Finally, the filtrate was distilled, and 2 g. of the dimer, b.p. 175–180° (15 mm.), collected. The crude dimer was recrystallized from ethanol; yield was 15.5 g. (55%); m.p. 164–165°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09; mol. wt., 220. Found: C, 75.90; H, 9.00; mol. wt., 218.

Reaction of Monomer with Aniline.—One gram of pure monomer was added slowly to an equivalent amount of aniline in 10 ml. of anhydrous diethyl ether. The crude anilide was recrystallized from petroleum ether. Observed m.p. was 139–140°; reported[6] m.p. for hexahydrobenzoanilide is 141°; mixed m.p. was 140–141°.

Reaction of Monomer with Alkali.—To 1 g. of the monomer was added dropwise 10 ml. of 10% sodium hydroxide. The alkaline solution was extracted with diethyl ether and acidified with dilute hydrochloric acid. The acid solution was extracted with several small portions of ether and the combined extracts dried. Evaporation of the solvent left 0.7 g. of hexahydrobenzoic acid, m.p. 29.5–30.5°. Mixed m.p. with authentic sample of hexahydrobenzoic acid was 30–31°.

Reaction of Dimer with Hydroxylamine.—One gram of dimer, 10 ml. of ethanol and 1 g. of pyridine were warmed under reflux to 60°; and a solution of 0.3 g. of hydroxylamine in 5 ml. of water was added slowly. After heating for two hours, the reaction mixture was evaporated by a stream of dry air. The residue was triturated with a small portion of hot chloroform and filtered. Chilling of the filtrate precipitated 0.3 g. of the monoxime, m.p. 171–172°.

Anal. Calcd. for $C_{14}H_{21}O_2N$: N, 5.95. Found: N, 5.93.

Catalytic Hydrogenation of Dimer.—Two grams of the dimer and 50 ml. of ethanol, mixed with 0.5 g. of Raney nickel, were treated with hydrogen at 1,000 p.s.i. and 80° for two hours. After removal of the catalyst by filtration, the solution was concentrated by distillation. The solid residue was recrystallized from dilute ethanol. The hydrogenated product was further purified by sublimation; m.p. 121–122°; yield 1.64 g. (77%). This product formed a semicarbazone, m.p. 141–142°, and a phenylurethan, m.p. 151–152°.

Alkaline Hydrolysis of Hydrogenated Product.—To 2 g. of the hydrogenated product was added 10 ml. of 10% sodium hydroxide solution. The mixture was warmed over a water-bath. The oil which formed was extracted with ether. Removal of the ether left 1 g. of an oily liquid, b.p. 211–213° (755 mm.), which formed an oxime, m.p. 157–158°. Melting point of the oxime prepared from an authentic sample of dicyclohexyl ketone was 157–158°; mixed m.p. 158–159°.

Anal. Calcd. for $C_{13}H_{23}ON$: N, 6.70. Found: N, 6.77.

The alkaline solution from above was acidified with sirupy phosphoric acid and distilled. The distillate reacted acid to litmus, reduced potassium permanganate and mercuric nitrate solutions and gave a negative test with the Schiff reagent.

Reaction of Dimer with Sodium Hydroxide.—Two grams of the dimer was refluxed with 50 ml. of 15% sodium hydroxide solution for 48 hours. The cooled reaction mixture was extracted with diethyl ether. Removal of the ether by distillation gave 0.9 g. (53%) of an oil, b.p. 145–147° (12 mm.). Treatment of this oil with hydroxylamine produced an oxime, m.p. 158–159°; mixed m.p. with an authentic sample of dicyclohexyl ketone oxime was 157–158°.

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[3] All melting points are corrected.

[4] V. Meyer, *Ber.*, **30**, 1941 (1897).

[5] J. S. Lumsden, *J. Chem. Soc.*, **87**, 92 (1905).

[6] N. J. Edson, *J. Soc. Chem. Ind.*, **53**, 138 (1934).

Cyclization of N-β-Cyanoethylanilines

BY WILLIAM S. JOHNSON AND WILLIAM DEACETIS[1]

RECEIVED FEBRUARY 2, 1953

A recent publication of Braunholtz and Mann,[2] in which the monocyclization of N,N-bis-(β-cyanoethyl)-*m*-toluidine, II ($R = CH_3$) was mentioned, prompts us to announce our interest in this problem. Our studies, which are yet at a preliminary stage, have been aimed at finding a facile synthesis of 4-keto-7-chloro-1,2,3,4-tetrahydroquinoline III (R = Cl), which has recently been shown[3] to be easily converted to the important antimalarial, chloroquine.

We have been able to obtain III (R = Cl) by direct cyclization of I (R = Cl),[4] but since we have found that cyclizations of this type proceed more readily with cyanoethyl derivatives of alkylanilines (having a tertiary nitrogen atom),[5] we have considered the feasibility of monocyclization of II (R = Cl) to IV (R = Cl) followed by β-elimination of the N-cyanoethyl group to give III (R = Cl). Some of our experiments are reported below.

The addition of acrylonitrile to aniline and to *m*-

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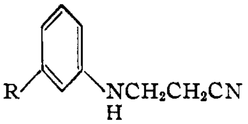
[1] Wisconsin Alumni Research Foundation Research Assistant, 1950–1952.

[2] J. T. Braunholtz and F. G. Mann, *J. Chem. Soc.*, 3046 (1952).

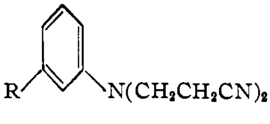
[3] W. S. Johnson and B. G. Buell, THIS JOURNAL, **74**, 4513 (1952).

[4] Details of this work will be reported in a future publication.

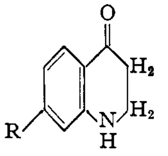
[5] *Cf.* French patent 806,715 [*C. A.*, **31**, 4991 (1937)].



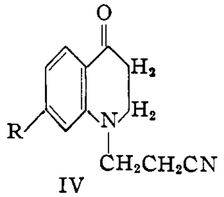
I



II



III



IV

chloroaniline according to the procedure of Smith and Yu[6] yielded the bis-cyanoethyl compounds II (R = H), and II (R = Cl), respectively. Braunholtz and Mann[2] have described an excellent procedure for the aluminum chloride-catalyzed double cyclization of the former substance to give the tricyclic diketone, 1,6-diketojulolidine, in 89% yield. Using a 5:1 instead of 6.7:1 molar ratio of aluminum chloride they obtained a "small yield" of a monocyclization product from II (R = CH_3). Employing essentially the procedure of Mann and Smith[7] for double cyclization, but reducing the ratio of catalyst to 2.5:1, we have effected monocyclization of II (R = H) into IV (R = H) in about 72% yield. The crude product thus obtained was converted into crystalline oxime in 79% yield. In the *m*-chloro series the same conditions, however, gave the monocyclization product, presumably IV (R = Cl), in only 6% yield isolated as the 2,4-dinitrophenylhydrazone, and considerable dicyano compound II (R = Cl) was recovered. When the temperature was raised to 175–200° (*o*-dichlorobenzene solvent) 7-chloro-1,6-diketojulolidine was produced in 47% yield; therefore it seems likely that some intermediate temperature will give improved yields of IV (R = Cl).

Preliminary attempts to eliminate the cyanoethyl group from IV (R = H) with base were not successful. Treatment with a mixture of concentrated hydrochloric acid and excess acetic anhydride however, yielded III (R = H), isolated as the N-acetyl derivative.

Experimental[8]

N-β-Cyanoethyl-4-keto-1,2,3,4-tetrahydroquinoline (IV, R = H).—A mixture of 3.0 g. of the dicyano compound II (R = H),[6] m.p. 82–83.5°, 5.02 g. of powdered aluminum chloride, 15 ml. of chlorobenzene and 0.5 ml. of concentrated hydrochloric acid was heated with stirring at 140–145° (oil-bath) for 6 hours. The mixture was cooled, and 100 ml. of water was added slowly with cooling. The chlorobenzene was removed by steam distillation and the residue extracted with chloroform. The chloroform extracts were washed with 10% sodium bicarbonate solution, water, saturated salt solution and dried over sodium sulfate. Evaporation of the solvent and evaporative distillation of the reddish oily residue at 75–85° (0.01 mm.) gave 2.17 g. (72% yield) of clear yellow oil which could not be induced to crystallize. The analysis for carbon was about 2.6% below that calculated for IV (R = H), but on treatment with hydroxylamine hydrochloride in pyridine, an oxime was produced in 79% yield. From 0.50 g. of the oil was thus obtained 0.426 g. of pale yellow oxime, m.p. 175–178° (dec.). Recrystallization from benzene–petroleum ether (60–68°) gave yellow prisms, m.p. 178–185° (dec.). Further recrystallization did not change the m.p. of this material which may consist of a mixture of *syn* and *anti* forms.

Anal.[9] Calcd. for $C_{12}H_{13}ON_3$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.62; H, 5.92; N, 19.35.

The pure ketone was isolated from the crude cyclization product by chromatography on alumina. The product came off the column with benzene, and after two recrystallizations from diisopropyl ether was obtained as pale yellow plates, m.p. 79–79.5°.

Anal. Calcd. for $C_{12}H_{12}ON_2$: C, 71.97; H, 6.04; N, 13.99. Found: C, 71.96; H, 6.10; N, 13.83.

N,N-Bis-(β-cyanoethyl)-*m*-chloroaniline (II, R = Cl) was prepared according to the procedure of Smith and Yu[6] for the parent compound (II, R = H) from 102 g. of *m*-chloroaniline, 95.4 g. of acrylonitrile, 20 ml. of acetic acid and 8.0 g. of cuprous chloride. The crude reddish oily product was dissolved in hot alcohol, and on cooling 14.9 g. of II (R = Cl) crystallized, m.p. 88–92°. The filtrate was concentrated and the residual reddish oil distilled through a 25-cm. Vigreux column to give 46.5 g. of N-β-cyanoethyl-*m*-chloroaniline, b.p. 135–150° (0.02–0.03 mm.), m.p. 41–47° and 14.5 g. of oil, b.p. 150–225° (0.02–0.03 mm.). Crystallization of the latter fraction from alcohol gave an additional 4.05 g. of II (R = Cl), m.p. 94–96°. A sample purified by repeated recrystallization from alcohol was obtained as long colorless needles, m.p. 98–99°.

Anal.[9] Calcd. for $C_{12}H_{12}N_3Cl$: C, 61.67; H, 5.18. Found: C, 61.85; H, 5.19.

N-β-Cyanoethyl-4-keto-7-chloro-1,2,3,4-tetrahydroquinoline (IV, R = Cl) was prepared from 3.0 g. of the dicyano compound II (R = Cl), m.p. 95.5–96.5°, 4.34 g. of aluminum chloride, 15 ml. of chlorobenzene and 0.5 ml. of concentrated hydrochloric acid as described above for IV (R = H). The heating period was 7 hours. The crude product obtained on evaporation of the chloroform was solid, m.p. 80–100°, and on crystallization from alcohol, yielded a total of 1.85 g. of uncyclized dicyano compound II (R = Cl). The filtrate was treated with 2,4-dinitrophenylhydrazine solution, and the **2,4-dinitrophenylhydrazone of IV (R = Cl)** separated immediately; yield 0.32 g.; m.p. 220–225° (dec.). Two recrystallizations from ethyl acetate gave red microcrystals, m.p. 242–243° (dec.) introduced at 220°.

Anal.[9] Calcd. for $C_{18}H_{15}O_4N_6Cl$: C, 52.12; H, 3.65; N, 20.26. Found: C, 52.14; H, 3.69; N, 19.78.

7-Chloro-1,6-diketojulolidine.—The cyclization described in the preceding experiment was repeated except that 20 ml. of *o*-dichlorobenzene was used in place of the chlorobenzene, and the mixture was heated for 0.5 hour at 200° and an additional 1.5 hours at 175°. Crystallization of the crude product from alcohol gave 1.09 g. of brown needles, m.p. 160–162° and a second crop amounting to 0.324 g. of darker material, m.p. 154–158°. Evaporative distillation of the residue from the filtrate at 120–130° (0.01 mm.) gave an additional 0.02 g., m.p. 159–162°, making the total yield of material of fair quality, 1.43 g.

Sublimation of a sample from the first crop, followed by repeated recrystallization from alcohol gave bright yellow needles, m.p. 164–165°.

Anal.[9] Calcd. for $C_{12}H_{10}O_2NCl$: C, 61.15; H, 4.28; N, 5.94. Found: C, 61.12; H, 4.42; N, 5.96.

Conversion of IV (R = H) into N-Acetyl-4-keto-1,2,3,4-tetrahydroquinoline.—A mixture of 0.490 g. of the keto nitrile IV (R = H), m.p. 79–79.5°, and 5 ml. of a solution of 100 g. of concentrated hydrochloric acid in 400 g. of acetic anhydride was heated under reflux for 3 hours. An additional 5 ml. of acetic anhydride was added and the refluxing was continued for another hour. The mixture was cooled, 20 ml. of water added, and the acids neutralized with solid potassium carbonate. The resulting basic solution was extracted with chloroform and the combined extracts were washed with saturated sodium bicarbonate solution, water, saturated salt solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave 0.471 g. of a pale yellow oil which crystallized from benzene–petroleum ether (60–68°) in colorless prisms, m.p. 150–155°. The nature of this product is uncertain, but after standing in contact with the mother liquor for several days, the crystals, which had turned to a semisolid, were redissolved in benzene and chromatographed on 10 g. of Florisil. From the column

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(6) P. A. S. Smith and T. Yu, THIS JOURNAL, **74**, 1096 (1952).

(7) F. G. Mann and B. B. Smith, *J. Chem. Soc.*, 1898 (1951).

(8) Melting points are corrected for stem exposure.

(9) Microanalyses by E. J. Eisenbraun and G. Winestock.

there was obtained 0.228 g. (47% yield) of pale yellow crystals, m.p. 88–92°. Recrystallization from a small amount of methanol gave small colorless prisms, m.p. 91.5–92.5° (reported[10], 94°), undepressed on admixture with authentic N-acetyl-4-keto-1,2,3,4-tetrahydroquinoline prepared from the free quinolone.[11]

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[10] G. R. Clemo and H. J. Johnson, *J. Chem. Soc.*, 2133 (1930).

[11] W. S. Johnson, E. L. Woroch and B. G. Buell, This Journal, **71**, 1901 (1949).

LABORATORY OF ORGANIC CHEMISTRY
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The Solubility of Lead Chloride in Sodium Chloride, Perchloric Acid and Hydrochloric Acid Solutions[1]

BY S. Z. LEWIN, JOHN E. VANCE AND LAWRENCE B. NELSON

RECEIVED FEBRUARY 13, 1953

In connection with an investigation of the crystal growth of lead chloride, measurements were made of the solubility of that compound at 25° in the media listed in Table I.

TABLE I

SOLUBILITIES OF $PbCl_2$ AT 25°

Medium (conc. in molality)	G. $PbCl_2$ per 1000 g. H_2O	Standard deviation	Lit. values (interpolated)
0.4723 *m* NaCl	1.870	0.008	1.87[a]
1.0125 *m* NaCl	1.784	.008	1.74[a]
2.0265 *m* NaCl	2.743	.010	2.72[a]
4.0216 *m* NaCl	8.367	.014	8.55[a]
0.5375 *m* HCl	1.561	.007	(3.68 g. at 0.50 *m*)[g]
0.5487 *m* $HClO_4$	10.88	.04	
1.0368 *m* $HClO_4$	10.56	.05	
2.3239 *m* $HClO_4$	7.421	.025	
3.4565 *m* $HClO_4$	5.183	.013	
6.4730 *m* $HClO_4$	1.781	.005	
Water	....	...	10.87[a], 10.84[b], 10.86[c], 10.75[d], 10.91[e], 10.76[f], 11.03[g], 10.84[h]

[a] G. E. R. Deacon, *J. Chem. Soc.*, 2063 (1927). [b] L. J. Burrage, *ibid.*, 1703 (1926). [c] W. R. Carmody, This Journal, 51, 2909 (1929). [d] T. P. Goulden and L. M. Hill, *J. Chem. Soc.*, 447 (1945). [e] L. Wilkinson, N. O. Bathhurst and H. N. Parton, *Trans. Faraday Soc.*, **33**, 623 (1937). [f] F. Flöttman, *Z. anal. Chem.*, **73**, 1 (1938). [g] H. E. Armstrong and J. V. Eyre, *Proc. Roy. Soc.* (*London*), **A88**, 238 (1913). [h] P. M. Lichty, This Journal, **25**, 469 (1903).

Sealed glass tubes containing solution and excess solid $PbCl_2$ were heated to about 100° for several hours, then placed into a thermostat and rotated at 25.00 ± 0.05° for at least 24 hours, after which samples were removed for analysis by suction through a plug of glass wool.

The concentration of acid was determined in each case by titration with standard NaOH to the brom cresol green end-point. Two procedures were used for the determination of lead chloride; (1) triple evaporation with sulfuric acid, followed by dilution with water and the usual gravimetric procedure with filtration on Selas crucibles, and (2) neutralization to the methyl orange end-point with ammonia, precipitation in hot solution with hydrogen sulfide, followed by solution of the precipitate in nitric acid and conversion to lead sulfate as before. Both procedures were followed in the case of the sodium chloride and hydrochloric acid solutions, and gave concordant results; only procedure (2) was used for the solutions containing perchloric acid. The concentration of sodium chloride was found as the difference between total chloride as obtained by the Volhard titration[2] and the amount of chloride as lead chloride calculated from the gravimetric determination of lead.

Demassieux[3] and Deacon[4] have reported that no double salts are formed between NaCl and $PbCl_2$, whereas Kendall and Sloan[5] offered analytical evidence that the solid phase in equilibrium with NaCl solutions of $PbCl_2$ is $NaCl \cdot 2PbCl_2$ for all concentrations in excess of 0.5 *N* NaCl. The solid phases in equilibrium with the 1, 2 and 4 *m* NaCl solutions of Table I were analyzed for lead according to procedure (1) above. The solid was removed from the liquid phase by filtration, and dried by pressing between filter papers without washing. The analytical results are given in Table II.

TABLE II

ANALYSES OF SOLID SAMPLES

Source of sample	$PbCl_2$, %
Mallinckrodt A.R. $PbCl_2$	100.16, 99.84, 99.96
1 *m* NaCl	98.36, 99.17
2 *m* NaCl	99.16, 98.05
4 *m* NaCl	98.13, 99.21

The analyses of the samples from the NaCl solutions are low as a result of contamination by NaCl, but the data clearly support the conclusion that no double salts form between NaCl and $PbCl_2$ for solutions up to 4 *m* in NaCl under the conditions of our experiments.

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[1] This work was supported in part under Contract No. AT (30-1)-1256 between the Atomic Energy Commission and New York University.

[2] I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," 3rd Ed., The Macmillan Co., New York, N. Y., 1952, p. 546, procedure 2.

[3] N. Demassieux, *Ann. chim.*, **20**, 267 (1923).

[4] G. E. R. Deacon, footnote *a* of Table I.

[5] J. Kendall and C. H. Sloan, This Journal, **47**, 2306 (1925).

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Anion-exchange Studies. VII.[1,2] Separation of Sulfuric Acid from Metal Sulfates by Anion Exchange

BY KURT A. KRAUS, FREDERICK NELSON AND JOHN F. BAXTER[3]

RECEIVED JANUARY 2, 1953

A strong base anion-exchange resin in the sulfate form (or in combination with other polyvalent anions) might be considered a base which can react with (adsorb) acids according to reactions of the type

$$(SO_4^{=})_r + HX \rightleftarrows (HSO_4^-)_r + (X^-)_r \qquad (1)$$

where subscript r stands for resin. In the case of the adsorption of sulfuric acid by a sulfate resin equation (1) becomes

$$(SO_4^{=})_r + H_3O^+ + HSO_4^- \rightleftarrows 2(HSO_4^-)_r + H_2O \quad (2a)$$

and

$$(SO_4^{=})_r + 2H_3O^+ + SO_4^{=} \rightleftarrows 2(HSO_4^-)_r + 2H_2O \quad (2b)$$

The fact that such acid adsorption, possibly according to equations (1) and (2), actually takes place can readily be demonstrated by passing sulfuric acid solutions through sulfate columns, and noting that a considerable volume of effluent is free of acid.

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[1] This document is based on work performed for the Atomic Energy Commission at the Oak Ridge National Laboratory.

[2] Previous paper, K. A. Kraus and G. E. Moore, This Journal, **75**, 1460 (1953).

[3] Summer Participant (1951) at Oak Ridge National Laboratory.

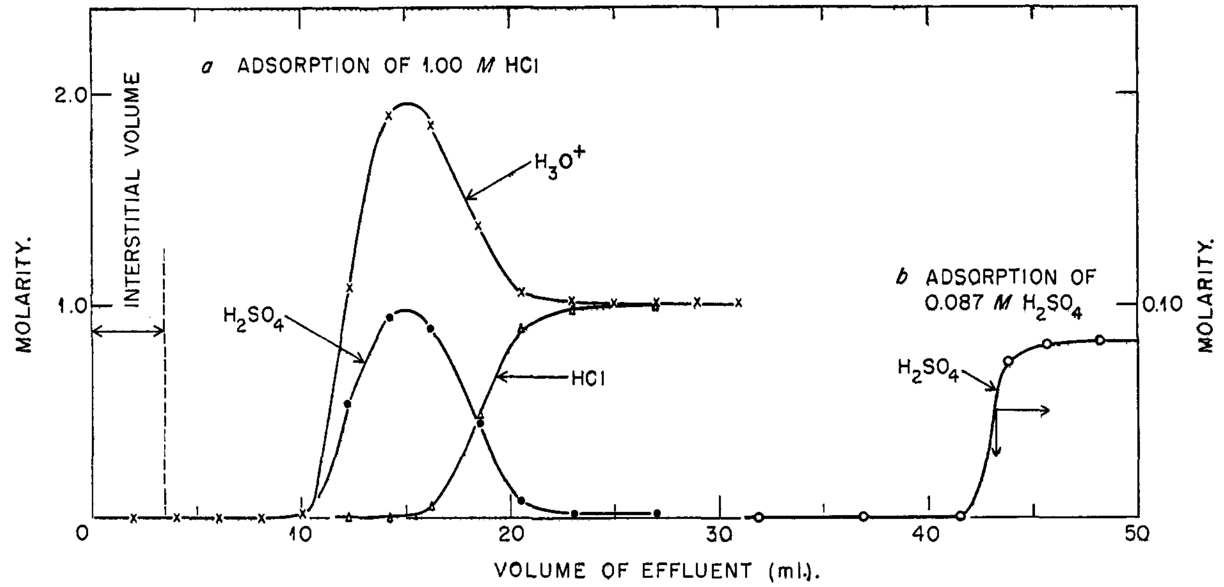

Fig. 1.—Adsorption of HCl and H_2SO_4 by Dowex-1-sulfate (0.488 cm.^{2} × 16.9 cm. column).

For example, 13 cc. of a 0.496 *M* and 42 cc. of a 0.082 *M* H_2SO_4 solution could be passed through 0.488 cm.^{2} × 14.5 and 17.0 cm. columns of the quaternary amine polystyrene–divinyl benzene resin Dowex-1 in the sulfate form, before the *p*H of the effluent dropped below 4 (see also Fig. 1).

Other acids (*e.g.*, HCl, $HClO_4$) have been similarly adsorbed by the sulfate form of the resin. The adsorption of HCl is typical of the behavior of strong acids and the results are shown in Fig. 1. A 1 *M* HCl solution was passed into a column of Dowex-1 in the sulfate form. The effluent initially had a *p*H > 4. Its acidity reached a maximum of *ca.* 2 *M* H_3O^+ and then decreased to 1 *M* H_3O^+. The increase in the acidity of the effluent over that of the eluent apparently is due to the fact that sulfuric acid is first eluted and that chloride ions substitute for acid sulfate (HSO_4) ions. The bulk of the sulfuric acid portion of the effluent was relatively free of chloride ions as also shown in Fig. 1.

This adsorption of sulfuric acid by a strong base exchanger implies that these resins can be used to separate sulfuric acid from non-adsorbable or weakly adsorbable metal sulfates. This separation is demonstrated below using a mixture of copper sulfate and sulfuric acid.

One-ml. portions of copper sulfate in sulfuric acid were placed on a 0.187 cm.^{2} × 9.3 cm. column (bed volume 1.74 cc.) filled with (well-washed) Dowex-1 in the sulfate form. The column was then eluted with distilled water. Approximately 1-ml. fractions of the effluent were collected and tested for copper and sulfuric acid. The copper concentration was determined spectrophotometrically after making aliquots 0.5 *M* in NH_3. The sulfuric acid concentration was determined either by *p*H measurements combined with a calibration curve or by titrations. The results of two experiments using 0.1 *M* $CuSO_4$–0.1 *M* H_2SO_4 and 0.1 *M* $CuSO_4$–0.5 *M* H_2SO_4 are shown in Fig. 2. Good separation of copper sulfate from the acid was obtained in both experiments with the copper containing effluent having a *p*H > 4.5.

The volume at which acid appears in the effluent depends on the amount of acid initially passed into the column (loading with respect to sulfuric acid) since in the water "elution" the acid will have to be moved through the remaining part of the sulfate column. In the experiment with 0.1 *M* H_2SO_4 acid appeared after *ca.* 8 column volumes of water while in the experiment with 0.5 *M* H_2SO_4 acid appeared after *ca.* 2 column volumes. In these experiments *ca.* 7.2 and 36%, respectively, of the adsorptive capacity of the column for H_2SO_4 were utilized (capacity 1.62 equivalents/1 bed).

Although the removal of sulfuric acid from the $CuSO_4$ solution was quite satisfactory the regeneration of the resin (removal of H_2SO_4 from the resin) using water only, rather than a stronger base, takes place slowly as also shown in Fig. 2. *Circa* 22 column volumes were necessary before the *p*H of the effluent rose to *ca.* 4.5.

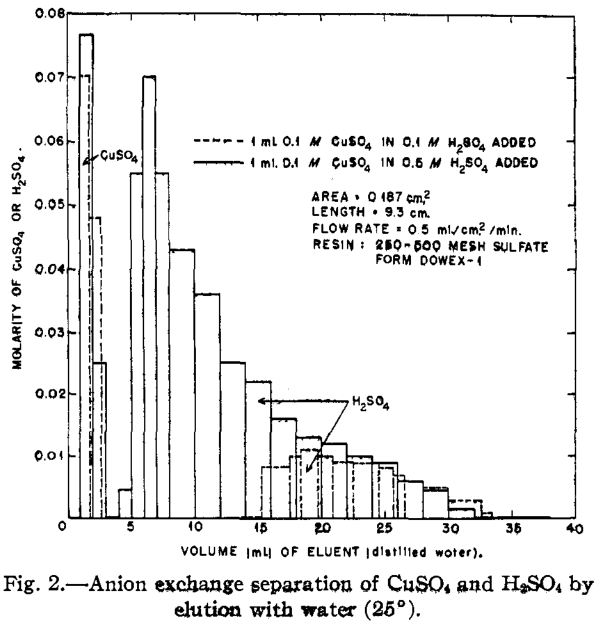

Fig. 2.—Anion exchange separation of $CuSO_4$ and H_2SO_4 by elution with water (25°).

In an attempt to increase the efficiency of the regeneration process an experiment was carried out at 60° since it was believed that slow rates of equilibration might be in part responsible for the trailing edge in the sulfuric acid elution. Operation at higher temperature not only does not improve the regeneration but actually the removal of H_2SO_4 takes more water (*ca.* 32 column volumes) than at lower temperature indicating that the tailing in the elution band is not due to slow rates of equilibration. It probably arises from a pronounced nonlinearity of the adsorption isotherm. It is interesting to note that the copper band at 60° definitely showed some adsorption, the apparent elution constant E^4 being *ca.* 1 instead of the theoretical maximum *ca.* 2.5 when no adsorption takes place. At the lower temperature the copper band was less strongly adsorbed, but did not travel with elution constant as large as 2.5.

(4) *E* has been defined (K. A. Kraus and G. E. Moore, This Journal, **73**, 9 (1951), as the distance (cm.) a band moves under equilibrium conditions, per cc. of eluent in a 1-cm.^{2} column.

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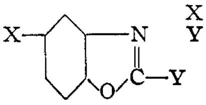
Preparation of Certain Derivatives of Benzoxazole

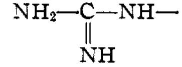
By Toyoyuki Nagano, Motoko Itoh and Konomu Matsumura

Received December 22, 1952

This note describes the preparation of several 2,5-disubstituted benzoxazoles, in the hope that they may be of therapeutic value.



X (5 position): Cl, HO_2C—, or BuO_2C—
Y (2 position): SH, OH, NH_2, or



$NH_2—C(=NH)—NH—$

Experimental

2-Benzeneazo-4-chlorophenol.—A modification of the method of Krause[1] was found to prevent the formation of tar. A solution of benzenediazonium chloride made from 0.1 mole (9.3 g.) of aniline was added at −3 to 0° with stirring over a period of two hours to a cold solution of 0.1 mole (12.9 g.) of *p*-chlorophenol, 4.0 g. of sodium hydroxide and 2.9 g. of sodium carbonate crystals in 100 ml. of 90% ethanol and 200 ml. of water. The stirring was maintained until there was no color reaction with alkaline β-naphthol, the solution then acidified with acetic acid, filtered, and the solid product (23 g. of orange yellow needles melting at 105–107°) washed with water. Recrystallization from 60% acetic acid gave orange prismatic needles melting at 110–111°.

2-Amino-4-chlorophenol.—To a stirred mixture of 4.64 g. of 2-benzeneazo-4-chlorophenol in 10 ml. of ethanol and 20 ml. of water was added 12.6 g. of sodium hydrosulfite during 15 minutes. Stirring was maintained until the mixture became colorless, and the ethanol was then removed on a water-bath. After standing overnight, the solution deposited 2.4 g. (83%) of colorless plates, melting at 138–140° with preliminary softening. Recrystallization from 50 ml. of hot water gave colorless rhombic plates melting at 140–141°. Popov[2] reported a melting point of 137–138°, and Korczynski and Obarski[3] a melting point of 185° for this product.

Anal. Calcd. for C_6H_6ClNO: N, 9.76. Found: N, 9.78.

The diacetyl derivative of 2-amino-4-chlorophenol gave colorless plates from benzene, melting at 173–175°. Korczynski and Obarski[3] reported a melting point of 201° for this derivative.

Anal. Calcd. for $C_{10}H_{10}ClNO_3$: N, 6.15. Found: N, 6.13.

The hydrochloride of 2-amino-4-chlorophenol gave colorless prisms from ethanol, melting at 258° with decomposition.

Butyl 4-Hydroxy-3-benzeneazobenzoate.—It has been found that the reaction of benzenediazonium chloride with 4-hydroxybenzoic acid gives only a small yield of 4-hydroxy-3-benzeneazobenzoic acid (the chief product being 2,4-bis-benzeneazophenol), but that substitution of the ethyl ester of the acid gives a good yield of ethyl 4-hydroxy-3-benzeneazobenzoate.[4] For this reason the butyl ester of 4-hydroxybenzoic acid was used in the present investigation.

A solution of benzenediazonium chloride made from 0.2 mole (18.6 g.) of aniline was added with stirring at −5 to −3° to a cold solution of 0.2 mole (38.8 g.) of butyl 4-hydroxybenzoate and 24 g. of sodium hydroxide in 400 ml. of water. After standing in the cold until there was no color reaction with alkaline β-naphthol, the solution was acidified with acetic acid, filtered and washed repeatedly with water. The product, crystallized from 100 ml. of 90% ethanol, weighed 46.0 g. (77%) and separated as orange yellow prisms (m.p. 75°), quite soluble in benzene and petroleum ether, and fairly soluble in warm ethanol and 80% hot acetic acid.

Anal. Calcd. for $C_{17}H_{18}N_2O_3$: N, 9.39. Found: N, 9.30.

The above coupling reaction also proceeds smoothly in sodium carbonate solution, although less rapidly than in sodium hydroxide.

Butyl 4-Hydroxy-3-aminobenzoate.—The reduction of butyl 4-hydroxy-3-benzeneazobenzoate, by the sodium hydrosulfite method outlined above, gave almost the theoretical yield of product melting at 72°. Recrystallization from glacial acetic acid gave colorless plates melting at 113°, but recrystallization from a chloroform–petroleum ether mixture gave colorless needles melting at 72°. Cavill[5] reported a melting point of 64–65° for this product.

Anal. (72°) Calcd. for $C_{11}H_{15}NO_3$: N, 6.70. Found: N, 6.69. *Anal.* (113°) Calcd. for $C_{11}H_{15}NO_3 \cdot C_2H_4O_2$: N, 5.20; $C_2H_4O_2$, 22.3. Found: N, 5.35, 5.10; $C_2H_4O_2$, 20.2 (titration).

Analysis indicated that crystallization from glacial acetic acid gives an acetate. Two recrystallizations of the acetate from chloroform–petroleum ether gave the substance melting at 72°.

The hydrochloride, prepared from the aminobenzoate and 10% hydrochloric acid, crystallized as colorless columns melting at 234° with decomposition.

4-Hydroxy-3-aminobenzoic acid was obtained by refluxing the ester with five times its weight of 20% hydrochloric acid for an hour. The acid separated as colorless rhombic plates melting at 202° with decomposition; the melting point is in agreement with that reported by Cavill,[5] and Auwers and Röhrig.[6] The hydrochloride of the free acid crystallized as colorless rhombic prisms melting at 250° with decomposition.

Hydrolysis of 5,5′-Dicarboxylic-dibenzoxazole-2,2′-disulfide.—A 400-mg. sample of the disulfide was dissolved in the calculated quantity of sodium carbonate solution, and the solution was immediately acidified with hydrochloric acid. Vigorous evolution of sulfur dioxide[7] (identified by odor and by a blue violet color with congo red paper) was followed by the separation of 300 mg. of solid melting at 265–271° with foaming. This material was separated into two fractions by recrystallization from 90% ethanol.

The more insoluble fraction, weighing 170 mg. and melting at 280° with foaming, separated as prismatic needles and was identified as 5-carboxylic-benzoxazole-2-thion by mixed melting point and analysis.

Anal. Calcd. for $C_8H_5NO_3S$: N, 7.18. Found: N, 7.55.

The more soluble fraction, weighing 110 mg. and melting at 248–249° with foaming, separated as prismatic needles

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[1] M. Krause, *Ber.*, **32**, 126 (1899).

[2] Popov, *Anilinokrasochnaya Prom.*, **3**, 391 (1933).

[3] Korczynski and Obarski, *Bull. soc. chim.*, [IV] **33**, 1823 (1923).

[4] Grandmougin and Freimann, *J. prakt. Chem.*, [2] **78**, 385 (1908).

[5] Cavill, *J. Soc. Chem. Ind.*, **64**, 212 (1945).

[6] K. Auwers and H. Röhrig, *Ber.*, **30**, 992 (1897).

[7] To our knowledge, the escape of sulfur dioxide has not heretofore been reported in similar reactions.

TABLE I

2,5-DISUBSTITUTED BENZOXAZOLES

Compounds 1, 5 and 8 were made by refluxing the corresponding aminophenol with ethanolic carbon disulfide for 60 hours. Compounds 2, 6 and 9 were made by fusion of the corresponding aminophenol hydrochloride with urea for two hours at 140–150°. Compounds 3, 7 and 10 were made by the reaction of the corresponding aminophenol with ethanolic cyanogen bromide for 50 hours at room temperature. Compound 4 and 11 were made from the corresponding aminophenol and dicyandiamide in ethanol–HCl by the method of Smith, *et al.* (THIS JOURNAL, **51**, 2522 (1929)). The hydrochloride of butyl 4-hydroxy-3-aminobenzoate (490 mg.), refluxed for two hours with 170 mg. of dicyandiamide in 2 ml. of 90% ethanol, gave 150 mg. of a hydrochloride melting at 175–180°. The base set free from this hydrochloride, repeatedly recrystallized from ethanol and from benzene, melted at 182–183°, and gave a mixed melting point of 182–184° with a specimen of 2-amino-5-carbobutoxybenzoxazole (m.p. 186°). *Anal.* Calcd. for $C_{12}H_{14}N_2O_3$: N, 11.97. Found: N, 12.49, 12.59.

Cpd.	X	Y	Formula	Description[i]	Solvent	Solubility	Yield, %	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
1	Cl	SH	C_7H_4ClNOS[a]	Needles	90% al.	V.s., Na_2CO_3	70	268 d.[b]	7.55	7.57
2	Cl	OH	$C_7H_4ClNO_2$	Fibrous needles	80% al.	V.s., al., ether, Na_2CO_3	92	189–190[c]	8.26	8.24
3	Cl	NH_2	$C_7H_5ClN_2O$[d]	Plates	50% al.	Sl.s., H_2O	88	182–183	16.62	16.55
4	Cl	$H_2N{-}\underset{\underset{NH}{\Vert}}{C}{-}NH{-}$	$C_8H_7ClN_4O$[e]	Elongated plates	Benzene	I., al., acetone	40	228 d.	24.51	24.63
5	$BuO_2C{-}$	SH	$C_{12}H_{13}NO_3S$	Needles	Dil. al.	V.s., al., ether, Na_2CO_3	76	134	5.58	5.48
6	$BuO_2C{-}$	OH	$C_{12}H_{13}NO_4$	Needles	Benzene–petroleum	S., org. solvents	90	99–100	5.96	5.97
7	$BuO_2C{-}$	NH_2	$C_{12}H_{14}N_2O_3$	Prisms	Ether	I., H_2O, sl.s., C_6H_6, v.s., al.	74	186	11.97	12.01
8	$HO_2C{-}$	SH	$C_8H_5NO_3S$[f]	Prisms	Water	V.s., al.	62	282 d.[g]	7.18	7.10
9	$HO_2C{-}$	OH	$C_8H_5NO_4$	Needles	Water	S., al.	70	>300	7.82	7.88
10	$HO_2C{-}$	NH_2	$C_8H_6N_2O_3$	Needles	90% al.	I., ether, C_6H_6 Sl.s., H_2O, al.	60	275 d.	15.73	15.68
11	$HO_2C{-}$	$H_2N{-}\underset{\underset{NH}{\Vert}}{C}{-}NH{-}$	$C_9H_8N_4O_3$[h]	Needles	Abs. al.	Sl.s., al., ethyl acetate	60	280 d.	25.45	25.52

[a] Na salt, colorless plates from ethanol, soluble in water. [b] Deck and Dains (THIS JOURNAL, **55**, 4989 (1933)) reported a melting point of 261–262°, and Korczynski and Obarski[3] reported a melting point of 283° for this substance. [c] Upson (*Am. Chem. J.*, **32**, 25 (1905)) reported a melting point of 184–185°, and an English patent (240,969 (1925)) reported a melting point of 189–190° for this substance. [d] Hydrochloride: needles melting at 229° with decomposition; hydrolyzed by water. *Anal.* Calcd. for $C_7H_5ClN_2O{\cdot}HCl{\cdot}H_2O$: N, 12.56. Found: N, 12.70. Hydrobromide: plates melting at 240° with decomposition. [e] Hydrochloride: needles from alcohol, melting at 273° with decomposition; slightly soluble in water. [f] Disodium salt: flat needles, hygroscopic and quite soluble in alcohol or water. Mono-sodium salt: long colorless columns from absolute alcohol, soluble in water. [g] French patent (54,436 (1933)) reported a decomposition temperature of 283–284°. [h] Hydrochloride: columns from ethanol–HCl, melting at 280° with decomposition; hydrolyzed by water. Sodium salt: plates from water, soluble in alcohol. [i] All compounds are colorless.

TABLE II

5,5′-DISUBSTITUTED-DIBENZOXAZOLE-2,2′-DISULFIDES

These compounds were made from the monosodium salts of the corresponding mercaptans by reaction with 0.1 *N* iodine–potassium iodide solution in water; the yields were practically quantitative. Compounds a and b are soluble in the usual organic solvents. Compound c is practically insoluble in organic solvents, but soluble in the calculated quantity of sodium carbonate solution.

Cpd.	X	Formula	Description	Solvent	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
a	Cl	$C_{14}H_6Cl_2N_2O_2S_2$	Prisms	Benzene	141–142	7.59	7.60
b	$BuO_2C{-}$	$C_{24}H_{24}N_2O_6S_2$	Needles	Benzene	115–116	5.60	5.62
c	$HO_2C{-}$	$C_{16}H_8N_2O_6S_2$	Prisms		237–238 d.	7.22	7.11, 7.31

and was identified as 5-carboxylic-benzoxazole by mixed melting point and analysis.

Anal. Calcd. for $C_8H_5NO_3{\cdot}H_2O$: N, 7.73. Found: N, 7.62.

5-Carboxylic-benzoxazole was independently synthesized by refluxing 300 mg. of 3-amino-4-hydroxybenzoic acid with an excess of formic acid for three hours, evaporating the excess formic acid, and finally heating the residue at 170° for three hours (94% yield). The product crystallized from dilute ethanol as prismatic needles melting at 249° with foaming, and gave no color with ferric chloride.

Anal. Calcd. for $C_8H_5NO_3{\cdot}H_2O$: N, 7.73. Found: N, 7.72.

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4,4′,4″-Trinitrotriphenylamine[1]

BY ROBERT IRVING WALTER

RECEIVED FEBRUARY 19, 1953

A trinitro compound prepared from triphenylamine by nitration with fuming nitric acid has been reported by Heydrich[2] and by Herz.[3] A substance having the same melting point, 280°, was subsequently described by Madelung, *et al.*,[4] who nitrated triphenylamine with nitrogen dioxide. None of these authors proposed a structure for his product, but Beilstein[5] lists the compound as 4,4′,4″-trinitrotriphenylamine on the basis of a private communication from Piccard, who also claimed that the melting point was 396°. There are no data in the literature in support of this assignment of structure.

Attempts in this Laboratory to repeat the nitration of triphenylamine using Herz's procedure[3] resulted in a yellow powder which gave yellow crystals melting at 383° from nitromethane. In no case has the nitration resulted in a substance melting at 280°, nor have the recrystallization

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[1] This work was carried out at Rutgers University in connection with contract number N7-ONR-45403 of the Office of Naval Research.

[2] C. Heydrich, *Ber.*, **18**, 2156 (1885).

[3] R. Herz, *ibid.*, **23**, 2539 (1890).

[4] W. Madelung, E. Reiss and E. Herr, *Ann.*, **454**, 36 (1927).

[5] Beilstein, "Handbuch der Organischen Chemie," Fourth Edition, Vol XII, Springer Verlag, Berlin, 1929, p. 717.

procedures in the literature given such a product.

To check the structure of the nitration product, an alternate synthesis was carried out from *p*-nitrochlorobenzene and *p*-nitroaniline in the presence of copper. (This reaction[6] occurs without rearrangement of the *p*-nitro group to give 4-nitrotriphenylamine both from diphenylamine and *p*-iodonitrobenzene[7] and from 4-nitrodiphenylamine and iodobenzene.[8]) The product was identical to the nitration product obtained by Herz's procedure, confirming the structural assignment in Beilstein.

The behavior of the substance on heating suggests the existence of more than one polymorphic form; the material reported to melt at 280° might have been an additional metastable crystal form of the same compound.

Experimental

Preparation of 4,4',4''-Trinitrotriphenylamine.—A number of runs of the nitration procedure of Herz[3] gave 75–80% of a fine yellow powder. Analysis showed that this was contaminated with lower nitration products. These impurities are more soluble in the common solvents than the very slightly soluble trinitro compound, but in nitromethane and nitrobenzene the latter seems to be the more soluble, for fractional crystallization gave successively purer crops of diamond-shaped plates. The third crop from nitromethane was taken for analysis.

Anal. Calcd. for $C_{18}H_{12}N_4O_6$: C, 56.84; H, 3.18; N, 14.73. Found: C, 56.94; H, 3.28; N, 14.84.

Alternatively, 138 g. (1 mole) of *p*-nitroaniline, 315 g. (2 moles) of *p*-nitrochlorobenzene, 160 g. of powdered anhydrous potassium carbonate, 5 g. of copper powder (copper bronze previously washed with ether was used) and 750 ml. of nitrobenzene were refluxed with stirring for 17 hours in an all-glass apparatus designed to condense nitrobenzene but pass water through.[9] The reaction mixture was steam distilled to remove nitrobenzene, filtered, and the pasty mass washed with acetone three times by decantation. Finally, it was extracted with acetone in a Soxhlet apparatus for two hours to remove unreacted reagents and nitrobenzene. The resulting coarse yellowish powder weighed 182 g., yield 48%. Continued extraction with acetone for 72 hours gave 0.8 g. of irregular crystals in the extract. *Anal.* Calcd. values above. Found: C, 56.74; H, 3.39; N, 14.59.

Behavior on Melting.—Observation on the Kofler hot stage, for which a 500° thermometer was calibrated, showed no melting at 280° of samples previously purified by recrystallization from nitromethane, nitrobenzene–ethanol or acetone. Instead, all samples sublimed, beginning at 270–280°, to give fine needles on the cover glass. (The synthetic material can be sublimed rapidly and quantitatively at 290°, and the product is pure. The nitration product is not purified by this procedure, since the partial nitration products also sublime.) Above 375°, the needle sublimate and any unsublimed residue undergo transition to irregular crystalline plates. These melt at 382–383°. Both preparations individually, and a mixture, showed this sequence of changes.

X-Ray powder photographs were taken of the plates prepared by recrystallization from nitromethane, the needle sublimate, and these needles heated to 375° under a cover plate. The patterns were identical, indicating that if any of these samples were polymorphs, the high temperature crystal forms reverted quickly to the room temperature form on cooling.

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(6) I. Goldberg, *Ber.*, **39B**, 1691 (1906).

(7) S. Kawai, *J. Chem. Soc., Japan*, **49**, 235 (1928), in *C. A.*, **24**, 80 (1930).

(8) J. Piccard and L. M. Larsen, THIS JOURNAL, **39**, 2008 (1917).

(9) F. D. Hager in "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 544.

A New Alkaloid from *Amianthium Muscaetoxicum* Gray

BY NORBERT NEUSS

RECEIVED FEBRUARY 23, 1953

Amianthium muscaetoxicum Gray, also called Stagger grass or Fly poison,[1] has long been known to be poisonous to cattle and sheep.[2] Over forty years ago, Alsberg[3] studied its pharmacology and found that it contained a very poisonous alkaloid which he was not able to crystallize. He claimed that the alkaloid resembled Veratrine chemically, although it did not produce a typical veratrinic response.

In view of these findings, we have undertaken a systematic investigation of Stagger grass alkaloids. The chromatographic separation of total alkaloids on acid-washed alumina, using Reichstein's technique,[4] yielded four fractions. One was readily identifiable as Jervine. Two were unidentified ester alkaloids (tentatively called Alkaloid E and F) which were shown to be responsible for the high toxicity and hypotensive action of the plant extract. The last fraction was an alkamine which has never been isolated previously. It was also isolated directly from the total alkaloids by treatment with acetone. Initial observations indicated that it might be related to steroidal alkamines. In view of recent interest in veratrum alkaloids, we would like to give our preliminary results now. The chemistry of the hypotensive principles of the plant will be published in detail later. The pharmacology of all active principles will be published elsewhere.

The new alkaloid, for which we propose the name Amianthine, is a C_{27} compound. This formulation as well as the presence of Jervine in total alkaloids and the close relationship of Stagger grass to *Veratrum* species favor the assumption that it might be a steroidal or modified steroidal alkamine.

When Amianthine is dissolved in concentrated sulfuric acid it gives a yellow color. However, it remains colorless in 84% sulfuric acid, and in this respect it is significantly different from most alkamines isolated from *Veratrum album* and *Veratrum viride*. The alkaloid has a pK_a value of *ca.* 9.7 and appears to be a tertiary base. The infrared spectrum does not show a resolved band corresponding to NH between the OH band at 2.87 μ and a very weak band at 3.14 μ. There is a very strong band corresponding to a conjugated CO at 6.06 μ and a band half as strong at 6.20 μ indicative of a carbon–carbon double bond. The ultraviolet absorption spectrum in alcohol exhibits a maximum at 250 mμ, log ϵ 4.04, which also corresponds to a conjugated CO.

It readily absorbs two moles of hydrogen in acetic acid or alcohol solution using platinum as a catalyst. The tetrahydro derivative formed is prob-

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(1) W. C. Muenscher, "Poisonous Plants of the U. S. A.," The Macmillan Co., New York, N. Y., 1951.

(2) C. D. Marsh, A. B. Clawson and H. Marsh, *U. S. Dept. Agr. Bull.*, 710 (1918).

(3) C. L. Alsberg, *Science*, **39**, 958 (1914); C. L. Alsberg, *J. Phar. Exp. Therap.*, **3**, 473 (1911–1912).

(4) T. Reichstein and C. W. Shoppee, *Discussion of the Faraday Society*, No. **7**, 305 (1949).

ably a mixture of stereoisomers. One stereoisomer could be isolated. As expected, this product does not show any ultraviolet absorption and its infrared spectrum does not have any bands between 5–6.8 μ. However, the intensity of the OH band is about twice as strong as in Amianthine itself.

Amianthine has one active hydrogen (Found: 0.96 mole) which is derived from a primary or a secondary OH because of the ease with which an O-acetate was formed in pyridine and acetic anhydride at room temperature. Its infrared spectrum shows a typical ester CO band at 5.8 μ in addition to the band of conjugated CO at 6.06 μ.

Acknowledgment.—We are indebted to Dr. H. Boaz for the infrared spectra and their interpretation, and to Messrs. G. M. Maciak, H. L. Hunter and W. J. Schenck for microdeterminations. We thank Mr. R. J. Armstrong for his assistance in extraction of the crude drug. We are grateful to the late Prof. Friesner, of Butler University, for confirming the identity of the plant.

Experimental[5]

Extraction of the Roots and Leaves of Amianthium Muscaetoxicum Gray.—Ground dried roots and leaves (25 kg.) were extracted, after moistening with 15 l. of dilute ammonia, with three 150-l. portions of benzene. Each extraction was made by stirring for 5 hr. and allowing to macerate for 16 hr. The extracts were drained through filter pads into a stainless steel vacuum still. The combined extracts were concentrated to 5 l. at reduced pressure, and extracted exhaustively with a total of 3 l. of 5% tartaric acid. The aqueous phase was filtered from resinous material and made basic (*p*H 8–9) with concentrated ammonia. The free bases were extracted five times with chloroform, filtered and dried over anhydrous sodium sulfate and evaporated to dryness in vacuum. The yield was 25 g. of total alkaloids (0.1%).

Amianthine.—The amorphous mixture of total alkaloids (10 g.) was dissolved in 25 ml. of acetone and allowed to stand for 72 hr. After this time, the alkaloid crystallized in long prisms (550 mg.). After three recrystallizations from acetone, 250 mg. of pure material was obtained, m.p. 251–253° (dec.), $[\alpha]^{20}D$ −87° (*c* 0.1728 in $CHCl_3$). Identical material was obtained by chromatography of total alkaloids, after elution of ester alkaloids and Jervine, using a 1:1 mixture of methanol–chloroform. For analysis, the sample was dried at 120° (0.05 mm.) for 4 hr.

Anal. Calcd. for $C_{27}H_{41}O_2N$: C, 78.78; H, 10.03; N, 3.41. Found: C, 78.56; H, 9.82; N, 3.11.

Amianthine O-Acetate.—A mixture of 50 mg. of Amianthine in 5 ml. of anhydrous pyridine and 1 ml. of acetic anhydride was allowed to stand at room temperature for 12 hr. The reaction mixture was poured into ice-water, a few drops of concentrated ammonia added, and the whole extracted three times with chloroform. The chloroform extract was washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The amorphous colorless residue crystallized upon addition of dilute methanol. After two recrystallizations from dilute methanol long needles were obtained, m.p. 206–207° (dec.). For analysis the sample was dried at 120° (0.05 mm.) for 4 hr.

Anal. Calcd. for $C_{29}H_{43}O_3N$: C, 76.78; H, 9.55. Found: C, 76.52, 76.61; H, 9.56, 9.66.

Hydrogenation of Amianthine.—A mixture of 25 mg. of Amianthine in 95% methanol was hydrogenated using platinum catalyst. Absorption of two moles of hydrogen was complete after 90 minutes. After filtration of the catalyst and removal of the solvent, an amorphous residue resulted. Upon addition of aqueous methanol, the material crystallized forming thin needles and spherical crystals. The spherical modification could be mechanically separated under a magnifying glass. It melted at 266–267° (dec.). On admixture with Amianthine, it gave a depression of 25–30°. Lack of material prevented further characterization.

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The Reaction of Carbon Monoxide with Free Radicals

BY GERALD B. PORTER AND SIDNEY W. BENSON

RECEIVED FEBRUARY 10, 1953

Calculations based on the most recent experimental data[1,2] show that the reaction

$$CH_3 + CO \longrightarrow CH_3CO \qquad (1)$$

should have little or no activation energy. To investigate this reaction, the pyrolysis of di-*t*-butyl peroxide was chosen as a source of methyl radicals.[3] In a system containing di-*t*-butyl peroxide and carbon monoxide at a temperature greater than 150°, reaction 1 may occur and the acetyl radicals formed may either decompose

$$CH_3CO \longrightarrow CH_3 + CO \qquad (2)$$

or react with methyl radicals

$$CH_3CO + CH_3 \longrightarrow CH_3COCH_3 \qquad (3)$$

In addition, carbon monoxide may reduce *t*-butoxy radicals exothermically.

$$(CH_3)_3CO + CO \longrightarrow (CH_3)_3C + CO_2 \qquad (4)$$

Reaction 4 is analogous to the reaction suggested by Stone and Taylor[4] to explain the similar exothermic formation of carbon dioxide from carbon monoxide during the photolysis of hydrogen peroxide

$$OH + CO \longrightarrow CO_2 + H \qquad (5)$$

Radioactive monoxide provides a means of measuring the extent of reactions 3 and 4. Although experimentally, no radioactivity was detectable in the condensable products, maximum values of the rate constants of reactions 1 and 4 are still calculable.

The ratio of the yields of radioactive acetone to ethane is given by

$$\frac{\text{Yield of acetone*}}{\text{Yield of ethane}} \approx k_1k_3/k_2k_6(\text{CO})$$

leading to a maximum value for the rate constant, k_1, of 3 × 10^9 (moles/cc.)$^{-1}$ sec.$^{-1}$.

A similar calculation indicates that k_4 is less than 3 × 10^6 (moles/cc.)$^{-1}$ sec.$^{-1}$.

The fact that reactions 1 and 4 were not detectable in this system is not to be taken as indicating that these reactions will not occur at all. Rather, it shows the instability of acetyl and *t*-butoxy radicals under the conditions of these experiments. Indeed, it has been frequently observed that, because of reaction 2, no biacetyl is formed during the photolysis of acetone if the temperature is much above 100°.

We should like to express our appreciation to Dr.

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[5] All melting points are uncorrected. Infrared spectra were run in chloroform solution.

[1] M. Szwarc, *Chem. Revs.*, **47**, 75 (1950).

[2] D. H. Volman and W. M. Graven, *J. Chem. Phys.*, **20**, 919 (1952).

[3] J. H. Raley, F. F. Rust and W. E. Vaughan, THIS JOURNAL, **70**, 88 (1948).

[4] F. S. Stone and H. S. Taylor, *J. Chem. Phys.*, **20**, 1339 (1952).

A. W. Adamson for the radiocarbon used and to the Office of Ordnance Research for a grant which has made possible the present work.

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Some Bis-substituted Succinamides as Curare Substitutes. IV

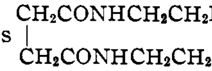
BY ARTHUR P. PHILLIPS

RECEIVED JANUARY 19, 1953

Earlier some series of dicarboxylic acid bis-aminoamides and their quaternary ammonium salts were described.[1,2] These had been made in conjunction with a family of bis-aminoalkyl esters of dicarboxylic acids and their quaternary ammonium salts[3] in a search for new drugs possessing curare-like activity. While powerful curariform agents were found in the ester series, most outstanding in the case of succinylcholine, the analogously constituted amides were nearly inactive in this sense. However, many of the series of bis-amides proved to act as powerful potentiators, both in duration and intensity of action, of the succinylcholine class of curare-like drugs. Succinylcholine potentiating ability in the various amide series was observed to occur in a wide range of chain lengths, from the malonic through the sebacic acid derivatives, but was frequently found to be maximal in the succinic, glutaric, adipic group. Thus it seemed useful to prepare a cross section of assorted bis-substituted amides from a particular dicarboxylic acid in the optimal region. This paper presents a number of such amides made from succinic acid.

TABLE I

SUBSTITUTED SUCCINAMIDES



$$\begin{array}{l} CH_2CONHCH_2CH_2R \\ | \\ CH_2CONHCH_2CH_2R \end{array}$$

R	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
$-CH(CH_3)_2$	141–142	$C_{14}H_{28}N_2O_2$	65.6	65.7	11.0	11.0	10.9	10.5
$-CH_2OCH_3$	146–147	$C_{12}H_{24}N_2O_4$	55.3	55.3	9.3	9.1	10.7	10.4
$-CH_2OCH(CH_3)_2$	122–123	$C_{16}H_{32}N_2O_4$	60.7	60.9	10.2	10.1	8.8	8.7
$-CH_2NHCH(CH_3)_2$	104–105	$C_{16}H_{34}N_4O_2$	61.1	61.1	10.9	10.6	17.8	17.8
$-CH_2N(CH_3)_2$	122–123	$C_{14}H_{30}N_4O_2$	58.7	58.5	10.5	10.2	19.6	19.8
$-CH_2N(CH_3)_3I$	211–212	$C_{16}H_{36}I_2N_4O_2$	33.7	33.7	6.4	6.4	9.8	9.7
$-CH_2N(CH_3)_2C_2H_5I$	167–168	$C_{18}H_{40}I_2N_4O_2$	36.1	35.9	6.7	6.4	..	..
$-CH_2N(CH_2CH_2)_2O$	125–126	$C_{18}H_{34}N_4O_4$	58.3	58.4	9.3	9.3	15.1	15.2
$-CH_2N(CH_2CH_2)_2O\cdot CH_3I$	162–163	$C_{20}H_{40}I_2N_4O_4$	36.7	36.7	6.2	6.2	..	..

The bis-isoamylsuccinamide, the first compound of Table I, is an isostere of one of the active potentiators of succinylcholine, the bis-dimethylaminoethylsuccinamide.[1] In Table I are summarized the details of structure, melting points and analytical data for a list of alkoxyalkyl- and alkylaminoalkylsuccinamides as well as for some derived bis-quaternary ammonium salts.

The pharmacology of these substances will be reported elsewhere. None of these compounds seemed to be as effective in prolonging the neuromuscular blocking action of succinylcholine as were the compounds described earlier.[1,2]

Experimental

The amides were prepared by the procedure of the previous publications.[1,2] Yields were nearly quantitative. The simple amides were purified by recrystallization from ethyl acetate, while the quaternary salts were recrystallized from methanol-ethyl acetate mixtures.

Acknowledgment.—The author is indebted to Mr. Samuel W. Blackman for the microanalyses included. The substituted propylamines were obtained through the courtesy of the American Cyanamid Company of Stamford, Conn.

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[1] A. P. Phillips, THIS JOURNAL, **73**, 5822 (1951).

[2] A. P. Phillips, *ibid.*, **74**, 4320 (1952).

[3] A. P. Phillips, *ibid.*, **71**, 3264 (1949).

5-Acenaphtheneacetic Acid

BY HENRY J. RICHTER

RECEIVED JANUARY 15, 1953

The preparation of an acenaphtheneacetic acid, from acenaphthene and α-chloroacetic acid, melting at 174–175° is described in the patent literature by Wolfram, *et al.*[1] In the equivalent British Patent, the acid is described as the 5-isomer,[2] but no melting point is indicated. In another patent[3] the same inventors describe the acid as 5-acenaphtheneacetic acid and give the melting point as 187°. Anderson and Wade[4] prepared 5-acenaphtheneacetic acid by the Willgerodt–Kindler reaction on the known 5-acenaphthenyl methyl ketone. The melting point reported is 179–180°. These authors indicate that they were unable to repeat the preparation of the acenaphthenacetic acid described by Wolfram, *et al.*, in the patent literature.

In this work 5-acenaphtheneacetic acid has been prepared by the condensation of α-chloroacetic acid and acenaphthene with the aid of ferric oxide and potassium bromide as catalysts.[5] The yield, based on the initial reactants, was quite low (28%). However, since a high proportion of the unreacted acenaphthene may be recovered, the preparation offers some advantage. A procedure for the purification of this acid involving fractional precipitation and crystallization of the sodium salt is de-

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[1] A. Wolfram, L. Schornig and E. Hausdorfer, German Patent 562,391 (Feb. 2, 1929); *C. A.*, **27**, 734 (1933).

[2] British Patent 330,916 (Feb. 19, 1929); *C. A.*, **24**, 6031 (1930).

[3] U. S. Patent 1,951,686 (March 20, 1934); *C. A.*, **28**, 3423 (1934).

[4] A. G. Anderson, Jr., and R. H. Wade, THIS JOURNAL, **74**, 2274 (1952).

[5] Y. Ogata and J. Ishiguro, *ibid.*, **72**, 4302 (1950).

scribed. The purified acid melted at 179.5–181°.[6] The position of the acetic acid residue in the acenaphthene nucleus was established by conversion to 5-acenaphthylmethylamine by the Curtius reaction[7] and treatment of the amine with nitrous acid to give 5-hydroxymethylacenaphthene.[8] A mixed melting point of this carbinol with that prepared by the lithium aluminum hydride reduction of the known 5-acenaphthoic acid showed no depression.

Experimental[9]

5-Acenaphtheneacetic Acid.—A mixture comprising 92 g. (0.6 mole) of acenaphthene, 28 g. (0.3 mole) of α-chloroacetic acid, 0.5 g. of potassium bromide and 0.2 g. of ferric oxide was heated on a sand-bath under gentle reflux for 24 hours. During this period of heating, the temperature of the melt reached 220°. The resulting dark mass was cooled and extracted exhaustively with warm 10% sodium hydroxide solution. Acidification of the dark alkaline extract precipitated 30 g. of dark and impure acid melting at 135–150°. There was also obtained 68 g. of dark, alkali-insoluble residue. The crude acid was dissolved in 250 ml. of warm alcohol, filtered, and the dark filtrate slowly diluted with water which precipitated a dark oil. The addition of water was continued until crystallization of the acid from the yellow liquor commenced, after which the solution was decanted from the precipitated oil. Further addition of water to the mother liquor yielded a pale yellow crystalline product, m.p. 150–160°. The precipitated oil was redissolved in alcohol and the separation repeated. There was thus obtained 18 g. of acid (28%, based on α-chloroacetic acid), which was further purified by solution in 300 ml. of hot 5% sodium hydroxide solution from which the sodium salt of the acid crystallized on cooling. It was filtered and washed with ice-water. Solution of the salt in warm water and acidification gave 13.5 g. of acid melting at 176–179°. Recrystallization of the sodium salt and final crystallization from dilute alcohol with the addition of decolorizing charcoal gave colorless needles, m.p. 179.5–181°.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.21; H, 5.70. Found: C, 79.24; H, 5.80.

Attempts to purify the crude alkaline extract of the reaction mixture by repeated crystallization and treatment with decolorizing charcoal were less satisfactory.

The amide was obtained as white needles from *n*-propanol, m.p. 236–237°.

Anal. Calcd. for $C_{14}H_{13}NO$: C, 79.58; H, 6.20. Found: C, 79.80; H, 6.53.

The phenacyl ester was obtained as fine white needles from alcohol, m.p. 89–90°.

Anal. Calcd. for $C_{22}H_{18}O_3$: C, 79.96; H, 5.48. Found: C, 80.00; H, 5.60.

The unreacted acenaphthene contained in the alkali insoluble residue was recovered by distillation, collecting the fraction boiling at 265–274°. There was obtained 39 g. (42% of the initial acenaphthene) which crystallized from alcohol as white needles, m.p. 95–96°, and formed a picrate, m.p. 161°.

Degradation of 5-Acenaphtheneacetic Acid.—The crude acid (7.2 g., 0.034 mole), m.p. 176–179°, was mixed with 40 ml. of dry benzene and 6 ml. of thionyl chloride and refluxed for 2 hours, after which the 5-acenaphtheneacetyl chloride was distilled collecting the fraction b.p. 185–195° at 11 mm. The yellow oil soon solidified; yield 4.6 g. (59%).

A mixture comprising 4.5 g. of the acid chloride, 2.2 g. of sodium azide, and 50 ml. of dry benzene was refluxed for 6 hours and then filtered. Concentrated hydrochloric acid, 40 ml., was added to the filtrate and the mixture refluxed for 4 hours, cooled, and the separated amine hydrochloride removed by filtration. There was obtained 2.8 g.—65%—of product which was recrystallized from dilute hydrochloric acid.[7]

Anal. Calcd. for $C_{13}H_{14}ClN$: N, 6.37; Cl, 16.16. Found: N, 6.30; Cl, 16.30.

The benzamide of the amine crystallized from dilute alcohol as fine white needles, m.p. 182–184°.

Anal. Calcd. for $C_{20}H_{17}NO$: C, 83.58; H, 5.97. Found: C, 83.33; H, 6.05.

The benzenesulfonamide crystallized as fine white needles from alcohol, m.p. 148–149°.

Anal. Calcd. for $C_{19}H_{17}NO_2S$: C, 70.56; H, 5.28. Found: C, 70.86; H, 5.33.

5-Hydroxymethylacenaphthene.—A solution of 0.2 g. of 5-acenaphthenemethylamine hydrochloride in 75 ml. of water was treated with 8 drops of 3 *N* hydrochloric acid followed by an excess of sodium nitrite solution. This mixture, on standing overnight at room temperature, deposited a white solid which was removed by filtration, dried and crystallized from benzene. The white needles melted at 156–157° (lit. 153.8–154°).[8] A mixed melting point of the 5-hydroxymethylacenaphthene obtained by the degradation of 5-acenaphtheneacetic acid and a sample prepared as described below by the reduction of the known 5-acenaphthoic acid showed no depression.

5-Acenaphthoic Acid.—This acid was prepared in 57% yield by treating 46 g. (0.2 mole) of 5-bromoacenaphthene in 125 ml. of absolute ether with *n*-butyllithium prepared from 30 g. (0.32 mole) of *n*-butyl chloride and 4.5 g. of lithium wire[10] in 200 ml. of ether. The resulting solution was poured on powdered solid carbon dioxide, allowed to stand one hour, acidified, and the precipitated acid filtered. This product was purified by washing a solution in 5% sodium hydroxide with ether followed by precipitation. There was thus obtained 22.5 g. of acid, m.p. 214–218°. Crystallization from dilute alcohol gave a product, m.p. 220–221°.[11]

5-Hydroxymethylacenaphthene by Reduction of 5-Acenaphthoic Acid.—Finely divided solid 5-acenaphthoic acid (19.8 g., 0.1 mole) was slowly added to a solution of 7.6 g. of lithium aluminum hydride in 600 ml. of dry ether[12] contained in a 2-l. three-neck flask fitted with a stirrer and reflux condenser. After stirring for 1 hour, the mixture was decomposed by the slow addition of 250 ml. of 10% sulfuric acid. The precipitated solid was filtered and extracted with warm 5% sodium hydroxide. There was thus obtained 13.8 g. of the carbinol. An additional 2.6 g. was obtained by evaporating the initial ether filtrate to give 16.4 g. (82%) of carbinol which crystallized from alcohol as fine white needles, m.p. 155–156°.

The acetate, obtained by reaction with acetic anhydride in pyridine, crystallized from hexane, m.p. 60.5–61.5°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.64; H, 6.22. Found: C, 79.9; H, 6.31.

Acknowledgment.—The author takes pleasure in thanking the Research Corporation for a Frederick Gardner Cottrell grant to support this work.

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[6] Anderson and Wade[4] were unable to cyclize this acid to 1-pyracenone. Our attempts to effect this ring closure likewise were unsuccessful.

[7] P. A. S. Smith, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 387.

[8] L. F. Fieser and J. E. Jones, THIS JOURNAL, **64**, 1667 (1942).

[9] All melting points are corrected.

(10) Metalloy Corp., Rand Tower, Minneapolis, Minn.

(11) H. Gilman, W. Langham and F. W. Moore, THIS JOURNAL, **62**, 2332 (1940).

(12) R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 2548 (1947).

Hydrogen Bonding Ability and Structure of Ethylene Oxides

BY SCOTT SEARLES, MILTON TAMRES AND ELLIS R. LIPPINCOTT

RECEIVED JANUARY 15, 1953

The very low electron donor ability of substituted ethylene oxides, compared with other cyclic ethers, in hydrogen bonding was reported recently.[1] The

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(1) S. Searles and M. Tamres, THIS JOURNAL, **73**, 3704 (1951).

parent compound, ethylene oxide, was not included in the series reported because its boiling point is below the principal temperature at which spectroscopic and calorimetric measurements were made. The study has now been extended to ethylene oxide by measuring the heat of mixing with chloroform at 3°.

The result, compared with similar data for other ethers, is presented in the table and confirms the effect of ring size on electron donor ability previously deduced for cyclic ethers: 3-membered ring < 6-membered ring < 5-membered ring < 4-membered ring. It is also apparent that the usual electronic effects of substituents are operative in the 3-membered ring.

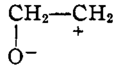
TABLE I

HEATS OF MIXING WITH CHLOROFORM AT 3°

Compound	ΔH (cal./mole)
Ethylene oxide	365
Propylene oxide	470
Epichlorohydrin	185
Styrene oxide	245
Cyclohexane oxide	666
Trimethylene oxide	760[a]
Tetrahydrofuran	750[a]
Tetrahydropyran	640[a]
Diethyl ether	650[a]

[a] From reference 1.

The concept of electron donor ability in hydrogen bonding being a measure of relative electron density[2] leads to the conclusion that the oxygen in 3-membered ring ethers is more positive (or electronegative) than in larger ring ethers or in acylic ethers. This observation may be of interest with regard to the recent proposals for the structure of ethylene oxide. It seems inconsistent with Zimakov's proposal that the structure is a resonance hybrid of I and II with a unit negative charge on each carbon atom,[3] for this would lead to the expectation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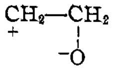
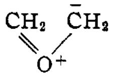
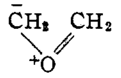

II

that the oxygen would be much less electronegative than usual. Also the C–O dipole would be much greater in ethylene oxide than in acyclic ethers, whereas it actually is about the same.[4-6] Walsh's structures for ethylene oxide and cyclopropane,[7] showing a high electron concentration in the center of the three-membered rings, would suggest that the exterior of such rings would have a lower electron density than normal for the atoms involved. This might explain the poor donor ability of ethylene oxide in hydrogen bonding, but these structural suggestions were not borne out by a recent quantum mechanical analysis.[8] The latter has indicated that, for strained systems, the hybridized orbitals employed for bonding attain maximum overlap in such a way that altered valence angles or "bent bonds" are realized. Detailed calculations were made on cyclopropane, but the results can be applied to other three-membered ring systems.[9]

The orbitals used in these exterior bent bonds of the ring are in a favorable position for some overlap with *p*-orbitals from adjacent atoms, thus giving rise to a conjugation or delocalization effect, which has been observed experimentally with cyclopropyl ketones,[10] α,β-epoxyketones,[7,9] and ethylenimine ketones.[9]

A similar effect can be employed to explain the positive nature of the oxygen atom in ethylene oxide. Since the *p*-orbitals of the oxygen are nominally filled, there can be no overlap of them with the bent bonds of the ring unless the unshared pair of electrons participates in bonding to the carbon atoms. This delocalization, which leads to a formal positive charge on the oxygen, may be expressed by resonance structures III and IV.


III


IV

The fact that the dipole moment of ethylene oxide is smaller and not larger than that of trimethylene oxide[4] is in agreement with these ideas. This delocalization does not cause significant alteration of the normal carbon–oxygen single bond distance,[11] which has been interpreted reasonably on a pure valence state approach (with bent bonds), indicating that III and IV do not make very large contributions. Small changes in electron distribution, however, should make relatively great differences in hydrogen bonding ability and in dipole moments. Such contributions of III and IV may also be partly responsible for the normal carbon–oxygen distance of 1.436 Å. observed in ethylene oxide.[11] Ordinarily one might expect it to be larger because of the weakness of the bond, which is evident from the ease of cleavage by reagents, but any double bond character due to forms III and IV would shorten up the bond.

A similar explanation will apply to other three-membered heterocyclics, the heteroatoms of which formally have unshared but filled p-orbitals. The low basicities observed with ethylenimine and ethylene sulfides (unpublished observations in these laboratories) are in accord.

A delocalization of unshared p-electrons on an atom bonded to a small carbocyclic ring has been postulated by Roberts and collaborators[12] to explain the electronegative character of such rings. In the present case, a delocalization of unshared p-elec-

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[2] M. Tamres, S. Searles, E. M. Leighly and D. W. Mohrman, Abstracts, 122nd Meeting of American Chemical Society, September, 1952, p. 41 M.

[3] P. Zimakov, *Acta Physicochem., U. R. S. S.*, **21**, 401 (1946).

[4] H. D. Robles, *Rec. trav. chim.*, **58**, 111 (1939).

[5] W. L. G. Gent, *Trans. Faraday Soc.*, **45**, 1021 (1949).

[6] There is some difficulty in making a direct comparison, because cyclic ethers normally have considerably higher polarity than their open chain analogs (H. C. Freeman, R. J. W. LeFevre and F. Maramba, *J. Chem. Soc.*, 1649 (1952)). Therefore, comparison with other cyclic ethers with larger rings may be more informative, and here the ethylene oxide dipole does seem abnormally low (ref. 4).

[7] A. D. Walsh, *Nature*, **159**, 712 (1947); *Trans. Faraday Soc.*, **45**, 179 (1949).

[8] C. A. Coulsen and W. E. Moffitt, *Phil. Mag.*, [7] **40**, 1 (1949).

[9] N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952).

[10] M. T. Rogers, THIS JOURNAL, **69**, 2544 (1947); R. P. Mariella and R. R. Raube, *ibid.*, **74**, 518 (1952).

[11] G. L. Cunningham, A. W. Boyd, R. J. Myers, W. D. Gwinn and W. I. LeVan, *J. Chem. Phys.*, **19**, 676 (1951).

[12] M. T. Rogers and J. D. Roberts, THIS JOURNAL, **68**, 843 (1946); J. D. Roberts and V. C. Chambers, *ibid.*, **73**, 5031 (1951).

trons on a heteroatom in a three-membered ring is employed to explain the electronegative character of that atom.

Experimental

Heats of Mixing Determinations.—The apparatus and method have been described previously.[13] The ethers were introduced in sealed ampoules in the manner described for volatile ethers in a previous paper.[1] A slightly different value (461 cal./mole) was reported previously for the heat of mixing of propylene oxide with chloroform, but the agreement is within experimental error.

[13] G. G. Zellhoefer and M. J. Copley, THIS JOURNAL, **60**, 1343 (1938).

DEPARTMENTS OF CHEMISTRY
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Tracer-diffusion in Liquids. V. Self-diffusion Isoelectric Glycine in Aqueous Glycine Solutions[1]

BY JUI H. WANG

RECEIVED JANUARY 8, 1953

The ordinary chemical concentration gradient diffusion of isoelectric glycine in its aqueous solutions has been measured by many workers.[2-4] The dependence of these chemical concentration gradient diffusion coefficients upon the concentration of solution have been compared[2] with those calculated from Gordon's formula[5] where D and D_0

$$D = D_0\left(1 + c\frac{\partial \ln y}{\partial c}\right)\frac{\eta}{\eta_0} \qquad (1)$$

are the diffusion coefficients of the solute in its solutions at molal concentration c and at infinite dilution, respectively, y the activity coefficient of the solute at concentration c, and η and η_0 are the macroscopic viscosities of the solution and pure solvent, respectively. Lyons and Thomas showed that for the case of aqueous glycine solutions, the factor (η/η_0) overcorrects the retardation of diffusion due to change in mobility of the glycine molecule. These authors inferred from their measured temperature dependence of the diffusion coefficient of glycine that the above overcorrection is due to the breaking down of the structure of water in the immediate vicinity of glycine molecules.

In self-diffusion, however, since the composition of solution is chemically uniform along the diffusion path, the activity coefficient of the diffusing tracer-molecules is constant, the term $(1 + c \times (\partial \ln y/\partial c))$ reduces to unity. Furthermore, since in self-diffusion there is no net transport of solvent in any direction, the "hydrodynamic effect" of Onsager and Fuoss[6] (which is often referred to as the "electrophoretic effect" in the diffusion of electrolytes) vanishes. We may thus expect the self-diffusion coefficient of isoelectric glycine to be theoretically simpler and hence possibly even more interesting. In the present work the self-diffusion coefficients of isoelectric glycine in its aqueous solutions at 25° are measured and discussed.

Experimental

Tracer Solution.—The radioactive glycine ($^{+}H_3NCH_2COO^{-}$) was supplied by Tracerlab, Inc., Boston, Mass., and obtained on allocation from the Isotopes Division, U.S. Atomic Energy Commission, Oak Ridge, Tennessee. The specific activity of this radioactive glycine was about 0.02 mc./mg. A dilute solution of this radioactive glycine in conductivity water was prepared and kept in a sterilized bottle at 0° as stock solution. In making radioactive solution for diffusion measurement, a small measured volume of this stock solution was evaporated to dryness in a platinum crucible under a heat lamp. The radioactive residue (practically invisible) was dissolved in inactive glycine solution of accurately known concentration and with pH at 5.98. The increase in total glycine concentration due to the dissolution of the above mentioned radioactive residue is negligible.

Diffusion Measurements.—All the measurements were carried out at 25.00 ± 0.01°. The experimental procedure is the same as that described in Paper I of this series.

Analysis of Samples.—The counting of the radioactive diffusion samples was carried out by means of a windowless flow counter: In order to eliminate errors due to self-absorption of the weak β-particles from C^{14}, the volumes of the c_0-samples were so adjusted that each of them contained approximately the same amount of solid material as the corresponding c_{av}-sample. All samples were dried in desiccators for more than 24 hours before counting. Consequently, the measured values of (c_{av}/c_0), which determine the values of Dt/l^2, are practically free from self-absorption errors.

Results and Discussion

The self-diffusion coefficients of isoelectric glycine in its aqueous solutions at 25° as determined in the present work are listed in Table I.

TABLE I

SELF-DIFFUSION COEFFICIENTS OF ISOELECTRIC GLYCINE IN AQUEOUS GLYCINE SOLUTIONS AT 25°

Concn., mole/l.	$D \times 10^5$, cm.²/sec.
0.01	1.06 ± 0.02
.10	1.05 ± .02
.25	1.03 ± .02
.50	0.990 ± .026
1.00	.929 ± .018
1.50	.871 ± .018
2.00	.830 ± .011

Each value listed in Table I is the average result of 3 to 12 measurements. These self-diffusion coefficients are plotted *vs.* volume molal concentration of glycine in Fig. 1. Diffusion coefficients of glycine for ordinary chemical concentration gradient diffusion as reported by Lyons and Thomas[2] are also included in Fig. 1 for comparison. From the definition of the diffusion coefficients, it is easy for us to see that at infinite dilution the self-diffusion coefficient of isoelectric glycine should be identical to that for chemical concentration gradient diffusion. Figure 1 indicates that as the concentration approaches zero, the two sets of diffusion coefficients tend toward the same limiting value. Since the optical method used by Lyons and Thomas has been developed to a high degree of precision, this agreement can be considered as a further confirmation on the general reliability of the present capillary method for measuring tracer-diffusion in liquids. The dotted curve in Fig. 1 represents values of $D/(1 + c(\partial \ln y/\partial c))$ in equation (1) calculated

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[1] Contribution No. 1135 from the Department of Chemistry of Yale University. Previous papers of this series: THIS JOURNAL, **74**, 1182, 6317 (1952); *ibid.*, 1611 (1952); *ibid.*, 1612 (1952); *ibid.*, **75**, 1769 (1953).

[2] M. Lyons and J. V. Thomas, *ibid.*, **72**, 4506 (1950).

[3] L. G. Longsworth, *ibid.*, **74**, 4155 (1952).

[4] See E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publ. Corp., New York, N. Y., 1943, p. 412 for earlier references.

[5] A. R. Gordon, *J. Chem. Phys.*, **5**, 522 (1937).

[6] L. Onsager and R. M. Fuoss, *J. Phys. Chem.*, **36**, 2689 (1932).

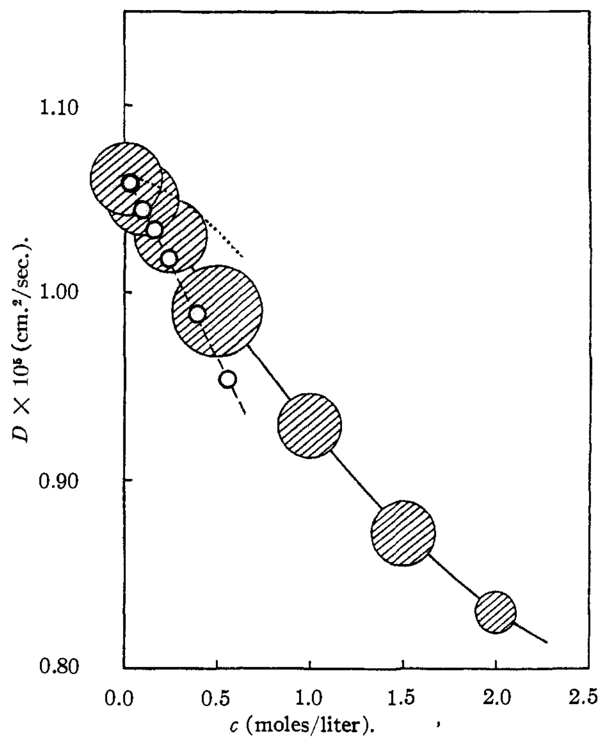

Fig. 1.—Diffusion coefficients of isoelectric glycine in its aqueous solution at 25°: ●, self-diffusion coefficients determined in the present work; O, chemical concentration gradient diffusion coefficients determined by Lyons and Thomas.

by Lyons and Thomas from their data. It may be seen from Fig. 1 that these values, which when corrected for "hydrodynamical effect" would represent the mobilities for chemical concentration gradient diffusion, are higher than the self-diffusion coefficients of isoelectric glycine at the corresponding concentrations. From this we may infer that the actual mobilities for the chemical concentration gradient diffusion of isoelectric glycine are still higher than the corresponding self-diffusion coefficients.

A possible cause of this decrease in self-diffusion coefficient of isoelectric glycine with increasing concentration in dilute solutions is that the actual driving force for self-diffusion (equal to the absolute temperature times the entropy gradient) is opposed by a smaller but finite force due to the time of relaxation effect. This time of relaxation effect is due to the interaction between dipolar ions and therefore should presumably increase with concentration of the solution. The effect of interaction between dipolar ions on the equilibrium properties of these solutions in the dilute concentration range have been discussed by Fuoss.[7] But the quantitative formulation of a theory for the relaxation effect in the self-diffusion of dipolar ions analogous to that for the diffusion of simple spherical ions[8] appears to be difficult because of the absence of spherical symmetry of charge distribution of both the diffusing dipolar ion and its surrounding atmosphere of dipolar ions. Thus, the equilibrium charge distribution surrounding a diffusing dipolar ion can be disturbed both by the translational motion of the center of mass of the dipolar ion (as in the case of self-diffusion of simple spherical ions), or by a pure rotation of the latter. Since these two mechanisms are probably linked together in the actual process of diffusion, it is difficult at this time to make quantitative calculations of the relaxation effect without introducing further simplifying assumptions of doubtful validity. It appears advisable, therefore, to postpone detailed discussion of the present subject until more data on the self-diffusion of dipolar ions have become available.

Acknowledgment.—The present work is supported by a du Pont de Nemours Grant-in-Aid and by Contract AT-(30-1)-1375 between the U. S. Atomic Energy Commission and Yale University.

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[7] R. M. Fuoss, THIS JOURNAL, **56**, 1024 (1934); *ibid.*, **58**, 982 (1936).

[8] L. Onsager, *Ann. N. Y. Acad. Sci.*, **46**, 241 (1945).

The Uronic Acid Component of Chondroitinsulfuric Acid[1]

BY M. L. WOLFROM AND W. BROCK NEELY

RECEIVED FEBRUARY 13, 1953

Hexosamine glycosides hydrolyze with difficulty and when hexosamines are glycosidically linked to a hexuronic acid, as in the cartilage heteropolysaccharide chondroitinsulfuric acid,[2,3] the acid conditions requisite to break this bond lead largely to the destruction of the uronic acid moiety. In the case of the related polysaccharides heparin and "mucoitinsulfuric acid,"[4] this difficulty was overcome by the employment of an oxidative hydrolysis with bromine and concentrated sulfuric acid at 0°, whereby the D-glucuronic acid entity present was recovered as D-glucaric (D-glucosaccharic) acid. We report herein the extension of this procedure to cartilage chondroitinsulfuric acid whereby its hexuronic acid component is adequately identified as D-glucuronic acid, in confirmation of the work of Bray, Gregory and Stacey,[5] who isolated a crystalline methyl ether of this substance on acid hydrolysis of the methylated, degraded polysaccharide. In early experiments, Levene and Jacobs[6] obtained a silver salt on treatment of chondroitinsulfuric acid, designated glycothionic acid by them, with hydrobromic acid and bromine under unspecified conditions. The silver content of this salt was in agreement with that required by a hexuronic acid but the substance was not further characterized.

Experimental

An amount of 500 mg. of purified barium chondroitinsulfate (from cartilage)[3] was dissolved at 0° in a mixture of 10 ml. of concentrated sulfuric acid (sp. gr. at 15.56°, 1.84), 4 ml. of water and 10 drops of bromine and maintained at 3° for 6 days. Additional quantities of bromine were added

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[1] Supported by fellowship funds granted by The Ohio State University Research Foundation to the university for aid in fundamental research (Project R-11670-P369).

[2] P. A. Levene, *J. Biol. Chem.*, **140**, 267 (1941).

[3] M. L. Wolfrom, R. K. Madison and M. J. Cron, THIS JOURNAL, **74**, 1491 (1952).

[4] M. L. Wolfrom and F. A. H. Rice, *ibid.*, **68**, 532 (1946); **69**, 1833 (1947).

[5] H. G. Bray, J. E. Gregory and M. Stacey, *Biochem. J.*, **38**, 142 (1944).

[6] P. A. Levene and W. A. Jacobs, *J. Exptl. Med.*, **10**, 557 (1908).

at intervals to hold it in excess. After bromine removal by aeration, the reaction mixture was poured slowly into 125 ml. of ice and water and the acid was neutralized in the cold with barium carbonate. The precipitate was removed by filtration and triturated with 30 ml. of 1% aqueous potassium hydroxide and again filtered. The combined filtrates were neutralized with acetic acid and concentrated under reduced pressure at 30–40° to a sirup which was treated with 80 ml. of a 1% solution of hydrogen chloride in anhydrous methanol and again concentrated under reduced pressure to a sirup. The sirup was extracted with 30 ml. of absolute ethanol, filtered and again concentrated to a sirup under reduced pressure. This sirup was dissolved in 4 ml. of water and the solution brought to *ca.* *p*H 7 with solid potassium bicarbonate. Glacial acetic acid (4 ml.) was added and the solution was maintained at 15° overnight. Crystals formed which were removed by filtration and were recrystallized by dissolving in aqueous potassium bicarbonate and adding an equal volume of glacial acetic acid; yield 50 mg., $[\alpha]^{24}\mathrm{D}$ +10° (*c* 1.8 as the dipotassium salt). The rotation was assayed by solution in water containing an equivalent (to phenolphthalein) quantity of potassium bicarbonate and was in agreement with the previously recorded[4] value (+10°). X-Ray powder diffraction data were in exact agreement with those produced by an authentic specimen of potassium acid D-glucarate (D-glucosaccharate): 4.439 (1), 3.934 (3), 3.302 (5), 2.771 (2), 2.392 (4).[7]

On repeating the above procedure with omission of the bromine oxidant, no potassium acid D-glucarate was isolable.

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[7] Interplanar spacing in Å. of the five most intense lines; estimated visually; 1 = strongest; λ = 1.5418 Å.

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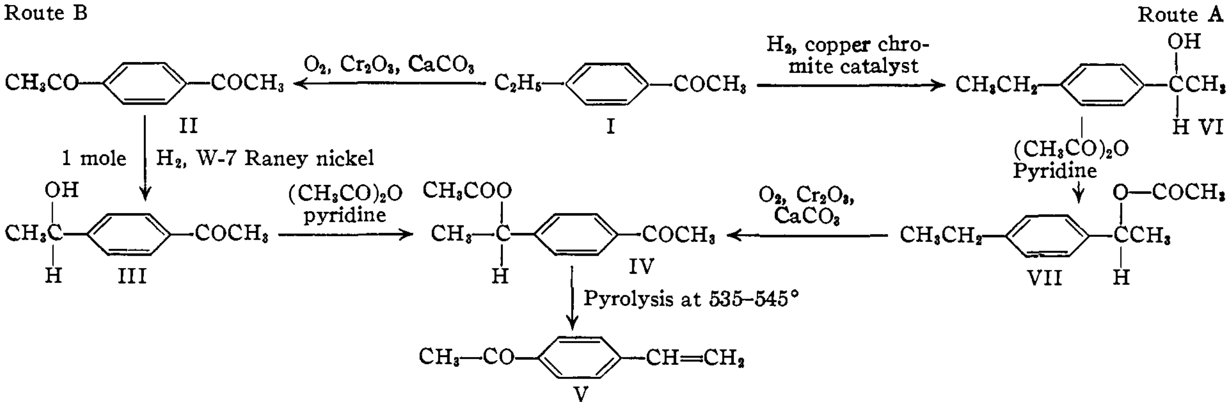
p-Vinylacetophenone: The Disproportionation of *p*-Acetophenylmethylcarbinol[1]

BY J. L. R. WILLIAMS

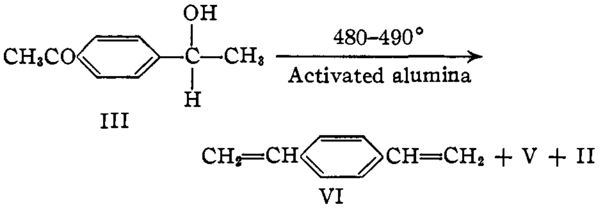
RECEIVED JANUARY 29, 1953

Two routes for the preparation of *p*-vinylacetophenone from *p*-ethylacetophenone which have been found are shown below.

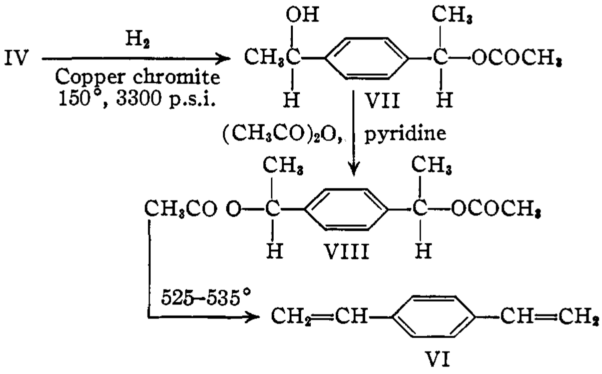


In route A, *p*-ethylacetophenone (I) was hydrogenated to *p*-ethylphenylmethylcarbinol (VI) which was acetylated and oxidized to *p*-acetophenylmethylcarbinol acetate (IV). By route B, *p*-ethylacetophenone was oxidized to *p*-diacetylbenzene (II) which was hydrogenated over W-7 Raney nickel to *p*-acetophenylmethylcarbinol (III) and then converted by acetylation to *p*-acetophenylmethylcarbinol acetate (IV). *p*-Acetophenylmethylcarbinol acetate from both routes was pyrolyzed at 530–545° over glass beads to yield *p*-vinylacetophenone (V).

p-Acetophenylmethylcarbinol (III) was alternately prepared by de-esterification of *p*-acetophenylmethylcarbinol acetate (IV) using sodium methoxide and methanol. Vapor-phase dehydration of *p*-acetophenylmethylcarbinol over activated alumina yielded not only *p*-vinylacetophenone but also *p*-diacetylbenzene (II) and *p*-divinylbenzene (VI) by disproportionation.



p-Divinylbenzene was also prepared from *p*-acetophenylmethylcarbinol acetate by the following scheme



Experimental

***p*-Ethylphenylmethylcarbinol Acetate (VII), Route A.**—A mixture of 250 g. (1.69 moles) of *p*-ethylacetophenone and 25 g. of copper chromite catalyst (Harshaw Cu-X-649-57-P) was hydrogenated in the usual way at 125° and 4500 p.s.i. until 1.69 moles of hydrogen had been absorbed. The resulting material was heated on the steam-cone for 16 hours with 250 cc. of acetic anhydride and 5 cc. of pyridine. Distillation through a 12-in. Vigreux column yielded 220 g. (66% of theory) of *p*-ethylphenylmethylcarbinol acetate, b.p. 79° (0.9 mm.), $n^{25}\mathrm{D}$ 1.4956.

***p*-Acetophenylmethylcarbinol Acetate (IV), Route A.**—In a liquid phase oxidizing apparatus consisting of a large test-tube equipped with a gas disperser, and a water take-off and reflux condenser, there was placed 220 g. (1.15 moles) of *p*-ethylphenylmethylcarbinol acetate, 1 g. of chromium sesquioxide and 15 g. of calcium carbonate. Air was forced through the disperser, and the temperature of the reaction mixture was maintained at 130–140° for 28 hours by means

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[1] Communication No. 1535 from the Kodak Research Laboratories.

of an electrically heated oil-bath. The reaction mixture was filtered free from catalyst and heated at 110° for two hours after the addition of 100 cc. of acetic anhydride and 25 g. of sodium acetate. The cooled reaction mixture was washed with two 500-cc. portions of water and the organic material was dried over anhydrous magnesium sulfate. Distillation through a 12-in. Vigreux-type column yielded the following fractions: (1) 98 g., b.p. 71–105° (0.25 mm.), n^{25}D 1.4962; (2) 58 g., b.p. 105° (0.25 mm.), n^{25}D 1.5150. On considering fraction (1) as recovered *p*-ethylphenylmethylcarbinol acetate, fraction (2) represented a 44.5% yield of *p*-acetophenylmethylcarbinol acetate.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8. Found: C, 69.7; H, 6.9.

The 2,4-dinitrophenylhydrazone of *p*-acetophenylmethylcarbinol acetate melted at 223–224°.

Anal. Calcd. for $C_{18}H_{18}O_6N_4$: C, 56.0; H, 4.7; N, 14.5. Found: C, 56.1; H, 4.8; N, 15.0.

***p*-Vinylacetophenone (V), Route A.**—A mixture of 52 g. (0.25 mole) of *p*-acetophenylmethylcarbinol acetate and 60 cc. of thiophene-free benzene was passed at a rate of one drop per second through a 25-mm. o.d. Pyrex tube packed for a distance of 30 inches with glass beads and maintained at 535–545° by means of an electrically controlled furnace. The reactants and products were flushed through the tube by a slow stream of nitrogen into a Dry-Ice trap. Six grams of polymer formed in the cooler portion of the reaction tube during pyrolysis. The trapped products were washed with two 100-cc. portions of water, dried over anhydrous magnesium sulfate, and distilled to yield 20 g. of material, b.p. 63–78° (0.31 mm.), m.p. 20–25°. Recrystallization from 25 cc. of hexane gave 15 g. (40.8% of theory) of *p*-vinylacetophenone, m.p. 34–35°. A sample recrystallized twice from hexane had m.p. 37–37.5°.

Anal. Calcd. for $C_{16}H_{10}O$: C, 82.3; H, 6.9. Found: C, 81.9; H, 6.7.

The 2,4-dinitrophenylhydrazone melted at 225–226.5°.

Anal. Calcd. for $C_{16}H_{13}O_4N_4$: C, 59.1; H, 4.0; N, 17.2. Found: C, 59.5; H, 4.6; N, 17.0.

The oxime melted at 118–119°.

Anal. Calcd. for $C_{10}H_{11}ON$: C, 75.1; H, 6.9; N, 8.7. Found: C, 74.6; H, 6.7; N, 9.2.

***p*-Acetophenylmethylcarbinol Acetate (IV), Route B.**—*p*-Diacetylbenzene was prepared by catalytic oxidation of *p*-ethylacetophenone, using chromium sesquioxide according to the method of Hochwalt.[2]

In a Parr low-pressure hydrogenation apparatus there was placed 64.8 g. (0.4 mole) of *p*-diacetylbenzene, 32 g. of freshly prepared, alcohol-washed W-7 Raney nickel,[3] and 175 cc. of methanol (Eastman Kodak Co., White Label). The reaction vessel was evacuated and flushed three times with hydrogen in the usual way and pressured to 50 p.s.i. After shaking for 32 minutes, the pressure drop was 30 pounds (theory 29 lb.), at which time shaking was stopped. The catalyst was removed and the reaction mixture evaporated at the water pump. At this stage the reaction mixture presumably consisted of *p*-ethylacetophenone, 1,4-bis-(α-hydroxyethyl)-benzene, and the desired product. No attempt was made to separate the products, but the reaction mixture was acetylated by heating with 150 cc. of acetic anhydride and 5 cc. of pyridine on the steam-cone for 16 hours. Distillation through a 6-in. Vigreux-type column resulted in the following fractions: (1) 1 g., b.p. 97–100° (0.2 mm.); (2) 2.0 g., b.p. 100–101° (0.2 mm.); (3) 15 g., b.p. 100–103° (0.2 mm.); (4) 50 g., b.p. 103–107° (0.2 mm.), n^{25}D 1.5168. Fraction (4) represented 60.5% of the theoretical yield of *p*-acetophenylmethylcarbinol acetate.

***p*-Vinylacetophenone (V), Route B.**—A solution of 41 g. (0.22 mole) of fraction (4) (*p*-acetophenylmethylcarbinol acetate) in 50 cc. of thiophene-free benzene was pyrolyzed as described above for route A. Distillation yielded the following fractions: (1) 3.0 g., b.p. 60° (0.3 mm.); (2) 5.0 g., b.p. 60–63° (0.29 mm.); (3) 14 g., b.p. 63–67° (0.29 mm.), m.p. 36–38° (porous plate). Fraction (3) represented 42.5% of the theoretical yield of *p*-vinylacetophenone. The 2,4-dinitrophenylhydrazone melted at 225°. A mixture of 1.1 g. of fraction (3) and 0.05 g. of benzoyl peroxide was heated at 65° for 16 hours to yield a clear, hard polymer.

***p*-Acetophenylmethylcarbinol (III).**—A mixture of 100 g. (0.48 mole) of *p*-acetylphenylmethylcarbinol acetate, prepared as above for route A, 250 cc. of methanol (Eastman Kodak Co., White Label) and 1.0 g. of sodium methoxide (Mathieson Chemical Corp.) was allowed to stand at room temperature (28°) for one-half hour. The reaction mixture was made acidic with 5% hydrogen chloride in methanol. The excess hydrogen chloride was removed at the water pump and the liquid distilled at atmospheric pressure to give 34 cc. of methyl acetate, b.p. 54–59°.

After all of the methanol had distilled, the residual liquid was distilled *in vacuo* through a 6-in. Vigreux-type column to yield the following fractions: (1) 19 g., b.p. 118–120° (0.4 mm.), n^{25}D 1.5444; (2) 34 g., b.p. 120° (0.5 mm.), n^{25}D 1.5462; (3) 8 g., b.p. 122° (0.6 mm.), n^{25}D 1.5452. The combined fractions weighed 61 g., representing 76.8% of the theoretical yield of *p*-acetophenylmethylcarbinol.

Anal. Calcd. for $C_{10}H_{11}O_2$: C, 73.1; H, 7.4. Found: C, 72.7; H, 7.7.

The 2,4-dinitrophenylhydrazone was prepared, and, after recrystallization from alcohol and water, it melted at 204–205°.

Anal. Calcd. for $C_{16}H_{16}N_4O_5$: C, 55.8; H, 4.7; N, 16.3. Found: C, 55.8; H, 5.0; N, 16.3.

The α-naphthylurethan of *p*-acetophenylmethylcarbinol melted at 133.5–134.5° after recrystallization from a mixture of hexane and ethyl acetate.

Anal. Calcd. for $C_{21}H_{19}O_3$: C, 75.7; H, 5.7; N, 4.2. Found: C, 75.7; H, 5.6; N, 3.9.

Disproportionation of *p*-Acetophenylmethylcarbinol during Dehydration over Activated Alumina.—Harshaw activated alumina (Al-0104-T-$^1/_8$ inch) was preheated in a stream of air for six hours at 550°. The catalyst was cooled to 480° and used immediately as follows.

One hundred grams (0.61 mole) of *p*-acetophenylmethylcarbinol was passed at a rate of one-half drop per second through a 25-mm. o.d. Pyrex tube packed for a distance of 1 in. with glass beads, followed by 28 in. of the above catalyst, then 1 in. of glass beads. The tube was maintained at 480–490° by means of an electrically heated furnace. The reactants and products were swept through the tube by means of dry nitrogen flowing at the rate of 6 l. per hour. Several Dry Ice traps were required to condense the gaseous products. The combined condensates were diluted with 200 cc. of benzene, 10 g. of water was separated, and the organic material dried over anhydrous magnesium sulfate. After the addition of a trace of picric acid, the benzene was removed at the water pump. An equal volume of hexane was added to the residue, and, after cooling in crushed ice, 6 g. of a white solid, m.p. 109–110°, was filtered off. This material was *p*-diacetylbenzene, as determined by a mixed melting point with an authentic sample of *p*-diacetylbenzene.

The hexane was removed from the mother liquors at the water pump, and the residue distilled *in vacuo* through a 6-in. Vigreux-type column to yield the following fractions: (1) 8.5 g., b.p. 48.5–60 (0.75 mm.), m.p. 4–10°, n^{25}D 1.5770; (2) 8.6 g., b.p. 60–73° (0.75 mm.), m.p. 22.5–24°, n^{25}D 1.5791; (3) 15.5 g., b.p. 73–83° (0.75 mm.), m.p. 24–28°, n^{25}D 1.5720.

One-gram portions of the above fractions were titrated for unsaturation by the standard bromide–bromate technique, using $^1/_{12}$ *M* solution:

	Bromide–bromate, cc.
Fraction (1)	46.7
Fraction (2)	26.19
Fraction (3)	24.57
Pure *p*-vinylacetophenone	28.0

These titrations indicated that fraction (1) contained considerable divinylbenzene, although it was not isolated in pure form. Fractions (2) and (3), when recrystallized from 20 cc. of hexane, gave 18.6 g. of *p*-vinylacetophenone (20.9% of the theoretical yield).

***p*-(α-Hydroxyethyl)-phenylmethylcarbinol Acetate (VII).**—A mixture of 54.6 g. (0.3 mole) of *p*-acetophenylmethylcarbinol acetate (IV) and 5 g. of copper chromite catalyst in a cyclohexane solution of 150 cc. total volume was hydrogenated at 150° and 3300 p.s.i. until 0.3 mole of hydrogen

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(2) C. A. Hochwalt, U. S. Patent 2,390,368 (Dec. 4, 1945); *C. A.*, **40**, 1878 (1946).

(3) H. Adkins and H. R. Billica, This Journal, **70**, 695 (1948).

had been absorbed. The cooled reaction mixture was removed from the bomb, filtered, and distilled to give 25 g. (54%) of *p*-(α-hydroxyethyl)-phenylmethylcarbinol acetate, b.p. 116–117° (0.5 mm.), n^{25}_{D} 1.5120.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.2; H, 7.6; acetyl, 21.3. Found: C, 69.3; H, 7.6; acetyl, 20.8.

1,4-Bis-(α-hydroxyethyl)-benzene Diacetate (VIII). Method A.—A mixture of 13.5 g. (0.065 mole) of *p*-(α-hydroxyethyl)-phenylmethylcarbinol acetate, 20 g. (0.2 mole) of acetic anhydride, and 5 drops of pyridine was heated on the steam-cone for 16 hours. Distillation of the reaction mixture yielded 21.0 g. (80%) of the diacetate, b.p. 104° (0.2 mm.), n^{25}_{D} 1.4955.

Method B.—1,4-Bis-(α-hydroxyethyl)-benzene was also prepared from *p*-diacetylbenzene. A mixture of 16.2 g. (0.1 mole) of *p*-diacetylbenzene, 8.1 g. of W-7 Raney nickel, and 200 cc. of methanol was hydrogenated in a Parr low-pressure apparatus at 50 p.s.i. The pressure drop was 13 p.s.i.; calcd., 12.8 p.s.i. After the catalyst had been filtered off, the methanol was evaporated to yield 12 g. of 1,4-bis-(α-hydroxyethyl)-benzene. A mixture of 9.0 g. (0.055 mole) of 1,4-bis-(α-hydroxyethyl)-benzene, 1.25 g. of acetic anhydride and 1 cc. of pyridine was heated on the steam-cone for 16 hours. Distillation of the reaction mixture gave 10.5 g. of 1,4-bis-(α-acetoxyethyl)-benzene, b.p. 110–112° (0.25 mm.), n^{25}_{D} 1.4932.

Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.2; H, 7.3. Found: C, 67.9; H, 7.4.

***p*-Divinylbenzene (VI).**—A solution of 21.0 g. (0.084 mole) of 1,4-bis-(α-hydroxyethyl)-benzene diacetate in 25.0 cc. of benzene was passed dropwise during the course of 1.5 hours through a 25-mm. o.d. Pyrex tube, packed for a distance of 30 inches with glass beads, and heated to 525–535° by means of an electrically controlled furnace. The reaction products were swept into a Dry Ice trap by a slow stream of nitrogen. The reaction products were melted, washed with water, and dried over anhydrous magnesium sulfate. Distillation yielded 7.7 g. (70% of the theoretical) of *p*-divinylbenzene, b.p. 34° (0.2 mm.). Titration of 0.52 g. of this material with $^1/_{12}$ *M* bromide–bromate solution required 30.2 cc., corresponding to a purity of 97.6%.

EASTMAN KODAK CO.
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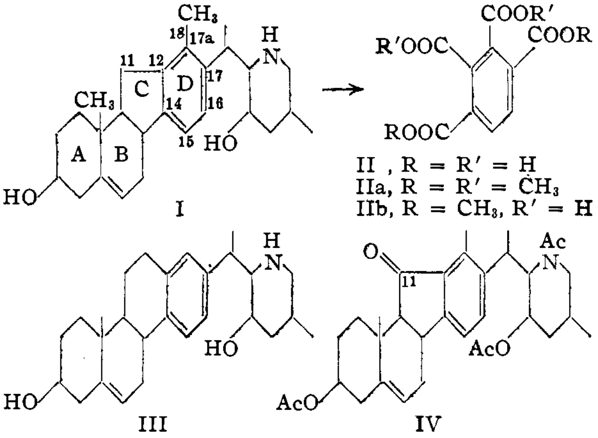
Degradation of Veratramine to Benzene-1,2,3,4-tetracarboxylic Acid

BY O. WINTERSTEINER, M. MOORE AND N. HOSANSKY

RECEIVED JANUARY 5, 1953

The structure I proposed by Tamm and Wintersteiner[1] for the secondary base veratramine from *Veratrum viride* Aiton requires that oxidative degradation of the alkaloid should result in the formation of II, benzene-1,2,3,4-tetracarboxylic acid (prehnitic acid[2]). This was indeed found to be the case. When veratramine was oxidized with hot alkaline permanganate and the mixture was worked up by the procedure described by Read and Purves[3] for the separation of the benzene polycarboxylic acids derived from coal and lignin, there was obtained a crystalline acid, m.p. 238–241°, $C_{10}H_6O_8$, identified as benzene-1,2,3,4-tetracarboxylic acid by analysis and comparison with an authentic sample.[4] The melting point of the tetramethyl ester (m.p. 128–130°) and of the (apparently slightly impure) 1,4-diester (160–167°, lit.[3] 171–172°) served to confirm this conclusion,[4] as did the identity of the infrared spectrum of the tetramethyl ester with that of an authentic specimen.



II, R = R′ = H
IIa, R = R′ = CH_3
IIb, R = CH_3, R′ = H

This result places the methyl group representing carbon atom 18 in the normal steroid skeleton into position 17a of ring D as visualized in formula I, and in conjunction with other facts[5,6] rules out the perhydrochrysene structure III proposed by Jacobs and Sato,[7] in which this carbon atom is incorporated in the ring system proper. Since there is ample evidence to show that rings A and B in veratramine are constituted as in normal steroids,[1,7] and that it is ring D which is aromatic,[1,5,7] it follows that ring C must be five-membered as postulated. These conclusions also apply to the related secondary alkaloid jervine, which has been correlated with veratramine[5] through one of its acetolysis products, the indanone IV.[6]

Experimental

The melting points were taken in capillaries and are corrected for stem exposure. The ultraviolet spectra were determined with a Cary self-recording spectrophotometer model 11-M. The infrared measurements were carried out with a Perkin–Elmer spectrophotometer model 12-B. The analytical samples were dried over phosphorus pentoxide at 110° (2 mm.).

Oxidation of Veratramine with Permanganate.—A suspension of veratramine (free base, 5 g.) in 500 cc. of water containing 8.0 g. of potassium hydroxide was brought to boiling in a vessel fitted with a reflux condenser, a separatory funnel and an air inlet tube extending to the bottom of the flask. Aqueous 3.5% potassium permanganate was added to the boiling mixture in 50-cc. portions at intervals governed by the consumption of the most of the reagent from the preceding addition. A stream of air admitted through the inlet tube served to prevent excessive bumping. When the last 50-cc. portion of a total of 1550 cc. added had remained unreduced for 5 hours (aggregate reaction time 30 hours), the contents of the flask were cooled and the excess permanganate destroyed by the addition of ethanol. The manganese dioxide was filtered off and washed thoroughly with hot water. The combined filtrate and washings were acidified to *p*H 2 with hydrochloric acid, filtered through a bed of Super-Cel, and concentrated *in vacuo* to about 200 cc. The solution was then brought to *p*H 10 by

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(1) Ch. Tamm and O. Wintersteiner, THIS JOURNAL, **74**, 3842 (1952).

(2) As pointed out by L. I. Smith and E. J. Carlson, *ibid.*, **61**, 288 (1939), the still widespread use in the contemporary literature of the trivial name mellophanic acid for this instead of for the 1,2,4,5-isomer is incorrect. We are following in this paper the suggestion of Read and Purves (ref. 3) to use the rational terms only.

(3) D. E. Read and C. B. Purves, *ibid.*, **74**, 116, 120 (1952).

(4) We wish to express our sincere thanks to Prof. C. B. Purves for making available to us samples of this acid and of its tetra and dimethyl esters.

(5) O. Wintersteiner and N. Hosansky, THIS JOURNAL, **74**, 4474 (1952).

(6) J. Fried, O. Wintersteiner, A. Klingsberg, M. Moore and B. M. Iselin, *ibid.*, **73**, 2970 (1951); O. Wintersteiner, B. M. Iselin and M. Moore, Abstracts, XIIth Internat. Congress of Chemistry, New York, N. Y., September 10–13, 1951, Medicinal Chemistry, p. 292.

(7) W. A. Jacobs and Y. Sato, *J. Biol. Chem.*, **191**, 71 (1951).

the addition of 2 *N* potassium hydroxide. After removal of a small amount of an amorphous precipitate by filtration, 10% barium chloride solution (147 cc.) was added, and the resulting suspension of precipitated barium salts was heated on the steam-bath for 30 minutes. The precipitate was collected after cooling to room temperature, washed with water, and dried (9.67 g., 56.9% Ba).

The barium salts were dissolved in hot 3 *N* hydrochloric acid (100 cc.) and decomposed by the addition of the calculated amount of 3 *N* sulfuric acid (27.8 cc.). The filtrate and hot water washings from the barium sulfate were concentrated to 50 cc. and placed in the refrigerator. The oxalic acid crystals which were deposited overnight were removed by filtration (3.57 g.). The filtrate, after reduction of its volume to 10 cc., was again placed in the refrigerator. The resulting mixture of large oxalic acid crystals and very small short rods was separated by aspirating the latter together with the mother liquor with a rubber-capped pipet. The fine crystals were collected by centrifugation (180 mg.). The mother liquor was brought to dryness (418 mg.), and the residue triturated with absolute ethanol. The insoluble portion, consisting of inorganic material, was removed by filtration, and the filtrate brought to dryness. The semicrystalline residue (375 mg.), as well as the original crop of fine rods, was treated separately with boiling concentrated nitric acid (3 cc.) under reflux till the evolution of brown nitrous gases ceased (*ca.* 1 hour). The solutions were concentrated on a hot-plate till crystallization commenced. Since the two batches of crystalline material collected after chilling did not differ materially in melting point and appearance, they were combined (185 mg.) and recrystallized again from boiling concentrated nitric acid, from which it formed small, clear-cut prisms melting with effervescence at 241–245° after softening beginning at 224°. The product did not depress the melting point of the reference specimen (244–248°, soft 224°) obtained from Professor Purves.[4] For analysis the compound was recrystallized from acetone–hexane (m.p. 235–238.5°, soft, 231°).

Anal. Calcd. for $C_{10}H_6O_8$ (254.1): C, 47.25; H, 2.38; neut. equiv., 63.5. Found: C, 47.43; H, 2.49; neut. equiv., 63.1.

The **tetramethyl ester** IIa was prepared in the usual manner by adding excess ethereal diazomethane to a solution of the acid in dry methanol. After recrystallization from acetone–hexane it melted at 127–130°, alone or in mixture with an authentic preparation of the same melting point.[4]

Anal. Calcd. for $C_{14}H_{14}O_8$ (310.3): C, 54.20; H, 4.55; OCH_3, 40.0. Found: C, 54.40; H, 4.77; OCH_3, 39.6.

The infrared spectrum (Nujol mull) of the ester was identical with that of the reference preparation[4]; 3.45 d, 3.87 ss, 5.76 d, 6.05 s, 6.27 ss, 6.36 ss, 10.48 ss, 10.56 m, 11.13 s, 11.54 m, 11.65 s, 12.79 s, 13.22 md, 13.62 sm, 14.30 s (d = deep, m = medium, s = small, ss = very small).

The **1,4-dimethyl ester** IIb was prepared by refluxing a solution of the acid (48 mg.) in 3% methanolic hydrogen chloride (3 cc.) for 6 hours.[3] The esterified material was separated into acidic and neutral fractions in the usual manner. The acidic fraction (47.3 mg.) was recrystallized from acetone–hexane, from which it formed rosettes of platelets melting at 160–167.5°. Further recrystallization failed to raise or sharpen the melting point. In mixture with the reference specimen[4] (m.p. 171–175°) the preparation melted at 167–173°.

Anal. Calcd. for $C_{10}H_{10}O_8$ (282.2): OCH_3, 22.0; neut. equiv., 141. Found: OCH_3, 21.9; neut. equiv., 138.

Ultraviolet Absorption Spectra of Acid II and its Esters.—The ultraviolet absorption spectra of the acid II and its esters IIa and IIb in ethanol are practically identical. They are characterized by a single maximum at 288 mμ (II, IIa) or 290 mμ (IIb), with ϵ 1260–1300, a shallow minimum at 279 mμ (II) or 275 mμ (IIa, IIb), with ϵ 1130–1250, and end absorption with an inflection at about 240 mμ, ϵ 8000–8300, which probably corresponds to the high band at 226 mμ in the spectrum of phthalic acid (butyl phthalate, λ^{alc}_{max} 226 mμ (9500), 272 mμ (1500)). The spectrum of the isomeric ester, tetramethyl benzene-1,2,4,5-tetracarboxylate[8] in ethanol shows the same general pattern (maximum at 291 mμ (2370), minimum at 275 mμ (1780), end absorption with inflection at 240 mμ (9050)). It would thus appear that these features are associated with the number of carboxyl functions (and hence of possible resonance structures) rather than with their distribution over the benzene ring. On the other hand, the segregation in the isomeric ester of the carbomethoxy groups into two pairs insulated from each other by unsubstituted ring carbon atoms seems to impart on each of these groupings something like the character of a separate chromophore, if the nearly twice as high extinction of the maximum over that of the corresponding band of the 1,2,3,4-substituted ester IIa can be so interpreted.

The authors are indebted to Mr. Joseph A. Alicino and his associates for the microanalyses, and to Dr. Nettie Coy for the ultraviolet and infrared measurements.

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(8) We are greatly indebted to Prof. R. T. Arnold of the University of Minnesota for making available to us a sample of this ester.

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COMMUNICATIONS TO THE EDITOR

N-PANTOTHENYLCYSTEINE AS A PRECURSOR FOR PANTETHEINE AND COENZYME A

Sir:

Pantetheine is readily converted *in vivo* to coenzyme A (CoA), and the intermediate reactions involved are now known.[1] In contrast, nothing is known of the mechanisms by which pantetheine arises from pantothenic acid. A study of this transformation revealed that in the presence of adenosine triphosphate and cysteine, extracts of acetone-dried cells of *Proteus morganii* transform pantothenate to a compound (I) essentially inactive in replacing pantothenate for *Saccharomyces carlsbergensis*, *Lactobacillus arabinosus* and *Lactobacillus casei*.[2] Pantethine was not formed.[2] However, the product (I) formed was considerably more active in promoting growth of *Acetobacter suboxydans*[2] than an amount of pantothenate equal to that inactivated by the enzyme preparation.

Since cysteine could not be replaced by β-mercaptoethylamine in the inactivation reaction with *P. morganii*, it appeared that I might be N-pantothenylcysteine (II). The corresponding disulfide,

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(1) G. D. Novelli and M. H. Hoagland. Abstract 26C, 123rd Meeting, Am. Chem. Soc., Los Angeles, March, 1953; G. D. Novelli, *Fed. Proc.*, in press.

(2) Free pantothenate was determined by assay with *S. carlsbergensis;* pantethine was determined with *Lactobacillus helveticus* 80 (J. Craig and E. E. Snell, *J. Bact.*, **61**, 283 (1951)) before and after digestion with intestinal phosphatase. Assays for pantothenate activity with *A. suboxidans* were conducted in the medium of L. A. Underkofler, A. C. Banz and W. H. Peterson (*J. Bact.*, **45**, 183 (1943)).