After separating and drying the crude product, it was dissolved in benzene–60° naphtha solution and decolorized twice with Norite, and the solution evaporated to dryness *in vacuo.* The residue was recrystallized from absolute alcohol–acetone solution to give 0.2 g. of XVII, m.p. 115.2–115.8°.

b. From XII.—Dehydrogenation of 0.7 g. of XII with an equivalent amount of roll sulfur was carried out using the above procedure giving 0.3 g. of XVII identical with that obtained from XV.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.07; H, 5.73. Found: C, 84.24; H, 6.02.

MISSOULA, MONTANA

NOTES

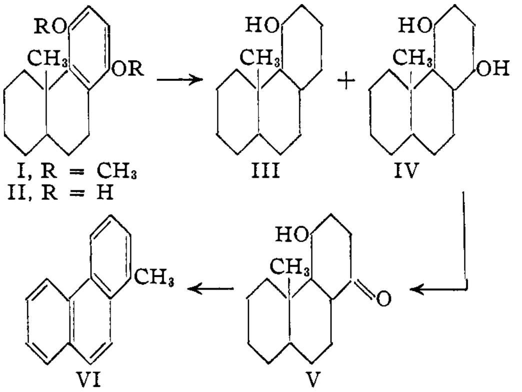
Synthesis of Phenanthrenes. VI. 5-Hydroxy-8-keto-4a-methylperhydrophenanthrene

BY RODERICK A. BARNES AND ALBERT H. SHERMAN[1]

RECEIVED JANUARY 2, 1953

Previous work[2-4] has been directed toward the preparation of octahydrophenanthrenes as possible intermediates for the synthesis of steroids. From such intermediates there are two main paths by which further progress toward the steroids might be achieved. The aromatic C ring may be reduced and then the D ring added or the two procedures might be reversed.

The purpose of this paper is to report some results which have been obtained in connection with the first approach. 5,8-Dimethoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (I), which has previously been described,[2] was treated with hydrogen bromide to cleave the methoxyl groups. The resulting hydroquinone (II) was rather unstable toward oxygen particularly in basic solution.

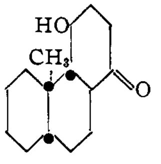


Two reductions of II were carried out; from the first there was isolated one isomer of 5,8-dihydroxy-4a-methylperhydrophenanthrene along with a large amount of unhydrogenated material. The second hydrogenation under more drastic conditions completely reduced the aromatic ring but also caused rather extensive hydrogenolysis. By chromatographic fractionation of the reduction product a single crystalline monohydroxy-4a-methylperhydrophenanthrene (III) and three additional isomers of diol IV were separated.

It is believed that III has the hydroxyl group at the 5-position. This seems likely because the hydrogenolysis requires the close approach of the catalyst surface and the hydroxyl-bearing carbon atom. Such a process would be sterically inhibited at the 5-position by the angular methyl group. Also, when III was oxidized and the resulting ketone treated with methylmagnesium iodide and then dehydrogenated no 4-methylphenanthrene was isolated. It is not surprising that the Grignard reagent would fail to add to the sterically hindered carbonyl group.

The oxidation of diol IV was investigated since most procedures for adding ring D require a keto group at the 8-position. N-Bromosuccinimide in aqueous dioxane oxidized the crude mixture of diols (from second hydrogenation) and after equilibration with base followed by distillation a single ketoalcohol (V) was isolated. It was anticipated that the sterically unhindered hydroxyl group (at the 8-position) would be preferentially oxidized. This was proved by treating V with methylmagnesium iodide and then dehydrogenating the addition product. The formation of 1-methylphenanthrene proved that the keto group of V must have been at carbon 8.

Although the stereochemistry of V has not been established some reasonable assumptions can be made. According to the theoretical considerations previously presented[2] the starting octahydrophenanthrene (II) should have the *cis* configuration of rings A and B.[5] If the results obtained by Cornforth and Robinson[6] in the hydrogenation of a similar *cis*-octahydrophenanthrene can be used as a basis for generalization it seems likely that the hydrogen at carbon 4b is *cis* to the angular methyl group.



Since V was obtained after equilibration with base the *trans* configuration of rings B and C is most probable. There is as yet no evidence bearing on the configuration of the hydroxyl group of V.

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[1] Abstracted from a thesis presented by A. H. Sherman to the Graduate School for the Ph.D. degree, November, 1952.

(2) R. A. Barnes, THIS JOURNAL, **75**, 3004 (1953).

(3) R. A. Barnes and M. D. Konort, *ibid.*, **75**, 303 (1953).

(4) R. A. Barnes, H. P. Hirschler and B. R. Bluestein, *ibid.*, **74**, 4091 (1952).

(5) The experimental verification of this prediction is currently in progress.

(6) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

The fact that only V was isolated when the mixture of diols IVb, c, and d was oxidized suggests that these three compounds may differ only in the configuration of the hydroxyl at carbon 8 and the hydrogen at carbon 8a.

Experimental[7]

5,8-Dihydroxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (II).—A mixture of 48% hydrobromic acid (100 ml.), acetic acid (165 ml.) and 5,8-dimethoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (7.5 g.) was heated at reflux temperature for 7 hours. The reaction mixture was diluted with water and the product extracted with ether. Evaporation of the ether left a greenish solid (6 g.). Recrystallization of 3 g. of this material yielded 1.5 g. (45%) of II which was nearly colorless and melted at 202–204° (capillary). The analytical sample prepared by further recrystallization from benzene melted at 200.1–200.7° (hot stage).

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.45; H, 8.70.

The ultraviolet spectral curve of II in ethanol had two maxima, one at 295 mμ (log ϵ 3.55), the other at *ca.* 225 mμ could not be determined accurately with our instrument.

An attempt to purify II by dissolving in aqueous alkali led to the formation of a brown tar from which a yellow solid could be isolated. An oxidation of II (0.93 g.) according to the procedure of Smith and Irwin[8] yielded 0.51 g. (55%) of crude quinone, m.p. 53–58°. Sublimation produced golden yellow crystals which melted at 60–62°. This quinone was extremely sensitive to air oxidation and darkened rapidly on standing. The ultraviolet spectral curve had maxima at 250 mμ (log ϵ 3.85) and 295 mμ (log ϵ 3.45).

5,8-Diacetoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene.—A mixture of II (0.6 g.), acetic anhydride (2.7 g.) and pyridine (5 ml.) was allowed to stand at room temperature for 40 hours. The reaction mixture was poured into ice-water containing hydrochloric acid (5 ml.) and the product extracted with ether. Evaporation of the ether left a crystalline product (0.5 g., 61%) which melted at 87–93°. The analytical sample was prepared by alternate recrystallization from methanol and ethyl ether–petroleum ether, m.p. 93.5–94.2°.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.09; H, 7.73.

Hydrogenation of II. A.—A solution of II (2.1 g.) in dioxane (50 ml.) was hydrogenated for four hours at 2800 p.s.i. and 170–185° using palladium-on-strontium carbonate (2.1 g.) as a catalyst. The catalyst was filtered from the solution and the solvents removed to leave a brown solid residue. Recrystallization of this substance from benzene yielded three crops of unchanged hydroquinone II (0.57 g.) in various stages of purity. The filtrate from these crystallizations was separated by chromatographic fractionation to yield two major components: (1) quinone, m.p. 52–57° formed by air oxidation of II during processing and (2) an isomer of 5,8-dihydroxy-4a-methylperhydrophenanthrene, IVa (0.12 g.) which melted at 193.5–195° after recrystallization from acetone.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.57; H, 11.00. Found: C, 75.43; H, 10.83.

B.—The hydrogenation was repeated using a solution of II (9 g.) in dioxane (115 ml.) and the catalyst (18 g.) at 220–230° and 3450 p.s.i. for 15 hours. An aliquot (1.5 g.) of the liquid hydrogenation product (7.5 g.) was separated by chromatography into four major fractions: (1) a liquid, probably 4a-methylperhydrophenanthrene (0.34 g.); (2) a solid (0.34 g.) which melted at 120.8–121° after recrystallization from hexane; (3) a solid (0.17 g.) which could not be recrystallized to a sharp melting compound and (4) a solid (0.10 g.) which melted at 172–175° after recrystallization from benzene or acetone.

Fraction 2 was a monohydroxy-4a-methylperhydrophenanthrene (III).

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.00; H, 11.78. Found: C, 80.67; H, 11.57.

Fraction 4 was a second isomer (IVb) of 5,8-dihydroxy-4a-methylperhydrophenanthrene.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.57; H, 11.04. Found: C, 75.68; H, 11.04.

Fraction 3 (100 mg.) was rechromatographed; the first fractions eluted (86 mg.) were soluble in methanol while the later fractions (7 mg.) were insoluble in methanol. The methanol-soluble fractions were combined and recrystallized from benzene or ethyl acetate to yield the third isomer (IVc) of 5,8-dihydroxy-4a-methylperhydrophenanthrene, m.p. 152–154°.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.57; H, 11.00. Found: C, 75.18; H, 10.87.

The methanol-insoluble fractions from two different chromatographic separations were combined and recrystallized from methyl ethyl ketone to yield isomer IVd, m.p. 203.5–204.5°.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.57; H, 11.00. Found: C, 75.47; H, 10.63.

The following melting points were observed for mixtures of the isomeric 5,8-dihydroxy-4a-methylperhydrophenanthrenes: IVa (194–195°) and IVd (202–203°), 175–192°; IVa and IVb (172–175°), 140–188°; IVb and IVc (152–154°), 115–151°.

Chromatographic Procedure.—Acid-washed, 80–200 mesh alumina, dried at 180° was used in all separations. The compounds were adsorbed on the column from a benzene solution (or ether-benzene if necessary) and solvents of increasing polarity were used to elute the various fractions (benzene, 2% ether in benzene, 4% ether in benzene, and finally 60% acetone in ether, 1% ethanol in 49.5% acetone–49.5% ether, 2% ethanol in 49% acetone–49% ether). Only fractions composing the major peaks in the chromatographic curve (fraction number plotted against weight of the fraction) were investigated. The solvents for elution of the various pure substances are listed: III, 20–40% ether in benzene; IVa, 8–30% acetone in ether; IVb, 2% ethanol in 49% acetone–49% ether; IVc and IVd, 15–30% acetone in ether.

Attempted Structure Proof for III.—A solution of III (464 mg.) in acetic acid (5 ml.) was oxidized by the dropwise addition at 0° of a solution of chromic anhydride (155 mg.) in water (0.5 ml.) and acetic acid (5 ml.). The reaction mixture was kept at 5° for 11 hours and at 30° for three hours. After processing there was obtained a pale yellow oil which did not crystallize. A few drops of this product were allowed to react with 2,4-dinitrophenylhydrazine to yield orange needles which melted at 210–213°. The major portion of the crude ketone (385 mg.) was added to a cold solution of methylmagnesium iodide prepared from methyl iodide (2.3 g.), magnesium (0.4 g.) and ether (10 ml.). After standing overnight at room temperature the reaction mixture was treated with ice and hydrochloric acid and the product extracted with ether. Evaporation of the ether left an oil (0.40 g.) which was directly dehydrogenated using 17% palladium-on-charcoal (0.08 g.) with diphenylamine (2.0 g.) as a solvent. About 50% of the theoretical amount of hydrogen was evolved. The dehydrogenated product was chromatographed but no crystalline phenanthrene was obtained.[9]

Oxidation of IV with N-Bromosuccinimide. A.—A portion (3 g.) of the crude product from the second hydrogenation was oxidized with N-bromosuccinimide (2.4 g.) in dioxane (22 ml.) and water (3 ml.) according to the procedure of Fieser and Rajagopalan.[10] The crude oxidation product was refluxed for 30 minutes with a 1% solution of potassium hydroxide in methanol (50 ml.). The reaction mixture was diluted with water and the product extracted with ether. A brown oil (2.78 g.) remained after evaporation of the ether. This product was separated by Girard reagent T[11] (5 g.) into a non-ketonic fraction (1.57 g.) and a ketonic fraction (1.16 g.). Evaporative distillation at 0.2 mm. of the ketonic fraction produced three fractions: (1) 0.16 g. (86–95°);

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[7] All melting points were determined using a Kofler hot stage. Analyses are by W. Manser, Zurich, Switzerland, and J. F. Alicino, Metuchen, New Jersey.

[8] L. I. Smith and W. B. Irwin, THIS JOURNAL, **63**, 1036 (1941).

[9] If the Grignard reagent only enolized the ketone, then subsequent dehydrogenation may have formed some 4-phenanthrol. However, the solvents used to remove any phenanthrene hydrocarbons would not be expected to elute a phenol from the column of alumina.

[10] L. F. Fieser and S. Rajagopalan, THIS JOURNAL, **71**, 3938 (1949).

[11] A. Girard and G. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

(2) 0.44 g. (95–110°) and (3) 0.20 g. (110–115°). Fraction 3 (ketoalcohol V) solidified on standing and after recrystallization from benzene-hexane melted at 177–180°.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.34; H, 10.39.

The infrared spectra of all three fractions had a strong carbonyl band at 5.85 μ. Only fraction 3 absorbed appreciably in the hydroxyl region (peaks at 2.75 and 2.85 μ).

B.—Diol IVb (409 mg.), m.p. 172–175°, was oxidized as in part A. The crude product (375 mg.) crystallized and after several recrystallizations melted at 183–185°. The filtrates from the recrystallizations containing most of the oxidation product (324 mg.) were treated with potassium hydroxide in methanol as in part A to yield V, m.p. 177–180° identical with the previous preparation. The melting point of a mixture of V and the crystalline product,[12] m.p. 183–185°, was 155–185°.

Structure Proof for V.—A solution of V (787 mg.) in ether (40 ml.) was added to methylmagnesium iodide prepared from methyl iodide (9.4 g.), magnesium (1.6 g.) and ether (50 ml.). The reaction mixture was processed as in the attempted structure proof of III. The product (756 mg.) crystallized on standing but was directly dehydrogenated without further purification. The first dehydrogenation with 5% palladium-on-charcoal and no solvent was incomplete. A portion (366 mg.) of the partially dehydrogenated mixture was dehydrogenated as in the previous case using freshly prepared palladium-on-charcoal (17%) and diphenylamine (2 g.) as a solvent. The main crystalline fraction of the dehydrogenation product (48 mg.) was recrystallized from ethanol to yield 1-methylphenanthrene which melted at 121–122°. The melting point of a mixture of this sample with authentic 1-methylphenanthrene (m.p. 118–119°)[13] was 118–120° (capillary). The picrate of this compound crystallized from ethanol as orange needles which melted at 136–139° (reported[13] 136–136.5°).

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[12] This is believed to be an isomer of V in which rings B and C are *cis*.

[13] Kindly furnished by Prof. R. C. Elderfield from the collection of the late Prof. W. E. Bachmann; W. E. Bachmann and A. L. Wilds, This Journal, **60**, 624 (1938).

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Monocyanoethylation of Certain Ketones

By Henry E. Baumgarten and Robert L. Eifert

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Other investigations in this Laboratory have required the preparation of relatively large quantities of γ-acetylvaleric acid (II) or of its derivatives. Trial of previously reported[1,2] procedures for the synthesis of II revealed that these procedures were lengthy, utilized costly starting materials and resulted in low over-all yields. Indeed, the most attractive procedure for the synthesis of II appeared to be the monocyanoethylation of methyl ethyl ketone to give γ-acetylvaleronitrile (I) followed by acid hydrolysis to II. However, as

$$CH_3COCH_2CH_3 + CH_2{=}CHCN \longrightarrow \underset{\text{I}}{CH_3COCH(CH_3)CH_2CH_2CN} \xrightarrow[HCl]{H_2O} \underset{\text{II}}{CH_3COCH(CH_3)CH_2CH_2CO_2H}$$

pointed out by Yoho and Levine,[3] numerous investigators have found that cyanoethylation of simple ketones leads to the formation of polycyanoethylated derivatives as the main reaction products or to very low yields of the monocyanoethylated derivatives in those few cases in which monocyanoethylation has been observed. In fact, the best yield of I thus far reported was 6% (obtained by Barkley and Levine[4] from the reaction of methyl ethyl ketone anion with β-chloropropionitrile).

As far as we have been able to determine, most of the previously reported cyanoethylation reactions have been run with the stoichiometric quantities of both reactants (*e.g.*, equimolar quantities for attempted monocyanoethylations) although it seems reasonable that the use of a large excess of ketone over acrylonitrile might lead to a larger yield of the monocyanoethylated derivative. In support of this thesis we found that, when a 10 to 1 molar ratio of methyl ethyl ketone to acrylonitrile was used (with benzyltrimethylammonium hydroxide as catalyst), the yield of I was 24–30%.[5] The hydrolysis of I with concentrated hydrochloric acid gave II in 91% yield. Although the over-all yield of II is not high by the usual standards, the relative low cost of the starting materials (the unused methyl ethyl ketone may be recovered and reused) recommends this procedure over those previously employed for the preparation of II.

Cyclohexanone has been reported[6] to react with a molecular equivalent of acrylonitrile to give a 10% yield of the monocyanoethyl derivative. With a 5 to 1 ratio of ketone to acrylonitrile, cyclohexanone gave a yield of 47% of the monocyanoethyl derivative. Acetone has been reported to give an 8% yield of the monocyanoethyl derivative when either a 1 to 1 ratio[7] or a 2 to 1 ratio[8] of ketone to acrylonitrile was used, although in the former instance the product was not isolated in the pure state. With a 10 to 1 ratio of ketone to acrylonitrile, acetone gave an 18% yield of the monocyanoethyl derivative.

Experimental

γ-Acetylvaleronitrile (I).—In a typical experiment a mixture of 2160 g. (30 moles) of methyl ethyl ketone and 5 ml. of a 40% aqueous solution of benzyltrimethylammonium hydroxide was cooled to 5° in a 5-l. three-necked flask fitted with a stirrer, dropping funnel, thermometer and reflux condenser. To the cooled and well-stirred mixture 159 g. (3 moles) of acrylonitrile was added at such a rate that the temperature did not rise above 10° (about 15 minutes was required). Stirring was continued for five minutes after addition was completed and the mixture was neutralized with dilute hydrochloric acid to congo red. The excess methyl ethyl ketone (and acrylonitrile, if any) was removed by distillation at atmospheric pressure through a 15-in. Vigreux column. The residue was fractionated under reduced pressure and the fraction boiling at 110–120° (15 mm.) was taken leaving a considerable quantity of higher boiling product in the stillpot. The recovered methyl ethyl ketone was dried over potassium carbonate for reuse in similar reactions. Occasionally subsequent reactions were a little harder to control due to the presence of some unreacted acrylonitrile in the recovered methyl ethyl ketone. The product from three runs was fractionated through the same Vigreux column, giving 330 g. (29.4%) of γ-acetyl-

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[1] F. March, *Ann. chim.*, [7] **26**, 295 (1902).

[2] F. Lions, *J. Proc. Roy. Soc., N. S. Wales*, **771**, 192 (1938).

[3] C. W. Yoho and R. Levine, This Journal, **74**, 5597 (1952).

[4] L. B. Barkley and R. Levine, *ibid.*, **72**, 3699 (1950).

[5] The remainder of the acrylonitrile appeared as the dicyanoethyl derivative, yield *ca.* 70%.

[6] H. A. Bruson and T. W. Riener, This Journal, **64**, 2850 (1942).

[7] O. W. Shannon, U. S. Patent 2,381,371; *C. A.*, **40**, 350 (1946).

[8] A. P. Terent'ev and S. M. Gurvich, *Vestnik Moskov. Univ.*, **5**, No. 5, Ser. Fix.-Mat. i Estest. Nauk No. 3, 47 (1950); *C. A.*, **45**, 7005 (1951).

valeronitrile, b.p. 114–115° (15 mm.), n^{25}_{D} 1.4332, d^{25}_{4} 0.951.

Anal. Calcd. for $C_7H_{11}NO$: C, 67.15; H, 8.85; N, 11.19. Found: C, 66.97; H, 9.07; N, 11.05.

Starting with quantities of from 0.1 to 3.0 moles of acrylonitrile and 10 molecular equivalents of methyl ethyl ketone, other experiments gave yields of γ-acetylvaleronitrile of 24–30%. After distillation of the product the residue in the flask solidified on cooling and could be recrystallized (two or three times) from ethanol to give a *ca.* 70% yield of γ-acetyl-γ-methylpimelonitrile, m.p. 66–67°. The reaction could be run starting at room temperature (*ca.* 25°) and maintaining the temperature of the reaction mixture below 50° without any appreciable effect on the yield. Under these conditions the addition of acrylonitrile required 60 to 90 minutes, and it was necessary to use two large capacity condensers and to provide a means for very rapid cooling to prepare for those occasional reactions which became suddenly and vigorously exothermic.

When 178 g. (1.0 mole) of γ-acetyl-γ-methylpimelonitrile was added in small portions to a well-stirred mixture of 1440 g. (20 moles) of methyl ethyl ketone and 10 ml. of the benzyltrimethylammonium hydroxide catalyst at 27° and later warmed to 60° for two hours, none of the monocyanoethyl derivative (I) could be found in the distillates from the reaction mixture, nor could the yield of the monocyanoethyl derivative in the typical procedure be increased by adding varying amounts of the dicyanoethyl derivative at the start of the reaction.

γ-Acetylvaleric Acid (II).—To 160 ml. of concentrated hydrochloric acid was added 70 g. (0.64 mole) of freshly distilled γ-acetylvaleronitrile. The solution became red and boiled gently. A white solid appeared (amide?) which slowly disappeared as the solution was heated under reflux for four hours. The cooled mixture was diluted with enough water to dissolve the precipitated ammonium chloride (extraction at this point with five portions of ether gave *ca.* 60% of the desired product). The solution was neutralized with strong sodium hydroxide solution, made just acid to congo red with hydrochloric acid, saturated with sodium chloride, and extracted ten times with 50-ml. portions of ether. The ethereal solution was dried over magnesium sulfate and distilled from a Claisen flask, giving 74 g. (91%) of γ-acetylvaleric acid, b.p. 160–162° (16 mm.), semicarbazone m.p. 160–161° (dec.) (lit.[2] m.p. 159–162° (dec.)).

2-(Cyanoethyl)-cyclohexanone.—To a mixture of 370 g. (3.78 moles) of cyclohexanone and 10 ml. of a 40% aqueous solution of benzyltrimethylammonium hydroxide in a flask fitted with a stirrer, reflux condenser and dropping funnel and heated on the steam-bath to 60° was added dropwise with stirring 40 g. (0.76 mole) of acrylonitrile, the addition requiring about 20 minutes. The temperature of the reaction mixture rose above 60° but the mixture did not boil nor was there any appreciable amount of acrylonitrile condensing in the condenser. The mixture was allowed to stand until the temperature fell to 40°, the catalyst was neutralized with hydrochloric acid to congo red, and the mixture was washed with water, dried over magnesium sulfate, and distilled through the 15-in. Vigreux column, giving 52 g. (47%) of 2-(cyanoethyl)-cyclohexanone, b.p. 147–150° (14 mm.), 5 g. of material boiling at 150–200° (1 mm.), and 49 g. of residue.

When the above reaction was attempted at room temperature (26°) for a period of two hours, only traces of the above products were obtained.

γ-Acetylbutyronitrile.—A mixture of 580 g. (10 moles) of acetone and 5 ml. of 40% aqueous benzyltrimethylammonium hydroxide was heated to boiling under reflux and to the hot solution was added 53 g. (1.0 mole) of acrylonitrile dropwise over a period of one hour. The mixture was heated an additional hour under reflux. The catalyst was neutralized with hydrochloric acid to congo red and the solution was distilled through the 15-in. Vigreux column, giving 20 g. (18%) of γ-acetylbutyronitrile, b.p. 108–112° (14 mm.), 2,4-dinitrophenylhydrazone m.p. 154–155° (lit.[9] m.p. 154–155°).

When the above reaction was attempted at room temperature for two hours, the yield of the product indicated was 7%.

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[9] N. F. Albertson, THIS JOURNAL, **72**, 2594 (1950).

Fluorinated Esters. V. Surface Tension and Parachor Studies[1,2]

BY ROBERT FILLER

RECEIVED JANUARY 28, 1953

The surface tensions of a number of fluorocarbons have been reported by Simons and Pearlson[3] and by Fowler and co-workers.[4]

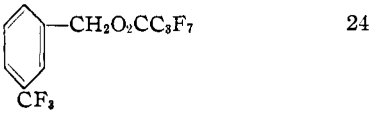
The values for these compounds are the lowest known and are considerably lower than those of analogous hydrocarbons. Schulman and Zisman[5] have recently reported the surface tensions of several fluorinated compounds including a number of perfluoroamines, chlorofluorocarbons and "pseudo-perfluoroalcohols" of the type $H(CF_2)_xCH_2OH$.

In a continuation of the study of the relation of structure to physical properties of fluorine-containing esters and diesters,[6] the surface tensions of several of these esters were measured and the influence of fluorine on this property was noted.

In Table I are listed the surface tensions of eleven fluorinated esters and diesters and these are correlated with the percentage of fluorine in the molecule. The measurements were made by the ring method and the corrections for this method[7] included the use of the extended tables recently de-

TABLE I

SURFACE TENSIONS OF FLUORINATED ESTERS

Compound	γ, dynes/cm.	*t*, °C.	Fluorine, %
$C_2H_5O_2C(CF_2)_4CO_2C_2H_5$	22.7	27.0	43.9
$C_3H_7CH_2O_2C(CF_2)_4CO_2CH_2C_3H_7$	22.2	26.0	37.8
$C_3F_7CH_2O_2C(CH_2)_4CO_2CH_2C_3F_7$	20.4	25.8	52.2
$C_3H_7CO_2CH_2(CF_2)_4CH_2O_2CC_3H_7$	23.9	26.0	37.8
$CF_3CO_2(CH_2)_5O_2CCF_3$	24.4	26.2	38.5
$C_3F_7CO_2(CH_2)_5O_2CC_3F_7$	20.6	26.2	53.6
$C_3F_7CO_2(CH_2)_6O_2CC_3F_7$	22.2	26.2	52.2
$C_7F_{15}CO_2(CH_2)_5O_2CC_7F_{15}$	19.1	26.2	63.6
$C(CH_2O_2CC_3F_7)_4$[a]	18.5	26.0	57.8
	24.8	26.5	51.1
$C_3F_7CO_2CH_2CH_3$[b]	17.0	26.0	55.0

[a] Courtesy Minnesota Mining and Manufacturing Co., St. Paul, Minn. [b] This value is undoubtedly low since the density of the vapor of this compound (b.p. 96°) was neglected in the correction.

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[1] Part of the data in this paper was presented before the Fluorine Symposium at the 122nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1952.

[2] Opinions expressed are those of the author and do not necessarily express the official opinions of the U. S. Air Force or the Wright Air Development Center.

[3] J. H. Simons and W. H. Pearlson, Fluorine Symposium, 112th Meeting of the American Chemical Society, New York, September, 1947.

[4] R. D. Fowler, J. M. Hamilton, Jr., J. S. Kasper, C. E. Weber, W. B. Burford, III, and H. C. Anderson, *Ind. Eng. Chem.*, **39**, 375 (1947).

[5] F. Schulman and W. A. Zisman, NRL Report 3950, April 1952.

[6] M. Hauptschein, J. F. O'Brien, C. S. Stokes and R. Filler, THIS JOURNAL, **75**, 87 (1953); R. Filler, J. F. O'Brien, J. V. Fenner and M. Hauptschein, *ibid.*, **75**, 966 (1953); R. Filler, J. V. Fenner, C. S. Stokes, J. F. O'Brien and M. Hauptschein, *ibid.*, **75**, 2693 (1953); G. Rappaport, M. Hauptschein, J. F. O'Brien and R. Filler, *ibid.*, **75**, 2695 (1953).

[7] W. D. Harkins and H. F. Jordan, *ibid.*, **52**, 1751 (1930); B. B. Freud and H. Z. Freud, *ibid.*, **52**, 1772 (1930).

scribed by Fox and Chrisman[8] for liquids of high density and low surface tension.

The difference in surface tension between a fluorinated diester and its hydrogen-containing analog is illustrated by diethyl octafluoroadipate (22.7 dynes/cm.) and diethyl adipate (28.0 dynes/cm.). This difference is comparable to that observed for fluorocarbons and hydrocarbons. It will also be noted that, with the exception of *m*-trifluoromethylbenzyl heptafluorobutyrate,[9] the surface tension generally decreases with increasing fluorine content. A corollary to this observation may be drawn by noting the effect of increasing numbers of $-CF_2$ groups. While the addition of a methylene group is normally attended by an increase in surface tension (as illustrated by 1,5-pentanediol diheptafluorobutyrate and the corresponding 1,6-hexanediol ester), the value is lowered by the addition of $-CF_2$ groups, though this decrease becomes much smaller with increasing length of the fluorinated chain. This may be seen in the homologous series, $CF_3CO_2(CH_2)_5O_2CCF_3$, $C_3F_7CO_2(CH_2)_5O_2CC_3F_7$ and $C_7F_{15}CO_2(CH_2)_5O_2CC_7F_{15}$. Similar results were reported by Schulman and Zisman.[5]

In Table II are listed the experimental parachors of a few of these compounds, which were calculated from the surface tensions by the Sugden equation.[10] These values are compared with those calculated from the atomic and structural constants of Sugden[10] and of Mumford and Phillips.[11]

TABLE II

PARACHOR DATA

Compound	Calcd. parachor Sugden	Calcd. parachor M.p.,°C.[11]	Expl. parachor	P_F
$C_2H_5O_2C(CF_2)_4CO_2C_2H_5$	544.6	530.0	538.0	24.9
$C_3F_7CH_2O_2C(CH_2)_4CO_2CH_2C_3F_7$	752.2	750.6	728.7	24.0
$C_3F_7CO_2(CH_2)_5O_2CC_3F_7$	713.2	710.6	704.8	25.1
$C_3F_7CO_2(CH_2)_6O_2CC_3F_7$	752.2	750.6	753.8	25.8
$C_7F_{15}CO_2(CH_2)_5O_2CC_7F_{15}$	1162.8	1192.2	1114.0	24.1

The atomic parachor for fluorine (P_F), obtained from the experimental values using the Sugden constants (except for fluorine), range from 24.0 to 25.8. If the more recent constants given by Vogel[12] are employed, values from 22,2 to 24.0 are obtained. Schulman and Zisman[5] found similar variances in the few examples they studied. Fowler[4] reported values of 24.4–24.8 for P_F in fluorocarbons, which are lower than those assigned by Sugden[10] (25.7), Mumford and Phillips[11] (25.5) or Vogel[12] (26.1).

It is therefore difficult with the data now available to assign a definite value or a narrow range for the atomic parachor for fluorine, though what data have been accumulated seem to indicate that the earlier values may be somewhat high. It may, perhaps, be advisable to assign a parachor value to the CF_2 group instead of to a single fluorine atom. This system of assigning values to whole groups rather than to individual atoms has been suggested by Gibling.[13] It also takes into account the slight increase in parachor of the methylene group as the number of carbon atoms increases. This might also be applied to the CF_2 group. The bond parachors suggested by Vogel[14] may also prove useful. In this system a preliminary value of 28.2 has been assigned for the C–F bond. The present diesters give C–F bond parachors varying from 24.4 to 26.2.

Experimental

Measurements were made with a Du Noüy Interfacial Tensiometer (Precision direct reading model), using a platinum–iridium ring with a circumference of 6.015 cm. and $R/r = 53.8$.

Acknowledgment.—The author wishes to thank Mr. Ray Robinson for his assistance with the measurements.

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(8) H. W. Fox and C. H. Chrisman, Jr., *J. Phys. Chem.*, **56**, 284 (1952).

(9) This compound has not been described previously. Physical constants include: b.p. 52–53° (0.8 mm.), $n^{25}D$ 1.3824 and d^{25}_4 1.491.

(10) S. Sugden, "The Parachor and Valency," Routledge and Sons, Ltd., London, 1930.

(11) S. A. Mumford and J. W. C. Phillips, *J. Chem. Soc.*, 2112 (1929).

(12) A. I. Vogel, *J. Chem. Soc.*, 1842 (1948).

(13) J. W. Gibling, *ibid.*, 299 (1941); *ibid.*, 661 (1942); *ibid.*, 146 (1943).

(14) A. I. Vogel, W. T. Cresswell, G. J. Jeffery and J. Leicester, *Chemistry and Industry*, 358 (1950).

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The Compounds Formed between Nickel(II) and Dimethylglyoxime by Alkaline Oxidation

BY E. BOOTH AND J. D. H. STRICKLAND[1]

RECEIVED NOVEMBER 21, 1952

The determination of traces of nickel by dimethylglyoxime in the presence of alkaline oxidizing agents is established analytical practice. Difficulties still encountered, in particular the formation[2a] of a "metastable" complex, are largely explained by the discovery by Hooreman[2b] of two complexes with markedly different absorption spectra, and containing nickel and dimethylglyoxime (DMGOH) in the ratio 1:2 and 1:4. (For brevity we shall refer to them as complexes I and II, respectively.)

Isolation in the solid state of these complexes is very difficult and we believe that the substances isolated and analyzed by authors such as Feigl,[3] Kuras and Ruzicka[4] or Okac and Polster[5] are not the same as those present in solution during analytical methods for traces of nickel. Whilst disagreeing with the findings of Babko,[6] we do agree that techniques such as spectrophotometry are the most reliable for elucidating the formulas of compounds of this type and we have used such methods exclusively.

Experimental

Absorption Spectra.—The absorption spectra of complex I and complex II, were obtained at 3.75×10^{-5} *M* concentrations.

Complex I had two peaks in the visible, the molar extinction coefficients being 1.16×10^4 (442 mμ) and 0.52×10^4 (530 mμ). The oscillator strength, *f*, of the main peak was approximately 0.16 per nickel atom. The single broad peak of complex II had a molar extinction coefficient of 1.28 ×

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(1) The British Columbia Research Council, Vancouver 8, Canada.

(2) (a) N. H. Furman and B. McDuffie, Atomic Energy Commission Classified Report AEC-M-4234 (1947); (b) M. Hooreman, *Anal. Chim. Acta*, **3**, 635 (1949).

(3) F. Feigl, *Ber.*, **57**, 758 (1924).

(4) M. Kuras and E. Ruzicka, *Chem. Listy*, **45**, 100 (1951).

(5) A. Okac and M. Polster, *Collection Czechoslov. Chem. Communs.*, **13**, 561 (1948).

(6) A. K, Babko, *Zhur. Anal. Khim.*, **3**, 284 (1948).

10^4 (460 mμ) with an oscillator strength of approximately 0.32 per nickel atom.

The Ratio of Combined Nickel and Dimethylglyoxime.—Having established conditions under which either one of the pure complexes could be formed, the ratio of reactants was established by a simplification of the method of variations. Plots of moles of DMGOH against the extinction of complex formed per mole of nickel reacting showed breaks at Ni: DMGOH ratios of 1:2 and 1:4, confirming the findings of Hooreman.[2]

Oxidation State of the Complex.—The amount of oxidant required to form a known amount of complex is made difficult to determine by the variety of side reactions which can take place. The concentrations of reactants must be less than about 10^{-3} M and the alkali stronger than 0.05 M; otherwise the red divalent complex is precipitated before oxidation is complete. The only way of ensuring no complications is to have stoichiometric quantities of nickel and DMGOH initially present and to find conditions such that these react to give a complete yield of complex.

Figure 1 shows experiments with complex II under these conditions, it will be seen that three electrons per nickel atom are involved in the formation of this substance.

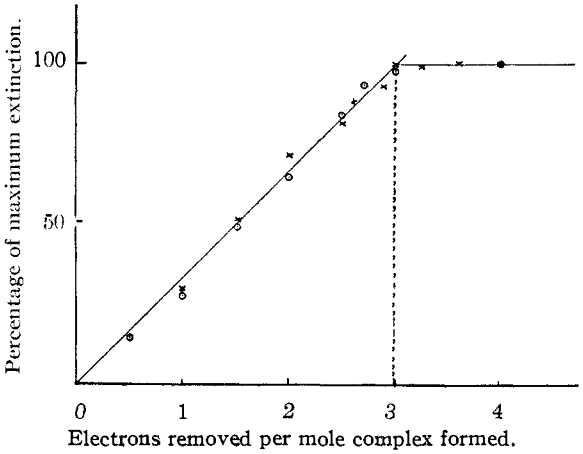

Fig. 1.—Oxidation state of complex II: x-x-x, 2.5 × 10^{-4} M complex formed; ·-·-·, 5 × 10^{-5} M complex formed.

Comparable experiments with complex I were only semi-quantitative due to the possibility of oxidation of the ammonia, which is necessary for the formation of this complex. However, if two moles of DMGOH is added to a solution of one mole of complex I a rapid transformation of this compound into complex II occurs, the speed or completion of this reaction being unaltered by the presence or absence of dissolved air or hypohalite (the oxidant used for the formation of the complexes). It occurs equally readily even in the presence of excess of arsenite. These facts, and the general similarity of the two compounds, indicate that they are both in the same, $-3e^-$, oxidation state. Furthermore if the black unstable compound of trivalent nickel described by Edelman[7] is shaken with aqueous alkali, complexes I or II are formed according to whether the alkali is ammonia or sodium hydroxide.

The Nature of the Complexes in Solution.—Complex II is anionic. It is not extracted by organic solvents and migrates to the anode in electromigration experiments. It enters the resin phase when shaken with an anion exchanger, *e.g.*, Amberlite 400, and using this resin and the technique recently outlined[8] the ion was shown to be monovalent.

Complex I, however, would not enter the resin phase of either an anion or a cation exchanger. It remained inert during electromigration experiments and could be extracted into *n*-butyl alcohol. The molecule must be assumed to be neutral.

Both compounds are destroyed by acidifying solutions but in alkali ($pH > 10.5$) complex II is stable indefinitely. Complex I, however, decomposes appreciably over a period of hours. According to conditions it will either decompose completely, form the red Ni(II) complex or change partially to complex II. The latter, although formed easily from complex I by adding DMGOH, cannot, once formed, be converted back to complex I by any means we have been able to devise.

The Number of Hydroxyl Ions Required.—Acidity changes occurring during the formation of complex I and II are difficult to measure by *p*H experiments as the concentrations of the reacting species are necessarily small in comparison with the concentration of alkali which must be present for the reaction to take place satisfactorily. With complex I, where ammonia must be present, the further complication of buffering makes such experiments almost impossible but the number of OH^- groups used up in the reaction to form complex II has been measured as follows.

One hundred fifty ml. of 0.2 N sodium hydroxide was neutralized by 0.2 N acid to *p*H 7. Fifty ml. of water was added and 0.1 N sodium hydroxide (w equivalents) to bring the *p*H to ϕ (about 10.5). This experiment was repeated but adding x moles of DMGOH as pure solid and a larger, w_1, number of equivalents of 0.1 N akali to make the *p*H ϕ $w_1 - w$ equivalents were thus used to ionize the DMGOH to $DMGO^-$.[9]

In the main experiments x moles of DMGOH was added to 150 ml. of 0.2 N alkali followed by w_1 equivalents of alkali, and water to give a volume of exactly 200 ml. Twenty ml. of a solution of nickel nitrate (0.25 x equivalent Ni^{II}) in bromine water (1.5–1.75 times the theoretical oxidant) was introduced dropwise at a temperature of 35°. The solution was then cooled to 25° and 5 ml. withdrawn to determine the fractional yield, p, of complex II formation. The solution was slowly titrated to *p*Hϕ with 0.2 N acid, and the number of equivalents, y, determined. A blank experiment was carried out exactly as above but adding no DMGOH and only w equivalents of excess alkali. Small additions of bromine, $nickel^{II}$ and DMGOH were made to the blank, these being equivalent to any such amounts left unreacted in the main experiment. Five ml. of solution was removed and discarded. If y_1 equivalents were then needed in the back titration of the blank then the number of equivalents of OH^- used up per mole of complex II formed is given by

$$\frac{4[(y_1 - y) + (w_1 - w)]}{\text{p.x.}} \times 220/215$$

the factor 220/215 being a volume correction.

The difference $y_1 - y$ on which the accuracy of this work depended was of the order of 5 ml. the over-all accuracy being better than ±0.5 of a mole of OH^-. Results of four such experiments are shown in the table. The mean value approximates to 6.

x = No. of moles of DMGOH; ϕ = *p*H to which all titrations are taken; w = equivalents of OH^- to give ϕ without DMGOH present; w_1 = equivalents of OH^- to give ϕ with DMGOH present; y = back titer, in equivalents; y_1 = blank back titer, in equivalents; p = yield of complex.

$x \times 10^4$	ϕ	$w \times 10^4$	$w_1 \times 10^4$	$(w_1 - w) \times 10^4$	$y \times 10^4$	$y_1 \times 10^4$	$(y_1 - y) \times 10^4$	p	No. of OH^- ions used
6.90	10.46	1.46	4.26	2.80	295.2	302.4	7.2	1.00	5.9
6.90	10.46	1.46	4.26	2.80	294.2	302.3	8.1	1.00	6.4
13.80	10.68	2.36	10.06	7.70	268.4	280.5	12.1	0.93	6.3
13.80	10.68	2.36	10.06	7.70	268.4	280.5	12.1	0.93	6.3

Combined Ammonia in Complex I.—Although complex II may be prepared in alkali hydroxide as well as ammoniacal solutions, and thus cannot contain combined ammonia molecules, all evidence points to the presence of the latter, in

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(7) L. E. Edelman, This Journal, 72, 5765 (1950).

(8) J. D. H. Strickland, *Nature*, 169, 620 (1952); *ibid.*, 169, 738 (1952).

(9) A. K. Babko and P. B. Mikhelson, *Zhur. Anal. Khim.*, 6, 267 (1951).

some form, in complex I. Thus complex I cannot be formed, whatever the nickel:DMGOH ratio, unless ammonia is present in solutions. When solutions of complex I are stripped of ammonia by diffusion, etc., the complex decomposes before the ammonia is completely removed. When primary amines, *e.g.*, monoethylamine, are used instead of ammonia a compound similar to complex I is produced having an absorption spectrum almost identical with complex I except that the peak at 530 mμ found with complex I, is altered in shape and size and it is to be inferred that this absorption arises from an ammonia group in the molecule. It is also significant that only ammonia will give complex I from Edelman's black solid.[7]

Discussion

The experimental data given above are mutually consistent and lead to the equation of formation of complex II to be given as

$$\mathrm{Ni^{2+} + 4DMGOH + 6OH^- \longrightarrow [Ni(OH)_2(DMGO)_4]^{1-} + 4H_2O + 3e^-}$$

with the compound having the empirical formula shown. However its structure remains to be determined. The valency of the nickel is also uncertain, although it seems likely that one electron is removed in raising $\mathrm{Ni^{II}}$ to $\mathrm{Ni^{III}}$ and the other two are removed from the two hydroxyl groups. The very high molecular extinction coefficient of this compound would indicate resonance.

It would be logical to assume complex I to be an analogous compound with amino groups replacing two of the four dimethylglyoxime groups, but in the absence of evidence of the number of ammonia molecules involved this cannot be verified.

Complex I is formed almost exclusively in all published analytical methods but it would be much better to use complex II, as the former is unstable and can either decompose or partially revert to complex II in a comparatively short time. To achieve rapid and quantitative formation of complex II a good initial excess of dimethylglyoxime should always be present with only the minimum amount of oxidant (2–3 ml. of 0.01 *N* iodine or bromine), so that excess dimethylglyoxime is not oxidized before it can convert any complex I to II. The ammonia present in solutions should be kept to a minimum and the correct alkalinity ($p\mathrm{H} > 11$) obtained by adding sodium hydroxide.

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Condensations of Primary Aliphatic Nitramines with Formaldehyde

BY LEON GOODMAN

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In the course of some studies of the chemistry of primary aliphatic nitramines we have observed a convenient condensation of formaldehyde with several primary nitramines in strong sulfuric acid leading to the formation of N,N′-dialkylmethylenedinitramines.

$$\mathrm{2RNHNO_2 + CH_2O \xrightarrow{\mathit{ca.}\ 90\%\ H_2SO_4} \underset{(I\text{–}IV)}{[RN(NO_2)]_2CH_2} + H_2O}$$

I, R = $\mathrm{CH_3}$
II, R = $\mathrm{C_2H_5}$
III, R = $n\text{-}\mathrm{C_4H_9}$
IV, R = $\mathrm{-CH_2-}$

Thus formaldehyde seems to stabilize the primary nitramines to strong sulfuric acid. Holstead and Lamberton[1] have recently noted a quite analogous reaction (equation A) in which intermediately formed formaldehyde and nitramide ($\mathrm{NH_2NO_2}$) condense with acetanilide under similar conditions.

$$\mathrm{AcO[CH_2N(NO_2)]_3CH_2OAc \xrightarrow[concd.\ H_2SO_4]{C_6H_5NHAc} (\mathit{p}\text{-}AcNHC_6H_4CH_2)_2NNO_2} \quad \text{(A)}$$

The yields from the condensation reaction are only fair, probably due to the concurrent decomposition of the nitramines in the strong acid.[2] Since low temperatures (below 0°) and very efficient stirring were found to be necessary for good results, *ca.* 90% sulfuric acid solutions were used to permit these conditions. A complete study of the reaction variables was not made and the listed yields are probably not optimum. Compound IV was more conveniently prepared by the cyclization of the monomethylol derivative of ethylenedinitramine[3] in the strong sulfuric acid solution. The methylol derivatives of primary aliphatic mononitramines are unknown, probably due to an unfavorable equilibrium.[4]

Cyclohexyl nitramine failed to react similarly to the other primary nitramines and it was not found possible to identify any products from the reaction. Nitrourethan also failed to condense with formaldehyde under the chosen experimental conditions and could be recovered from the acid solution. The very low basicity of the compound probably prevents the condensation. Attempts to employ chloral or paraldehyde in place of formaldehyde were unsuccessful.

The use of the Lewis acid, boron trifluoride, as a substitute for the sulfuric acid is briefly noted in the experimental section.

Compounds III and IV showed the typical secondary nitramine ultraviolet spectrum[5] having $\lambda_{\max}$ 240 mμ(ϵ 11,300) and $\lambda_{\max}$ 235 mμ (ϵ 11,500), respectively, when measured in absolute ethanol.

Compounds (I–IV) appear to be useful intermediates in the synthesis of some substituted hydrazines and experiments, with this object in mind, are in progress.

Experimental[6]

The primary mononitramines were prepared by nitration of the appropriate N-alkyl urethans,[7] ammonolysis, in dry

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[1] C. H. Holstead and A. H. Lamberton, *J. Chem. Soc.*, 1886 (1952).

[2] (a) A. P. N. Franchimont and E. A. Klobbie, *Rec. trav. chim.*, **7**, 12 and 236 (1888); (b) M. H. van Erp, *ibid.*, **14**, 1 (1895); (c) A. P. N. Franchimont and H. Umbgrove, *ibid.*, **17**, 287 (1898); (d) A. P. N. Franchimont, *ibid.*, **29**, 296 (1910); (e) J. Thiele and A. Lachmann, *Ann.*, **288**, 267 (1896); (f) A. H. Lamberton, *Quart. Rev.* (*London*), **5**, 75 (1951).

[3] (a) D. Woodcock, *J. Chem. Soc.*, 1635 (1949); (b) W. E. Bachmann, W. J. Horton, E. L. Jenner, N. W. MacNaughton and C. E. Maxwell, III, THIS JOURNAL, **72**, 3132 (1950).

[4] A. H. Lamberton, C. Lindley, P. G. Owston and J. C. Speakman, *J. Chem. Soc.*, 1641 (1949).

[5] R. N. Jones and G. D. Thorn, *Can. J. Research*, **27B**, 828 (1949).

[6] Melting and boiling points are not corrected.

[7] H. M. Curry and J. P. Mason, THIS JOURNAL, **73**, 5043 (1951)

ether, of the nitrourethans, and acidification of the resulting ammonium salts. Nitrourethan was prepared by a slight modification of the direct nitration of Brian and Lamberton[8] in which the nitration mixture was drowned in ice-water and then ether-extracted directly to give a 97% yield of product.

Ethylenedinitramine, (EDNA), was prepared from 2-imidazolidone according to the directions of Bachmann, *et al.*[3b]

2,4-Dinitro-2,4-diazapentane (I). (A).—To a solution of 2.5 g. of paraformaldehyde in 160 ml. of 90% (by weight) sulfuric acid, chilled in an ice-salt-bath (−2 to −6°), was added, in small portions and with vigorous stirring, 9.0 g. of methylnitramine. The solution was stirred about 10 minutes after the addition and was then poured onto a large quantity of ice. On standing 1.7 g. of material, m.p. 41–44°, slowly precipitated. Ether extraction of the filtrate gave a further 2.1 g. of product melting at 48–50.8°. These combined products represent a 39% yield. By recrystallization from a chloroform–hexane mixture an analytical sample, melting at 49.2–50.9°, was realized.

Anal. Calcd. for $C_3H_8N_4O_4$: C, 21.95; H, 4.91; N, 34.14. Found: C, 22.11, 21.92; H, 4.86, 4.79; N, 33.99.

(B).—A mixture of 1.5 g. of methylnitramine, 0.4 g. of paraformaldehyde, 16 ml. of trifluoroacetic anhydride and 10 drops of boron trifluoride etherate was stirred 2.5 hours with ice-bath cooling. After standing overnight in the refrigerator the mixture was poured onto ice, neutralized with sodium bicarbonate and ether extracted. The ether was dried over magnesium sulfate and was evaporated, leaving 0.3 g. of a brown oil which could not be induced to crystallize. The oil was dissolved in 10 ml. of chloroform, poured onto a one cm. (10 g.) column of activated alumina, and eluted with 40 ml. of chloroform. The eluate solidified on long standing.

Anal. Calcd. for $C_3H_8N_4O_4$: N, 34.14. Found: N, 33.97.

On recrystallization from chloroform–hexane the melting point was 49–51° and there was no melting point depression when mixed with the material from method (A).

3,5-Dinitro-3,5-diazaheptane (II).—To a solution of 0.7 g. of paraformaldehyde in 50 ml. of 90% sulfuric acid was added 3.0 g. of ethylnitramine as in method (A) for compound I. The drowned reaction mixture deposited 1.7 g. of a white solid melting at 74–77° and ether extraction of the filtrate gave 0.2 g. of solid for a total yield of 43%. An analytical sample, m.p. 75.7–77.2°, was realized by crystallization from hexane.

Anal. Calcd. for $C_5H_{12}N_4O_4$: C, 31.25; H, 6.30; N, 29.15. Found: C, 31.24, 31.31; H, 6.35, 6.28; N, 29.36, 29.48.

5,7-Dinitro-5,7-diazaundecane (III). (A).—Over a 40-minute period 8.4 g. of *n*-butylnitramine was added to a solution of 4.0 g. of paraformaldehyde in 150 ml. of 82.5% sulfuric acid according to the conditions for compound I. The drowned reaction mixture precipitated 4.2 g. of product melting at 65–70°. This constitutes a 48% yield. Use of 74% sulfuric acid gave a 13% yield of the condensation product. One recrystallization from hexane gave the analytical sample melting at 72–73.5°.

Anal. Calcd. for $C_9H_{20}N_4O_4$: C, 43.54; H, 8.12; N, 22.57. Found: C, 43.32; H, 8.00; N, 22.44.

(B).—A mixture of 1.6 g. of *n*-butylnitramine, 50 ml. of dry ether, 1.0 g. of paraformaldehyde and 5 ml. of boron trifluoride etherate was refluxed for 8 hours, giving a clear solution. This was washed with 5 portions of water, dried with magnesium sulfate, and evaporated to give a small amount (*ca.* 0.2 g.) of a brown oil which, taken up in hexane and chilled, deposited a white solid, m.p. 72–73.5°, which gave no melting point depression when mixed with the material from method (A).

1,3-Dinitro-1,3-diazacyclopentane (IV). (A).—To a solution of 1.2 g. of paraformaldehyde in 50 ml. of 87% sulfuric acid was added 3.0 g. of EDNA according to the conditions for compound I. The drowned reaction mixture gave 1.8 g. of a white solid melting at 95–115°. This was added to 10 ml. of commercial 100% nitric acid chilled in an ice–salt bath, let stand 10 minutes, and poured onto ice to give 0.9 g. (28% yield) of a white solid melting at 128.5–133.5° (softening at 122°). Recrystallization from 50 ml. of 95% ethanol gave 0.6 g. of product melting at 132.5–134°.

(B).—To 58 ml. of 89% sulfuric acid, chilled in an ice–salt bath, was added 6.8 g. of N-methylol EDNA[3] over a period of 20 minutes. After 20 minutes of additional stirring the viscous mixture was poured onto an excess of ice to give 5.2 g. (85% yield) of product melting at 132.5–134°. This was recrystallized from 95% ethanol (50 ml./g.) to give an analytical sample melting at 132.5–133.5°.

Anal. Calcd. for $C_3H_6N_4O_4$: H, 3.73; N, 34.56. Found: H, 3.72, 3.92; N, 34.30, 34.49.

N-Methylol EDNA was recovered unchanged after being stirred for several hours at room temperature in trifluoroacetic anhydride containing a catalytic amount of boron trifluoride etherate.

Attempted Condensations with Other Primary N-Nitro Compounds.—The use of nitrourethan with solutions of paraformaldehyde in 80 to 90% sulfuric acid gave only water soluble products on drowning. Ether extraction of the aqueous solutions gave nitrourethan, identified by mixed melting point with the starting material.

The addition of cyclohexylnitramine to a solution of paraformaldehyde in 90% sulfuric acid gave a small amount of non-crystallizable yellow oil which could not be separated into recognizable products. The use of 75% sulfuric acid gave about 50% recovery of the starting nitramine and no other identifiable products.

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Esterification Catalysis by Metal Halides

BY MARION E. HILL

RECEIVED SEPTEMBER 17, 1952

We have found that Friedel–Crafts type catalysts are very effective for accelerating the rate of reaction at low temperature between acid chlorides and polar alcohols, such as 2,2,2-trichloroethanol and 2,2,2-tribromoethanol. Anhydrous aluminum chloride is most active and ferric chloride, titanium tetrachloride, antimony pentachloride, boron fluoride, stannic chloride, zinc chloride and mercuric chloride are also useful in varying degree.

Examples of the catalytic effect of aluminum chloride are the preparations of β,β,β-trichloroethyl acetate and β,β,β-trichloroethyl 3,5-dinitrobenzoate. β,β,β-Trichloroethyl acetate has previously been prepared from acetyl chloride and trichloroethanol by methods requiring high temperature and long reaction periods.[1,2] The use of anhydrous aluminum chloride permits this reaction to occur easily in a solvent at low temperature.

At room temperature 1.56 g. (0.020 mole) of acetyl chloride and 3.00 g. (0.020 mole) of trichloroethanol were dissolved in 5 ml. of chloroform. Very little reaction was observed. The addition of 0.13 g. (0.001 mole) of crushed anhydrous aluminum chloride caused a vigorous exothermic reaction with copious evolution of hydrogen chloride gas. After five minutes 0.39 g. (0.003 mole) of additional aluminum chloride was added and the reaction continued vigorously for 10 minutes and then subsided. Warming to 45° completed the reaction in 20 minutes. The chloroform was evaporated and the residue treated with ice-cold dilute hydrochloric acid, extracted with ether, and distilled under vacuum after removal of the ether. A yield of 2.75 g.

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[8] R. C. Brian and A. H. Lamberton, *J. Chem. Soc.*, 1633 (1949).

[1] R. Nakai, *Biochem. Z.*, 152, 272 (1924).

[2] K. Garzarolli-Thurnlackh, *Ann.*, 210, 63 (1881).

(72%) of trichloroethyl acetate, b.p. 62° (13 mm.), was obtained. *Anal.* Calcd. for $C_4H_5O_2Cl_3$: C, 25.09; H, 2.63; Cl, 55.56. Found: C, 24.94; H, 2.57; Cl, 56.31.

Similarly trichloroethyl 3,5-dinitrobenzoate, m.p. 142–143°, was prepared in 81% yield in carbon tetrachloride within an hour. The quantity of aluminum chloride used was 30% of the molar quantities of the reactants. A control experiment was made at the same time in which no aluminum chloride was used. No reaction was observed and a quantitative recovery of the acid chloride was made. *Anal.* Calcd. for $C_9H_5O_6N_2Cl_3$: C, 31.46; H, 1.47; N, 8.15; Cl, 30.96. Found: C, 31.25; H, 1.44; N, 8.09; Cl, 30.43.

With aluminum bromide as catalyst, β,β,β-tribromoethyl benzoate, m.p. 38°, and β,β,β-tribromoethyl 3,5-dinitrobenzoate, m.p. 164–165°, were easily prepared in 80–90% yields in carbon tetrachloride. These esters do not appear to have been reported previously. *Anal.* Calcd. for $C_9H_7O_2Br_3$: Br, 61.97. Found: Br, 61.80. Calcd. for $C_9H_5O_6N_2Br_3$: Br, 50.27. Found: Br, 50.92.

The use of aluminum chloride in the esterification of an ordinary alcohol and acid chloride was first reported by Combes,[3] who isolated an acetyl chloride–aluminum chloride complex and poured it into cold ethanol. The resulting energetic reaction gave a mixture of several products. However, our work indicates that the application of metal halide catalysts to esterifying unreactive alcohols and acid chlorides in the manner outlined above gives good yields of esters. Investigation is being continued in exploring the applicability of the method and the relative efficiency of various Friedel–Crafts type catalysts.

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[3] A. Combes, *Compt. rend.*, **103**, 814 (1887).

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Detection of Some Unknown Porphyrin Products Related to Deuteroporphyrin IX by Paper Chromatography[1]

BY T. C. CHU AND EDITH JU-HWA CHU

RECEIVED FEBRUARY 2, 1953

In the course of preparing deuteroporphyrin IX dimethyl ester[2] from red blood cells and resorcinol, several unknown porphyrin products have been detected by paper chromatography.[3] This paper reports the separation of these compounds and a study of their properties.

Experimental

(I) **Preparation and Separation.**—The method of preparation of deuteroporphyrin IX dimethyl ester and the presence of other porphyrins in the crude product were described in a previous paper.[2] When the crude product was chromatographed on a $CaCO_3$ column with a mixture of ethyl acetate and benzene (1:12), the porphyrin esters separated into three red fluorescent zones under ultraviolet light. The lowest main zone R_1 was identified as deuteroporphyrin IX dimethyl ester. The other two zones as shown by paper chromatography were still mixtures. Repeated secondary chromatography with the same solvent system (1:10) resolved the middle zone into R_2 and a less adsorbed minor component R_3, and the top zone with the solvent system (1:8) into R_4 and another less adsorbed minor component R_5. The paper chromatographic R_f values for both the free porphyrins and esters in different solvent systems are listed in Table I.

(II) **Properties.**—Due to the extremely small quantities isolated these porphyrin products were not obtained in crystalline form. Although attempt was made to crystallize R_2 from different solvents even under solid CO_2 cooling or vacuum drying for many months, no crystals were obtained and its copper complex was also not crystalline. However, R_2 could be precipitated by CCl_4 from ethyl acetate solution. The properties of R_2 and other members were studied on the chromatographically pure products. In general they are quite stable in most organic solvents and fairly so in acid, but very unstable in alkaline solutions.

(A) **Absorption Spectra.**—Absorption experiments were done with a Beckman DU spectrophotometer.[4] Its cell compartment has been equipped with a thermostatically controlled device to minimize the change of sample concentration. For comparison, their fluorescence intensities have been taken as a measure of concentration, with 2 γ coproporphyrin I in 10 ml. of 1% HCl solution as a standard. The measurements were made against the solvent at 25°. The spectra of pure crystalline dimethyl esters of deuteroporphyrin IX and protoporphyrin IX were also measured for reference (Fig. 1). The strong Soret band of each of them in the near ultraviolet region was observed but not measured.

(B) **Fluorescence—*p*H Curve.**—The relation between *p*H and the fluorescent property of these porphyrins was studied on a Coleman 14 universal spectrophotometer with the fluorescence attachment. Stock solutions were prepared from samples of known fluorescence intensity in ethyl acetate solution. Each vacuum-dried sample was dissolved

TABLE I

SOME PHYSICAL PROPERTIES OF THE PORPHYRIN PRODUCTS

	$R_f^{21\circ}$ (free/ester)		Absorptions, mμ (methyl ester)											
	KC–KP[b]	KCP[c]	Organic solvents: (E), ether; (EA), ethyl acetate						Acid soln. (HA)–HOAc, (%)–%HCl			HCl no.[a] Free	HCl no.[a] Ester	Yield,[d] %
R_1[e]	0.50/0.91	0.40/0.92	(E)	622	597	569	526	498–94	(5%)	590	547	0.4	1.5	74
			(EA)	621	596	568	527	498						
R_2	.30/ .50	0 / .49	(E)	624	596	570	530	499	(HA + 10%)	593	550	.4	1.5	19
			(EA)	623	595	569	532	499						
R_3	.30/ .50	0 / .63	(E)	625	596	570	534	500		...		...	...	1
R_4	0 / .35	0 / .08	(E)	627	600	572	533	500	(HA + 25%)	598	555	.9	1.2	5
			(EA)	625	599	569	534	502						
R_5	0 / .35	0 / .17	(E)	628	602	572	535	501	(HA + 25%)	598	555	1.0	1.8	0.5
			(EA)	626	599	569	535	502						
R_6	.. / .59	.. / .69	(E)	623	596	566	526	496		...		...	2.5	..
			(EA)	622	595	568	529	500						
CuR_2	....	....	(EA)	560	525				(HA)	562	527	...	...	..

[a] The concentration in % of HCl which will extract $^2/_3$ of the porphyrin from an equal volume of ether solution. [b] Kerosene, chloroform–kerosene, *n*-propyl alcohol solvent system.[3] [c] Kerosene, chloroform, *n*-propyl alcohol system.[2] [d] Relative yield of the products, based on fluorescence measurements from a typical preparation from RBC. [e] Deuteroporphyrin IX.

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[1] This investigation was supported by a research grant from The National Institutes of Health, Public Health Service.

[2] T. C. Chu and E. J.-H. Chu, THIS JOURNAL, **74**, 6276 (1952).

[3] T. C. Chu, A. A. Green and E. J.-H. Chu, *J. Biol. Chem.*, **190**, 643 (1951).

[4] The authors are indebted to Dr. T. M. Doscher and Mr. J. Myer of The University of Southern California for using the instrument.

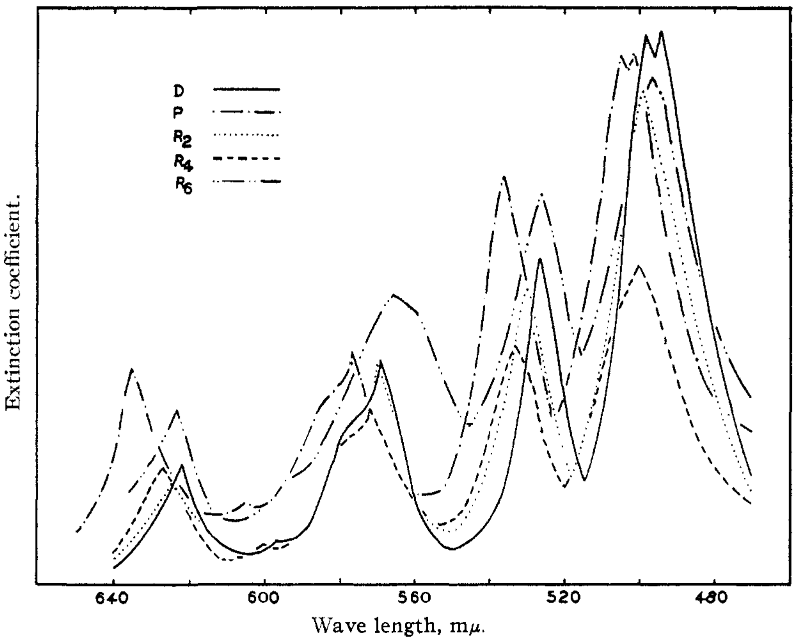

Fig. 1.—The absorption spectra of methyl esters of deuteroporphyrin IX (D), protoporphyrin IX (P), R_2, R_4 and R_6 in ether.

in calculated amounts of 5% HCl containing 5% acetic acid to a final concentration of "2 γ" per ml. in coproporphyrin I units. The solution was allowed to stand for 24 hours for complete hydrolysis. For each determination, 1 ml. of the stock solution was generally mixed with 9 ml. of sodium citrate buffer or HCl or NaOH of proper concentration as the case might be. In the *p*H region, the final *p*H of each solution after fluorescence measurement was determined in a Beckman G *p*H-meter. The curves for deutero- and protoporphyrin IX were also included in Fig. 2, but with 0.5-ml. samples.

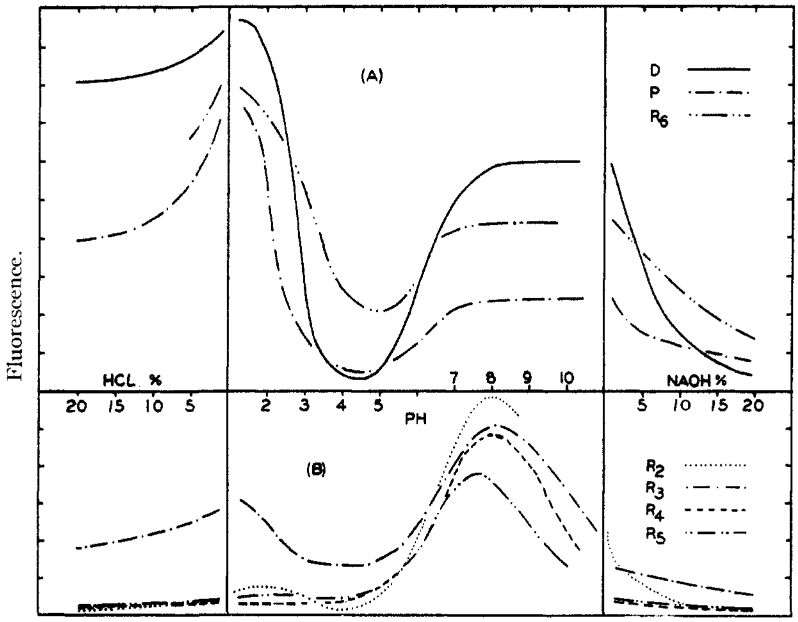

Fig. 2.—Fluorescence-*p*H curves of deuteroporphyrin IX (D), protoporphyrin IX (P), R_2, R_3, R_4, R_5 and R_6.

It has been observed that deuteroporphyrin, protoporphyrin, etc. (Fig. 2A), decreased their fluorescence values gradually on standing in strong alkaline solutions while other porphyrins (Fig. 2B) showed a tendency to increase. On the other hand, between *p*H 6–11 the latter group revealed a tendency to decrease their intensity while the former group was quite steady.

Analyses of the products recovered from these experiments by paper chromatography showed that the compounds of group (2B) had undergone some sort of change mainly into non-fluorescent substances and partly to other porphyrins including deuteroporphyrin. In the buffer solution of *p*H 6–11, more non-fluorescent products were formed.

(C) **Reaction with NaOH.**—When a solution of "5 γ" R_2 in 10 ml. of 4% NaOH was irradiated in the Coleman, the intensity of fluorescence increased to a maximum in about 20 minutes, then decreased slowly and smoothly for about an hour to reach its half value. Neither 1 nor 10% NaOH was as effective as the 4% solution. Paper chromatographic analysis of the reacting mixture at various stages showed that (1) at the glowing stages, a new porphyrin designated hereafter as R_6 and deuteroporphyrin were formed (2:1) increasingly at the expense of R_2; (2) at the declining stages, no R_2 but reducing amounts of R_6 and deuteroporphyrin were found. The reaction between R_2 and NaOH took place even in the dark and under nitrogen atmosphere but at much slower rate. Meanwhile, the addition of an equal volume of 30% H_2O_2 to 4% NaOH solution of R_2 gave essentially the same result. It seems that the reaction is independent of any mild oxidizing agent.

In reaction with NaOH, R_3 gave rise to R_6 and deuteroporphyrin, whereas R_4 gave R_6 as the main porphyrin product and R_5 gave R_2, R_3 and R_6, but with even poorer yields in all cases.

(D) **Isolation of R_6 and Chromatographic Roll.**—When protoporphyrin IX dimethyl ester was used instead of red blood cells in the fusion mixture, more R_2 resulted. A total of "2200 γ" (copro-I units) of chromatographically pure R_2 was obtained from 25 mg. of protoporphyrin ester. R_3, R_4 and R_5 were also found together with some deuteroporphyrin.

For the preparation of R_6, larger quantities of R_2 were treated with 4% NaOH in a beaker under sunlight. A pilot sample was placed in the Coleman beforehand in order to find out the possible maximum intensity. After 5 minutes testing, samples were taken at short intervals to determine the right time of exposure. For instance, under the hazy Los Angeles sunshine in May, it took 7–8 minutes. The reaction mixture was then immediately neutralized with 15% HCl, extracted and esterified as usual. The separation was effected by means of a chromatographic roll. It was made by rolling a sheet of Whatman No. 1 paper (15 × 57 cm.) into a doubly coiled No. 16 nichrome wire frame. Instead of spotting, a sample was applied all along the basal line 2 cm. from the bottom. The roll was developed in a 2-l. beaker containing 20 ml. of kerosene–chloroform (1:1) for about 40 minutes. The compound R_6 appeared in the middle of the papergram as a clear band with deuteroporphyrin band almost at the top and the residual R_2 at the bottom. Several minor products of the reaction which were not shown in the spot papergram were thus detected as faint bands between main ones. These bands were cut out from the dried papergram along pencil tracings made under ultraviolet light, and extracted with ethyl acetate. An average yield of "3 γ" of R_6 was obtained from "100 γ" of R_2.

As far as the fluorescence property is concerned, R_6 resembles deuteroporphyrin more than R_2, R_3, etc. In NaOH solution, its fluorescence disappears almost at the same rate as that of deuteroporphyrin; but in organic solvents it is not as thermostable as that of the latter. For instance, it loses its fluorescence considerably even at 105°. R_3 is also very unstable around this temperature, changing partly into the more stable R_2.

HCl numbers of these products and absorption data of the copper complex of R_2 ester are listed together in Table I.

Discussion

The absorption data of these porphyrin products indicate the absence of vinyl groups. This point has been supplemented by the negative qualitative test for the vinyl group.[5] Although R_2 is most probably an intermediate in the formation of deuteroporphyrin, it is not 4-vinyldeuteroporphyrin,[6] spirographisporphyrin,[7] monoformyl or diformyl deuteroporphyrin,[8] as evidenced by the spectroscopic data and negative chemical tests toward the reagents, diazoacetic methyl ester and hydroxylamine.

The different trends noted in the fluorescence changes of the group (Fig. 2B) are shown by the NaOH reaction. With a 4% NaOH, they give R_6 and deuteroporphyrin as the main fluorescent products. As shown in Fig. 2A, these porphyrins have more intense fluorescence in the strongly alkaline region. On the other hand a reacting medium with *p*H between 6–11 is favorable for the formation of non-fluorescent products.

The results of the NaOH reaction which may be outlined as $R_5 \rightarrow R_2(R_3) \rightarrow R_6 +$ deutero, support the view that they are most likely the precursors of deuteroporphyrin IX and should play some roles in the mechanism of the formation of deuteroporphyrin by the resorcinol fusion.

The authors wish to express their appreciation to Sister Agnes Ann Green for her interest in the work.

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[5] E. J.-H. Chu, *J. Biol. Chem.*, **166**, 463 (1946).

[6] H. Fischer and G. Wecker, *Z. physiol. Chem.*, **272**, 1 (1941).

[7] H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. II, 1937, p. 468.

[8] Ref. 7, p. 292.

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Heat Capacities at Low Temperatures and Entropies at 298.16°K. of Stannic and Stannous Sulfides

BY E. G. KING AND S. S. TODD

RECEIVED MARCH 7, 1953

Existing thermodynamic information on the sulfides of tin is rather meager, and low-temperature heat-capacity and entropy data have been entirely lacking. This paper presents the results of low-temperature heat capacity measurements of both stannic and stannous sulfides, with an evaluation of their entropies at 298.16°K.

Materials.—The stannic sulfide was prepared by K. R. Bonnickson of this Laboratory from reagent-grade stannous chloride dihydrate, sulfur and ammonium chloride. These ingredients were mixed in the molal proportion of 1:3:2 and heated in an open-end tube, first at 150° until evolution of water ceased and then for three hours at 300–350°, after which the tube was stoppered and cooled. The reaction mass was broken up, shaken with water, and centrifuged four times. It was then shaken with alcohol, centrifuged and dried at 60°. Finally the product was mixed with 10% by weight of sulfur and heated in vacuum for five hours at 300°, the excess sulfur being distilled off in the process. The product analyzed 64.95% tin, as compared with the theoretical 64.92%. The X-ray diffraction pattern agreed with that given for stannic sulfide in the A.S.T.M. catalog, except for the presence of four weak lines that could not be identified.

The stannous sulfide was furnished by M. J. Spendlove of the College Park, Md., Station of the Bureau of Mines. It was prepared by adding sulfur to an excess of molten tin, skimming off the reaction product, and roasting at 980° to remove excess sulfur and produce a crude grade of stannous sulfide. The crude material then was purified by sublimation in vacuum, which gave a well crystallized, dense product. Chemical analysis showed the substance to contain 99.2% stannous sulfide and 0.6% stannic oxide, leaving about 0.2% unaccounted for. Spectrographic analysis indicated less than 0.01% each of aluminum, bismuth, iron, magnesium, calcium, sodium and copper, while silicon and lead may run as high as 0.05%.

Measurements and Results.—The measurements were conducted with previously described apparatus.[1] The sample masses employed were 104.12 g. of stannic sulfide and 338.98 g. of stannous sulfide. The stannous sulfide results were corrected for the 0.6% stannic oxide content by means of the heat capacity data of Millar,[2] the correction ranging from 0.38% at the lowest temperature to zero at the highest. No correction of the stannic sulfide results was necessary.

The measured heat capacities appear in Table I, being expressed in defined calories (1 cal. = 4.1840 abs. joules) per deg. mole. Molecular weights accord with the 1951 International Atomic Weights.[3]

TABLE I

HEAT CAPACITIES

T, °K.	C_p, cal./deg. mole	*T*, °K.	C_p, cal./deg. mole	*T*, °K.	C_p, cal./deg. mole
SnS_2 (mol. wt., 182.83)					
52.75	4.139	114.65	10.24	216.55	15.16
56.45	4.453	124.72	11.02	226.55	15.38
60.65	4.874	135.98	11.80	236.88	15.62
65.17	5.389	146.13	12.43	246.21	15.84
70.05	5.900	155.79	12.92	257.06	16.02
74.92	6.407	166.54	13.44	266.82	16.21
80.28	6.976	176.14	13.85	276.28	16.39
84.04	7.387	186.22	14.24	287.38	16.58
93.66	8.356	196.28	14.56	296.54	16.76
105.07	9.435	206.63	14.87	(298.16)	(16.76)
SnS (mol. wt., 150.77)					
52.45	4.762	114.70	8.837	216.37	11.10
56.82	5.115	125.28	9.249	226.05	11.19
61.40	5.525	136.01	9.607	236.31	11.28
65.90	5.920	146.22	9.901	246.03	11.37
70.49	6.277	155.93	10.13	256.19	11.45
75.28	6.623	166.03	10.34	266.05	11.55
80.20	6.974	176.12	10.54	276.36	11.61
83.71	7.208	186.09	10.69	286.68	11.69
94.67	7.868	195.91	10.84	296.80	11.77
104.47	8.368	206.31	10.95	(298.16)	(11.77)

Both substances exhibit normal heat capacity curves. The only unusual feature is that, at tem-

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[1] K. K. Kelley, B. F. Naylor and C. H. Shomate, U. S. Bur. Mines Tech. Paper 686 (1946).

[2] R. W. Millar, THIS JOURNAL, **51**, 207 (1929).

[3] E. Wichers, *ibid.*, **74**, 2447 (1952).

peratures below 80°K., the stannic compound has the lower molal heat capacity, despite the extra atom of sulfur in its molecular composition. A similar phenomenon is evident in Millar's[2] results for stannic and stannous oxides, the former having the lower molal heat capacity at temperatures below about 155°K.

Entropies at 298.16°K.—The entropy increments for the measured temperature range, 51.00 to 298.16°K., were obtained by Simpson-rule integrations of plots of C_p against log T. The extrapolated portions, between zero and 51.00°K., were evaluated by means of the following empirical sums of Debye and Einstein functions which fit the measured heat capacities to within the limits and for the temperature ranges shown in parentheses.

$$\text{SnS}_2\text{:}\ D(172/T) + E(369/T) + E\left(\frac{415}{T}\right)\ (1.0\%,\ 51\text{–}170°\text{K.})$$

$$\text{SnS:}\quad D(146/T) + E(311/T)\ (1.0\%,\ 51\text{–}150°\text{K.})$$

Results of the entropy calculations are in Table II. The measured portions constitute 89.7 and 84.5%, respectively, of the totals at 298.16°K. for stannic and stannous sulfides.

TABLE II

ENTROPIES AT 298.16°K. (CAL./DEG. MOLE)

	SnS_2	SnS
0–51°K. (extrap.)	2.15	2.84
51–298.16°K. (meas.)	18.78	15.52
$S°_{298.16}$	20.9 ± 0.2	18.4 ± 0.2

Employing entropy values for white tin and rhombic sulfur listed by Kelley,[4] the entropies of formation of stannic and stannous sulfides are, respectively, $\Delta S_{298.16} = -6.6 \pm 0.2$ and $\Delta S_{298.16} = -1.5 \pm 0.2$ cal./deg. mole.

[4] K. K. Kelley, U. S. Bur. Mines Bulletin 477 (1950).

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Decomposition of Nitrosyl Disulfonate Ion. II. The Relation to the Mechanisms of Diazotization and Deamination

BY JAMES C. M. LI AND D. M. RITTER

RECEIVED FEBRUARY 16, 1953

In connection with the study of the decomposition of nitrosyl disulfonate ion,[1] we have studied the reaction of nitrous acid with nitrosyl disulfonate ion and with sulfamate ion[2]; and we have found both cases significantly related to the mechanisms proposed for diazotization and deamination.

The first reaction in one molar sodium acetate solution was kinetically second order with respect to molecular nitrous acid and zero order to nitrosyl disulfonate ion. This rate law was deduced from the concentration and pH dependence of the rate of disappearance of the colored nitrosyl disulfonate ion and the evolution of nitrous oxide product.

As one evidence for the validity of the treatment the dissociation constant of nitrous acid was obtained from a plot of $1/\sqrt{k}$ *vs.* $1/[H^+]$ as required by the relation

$$\frac{1}{\sqrt{k}} = \frac{K}{\gamma_- \sqrt{k'}} \cdot \frac{1}{[H^+]} + \frac{1}{\sqrt{k'}} \qquad (1)$$

In equation (1) k is the rate constant at a given pH, K the dissociation constant of nitrous acid, γ_- the activity coefficient of NO_2^- and k' the pH independent constant for the proposed rate law: rate = $k'(HNO_2)$.[2] The value obtained was $5 \pm 0.5 \times 10^{-4}\ \gamma_-$ close to $5.15 \times 10^{-4}\ \gamma_\pm^2$ obtained by Schmid, Marchgraber and Dunkl[3] at 25°.

Following Hammett's suggestion[4] for the second-order participation of nitrous acid, we have deduced the following mechanism

$$2HNO_2 \xrightarrow{k_1} N_2O_3 + H_2O$$

$$(SO_3)_2NO^- + N_2O_3 + 2H_2O \xrightarrow{\text{fast}} 2SO_4^{=} + NO^+ + NO + NOH + H_3O^+$$

$$(SO_3)_2NO^- + NO + H_3O^+ \xrightarrow{\text{fast}} (SO_3)_2NOH^- + NO^+ + H_2O$$

with NO^+ and 2NOH giving nitrous acid and nitrous oxide, respectively. The rate constant k_1 = 7,000 l./mole-min. was obtained at 25°. From the temperature dependence of k_1 between 35 and 10°, $k_1 = 300$ was obtained at 0° by extrapolation.

Compare this reaction with the diazotization of aniline[5] at 0° and mild acidity where the concentration dependences were zero order for amine and second order for nitrous acid. In the calculation, a value[3] of 3.55×10^{-4} was used for the dissociation constant of nitrous acid at 0° and the activity coefficient of NO_2^- was taken as 0.8 in the phthalate buffer solution. The following table shows results of calculations based upon data transcribed from the latter paper

pH	Rate/$(\Sigma\ HNO_2)^2$	$[1 + (K/[H^+]\gamma^-)]^2$	k_1
4.80	0.30	840	252
5.00	.14	2060	289
5.20	.063	5100	321

The agreement suggests that N_2O_3 is the actual reacting species in the acid decomposition of nitrosyl disulfonate ion as well as in some diazotization reactions.

The second reaction between sulfamate ion and nitrous acid was found kinetically first order with respect to each reactant in an acetate buffer solution, and the pH dependence showed the following rate law at 25° and 0.17 ionic strength

$$\frac{d(N_2)}{dt} = 7.0 \times 10^4 (HNO_2)(H^+)(^-SO_3NH_2) \text{ moles/liter-min.}$$

in agreement with Dusenbury and Powell[6] who suggested NO^+ or $H_2NO_2^+$ as the deamination agent.

We also have re-examined[7] the data of Taylor[8]

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[1] J. H. Murib and D. M. Ritter, THIS JOURNAL, **74**, 3394 (1952).

[2] Forthcoming papers III, IV of this series.

[3] H. Schmid, R. Marchgraber and F. Dunkl, *Z. Elektrochem.*, **43**, 337 (1937).

[4] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 294.

[5] E. D. Hughes, C. K. Ingold and J. H. Ridd, *Nature*, **166**, 642 (1950).

[6] J. H. Dusenbury and R. E. Powell, THIS JOURNAL, **73**, 3266, 3269 (1951).

[7] See also, A. T. Austin, E. D. Hughes, C. K. Ingold and J. H. Ridd, *ibid.*, **74**, 555 (1952).

[8] T. W. J. Taylor, *J. Chem. Soc.*, 1099, 1897 (1928).

and of Abel, Schmid and Schafranik[9] for methylamine and ammonia, respectively, using the curve-matching method of Dusenbury and Powell.[6] When all the values were considered, the rates corresponded exactly with the Taylor–Abel third-order rate equation over *p*H 3.5–4.6. The observed rates were somewhat larger than they should have been over *p*H 0.2–2.1, but they were closer to the third order rate law than to any other.

The results can all be reconciled by assuming two mechanisms. One is predominantly that followed in deamination

$$\mathrm{NO^+ + NH_3 \underset{k_b}{\overset{k_a}{\rightleftarrows}} N_2{-}H_3O^+}$$

$$\mathrm{N_2 - H_3O^+ + B^- \xrightarrow{k_c} N_2 + HB + H_2O}$$

where B^- is a generalized base. Steady state computation gives

$$\frac{\mathrm{d(N_2)}}{\mathrm{d}t} = \frac{k_a k_c(\mathrm{NO^+})(\mathrm{NH_3})(\mathrm{B^-})}{k_b + k_c(\mathrm{B^-})}$$

which gives at low (B^-) the Taylor–Able mechanism (when B^- is only NO_2^-) and at high (B^-) the mechanism of Dusenbury and Powell and those cases where chloride or bromide ions are catalysts. The second mechanism involving N_2O_3 appears peculiar to diazotization. However, only where the amine dependence is zero is it kinetically distinguishable from the Taylor–Abel case.

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[9] E. Abel, H. Schmid and J. Schafranik, *Z. physik. Chem., Bodenstein Festband*, 510 (1931).

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Absorption Spectra of Solutions of Pheophytin a in Methanol Containing Acid or Base[1]

BY ROBERT LIVINGSTON, RUDOLPH PARISER, LOU THOMPSON AND ALBERT WELLER

RECEIVED FEBRUARY 28, 1953

In the study of the kinetics of a photosensitized reaction it was necessary to use the extinction coefficients of pheophytin **a** at several different wave lengths and in solutions of varying acidity. Since such data were not available,[2] the absorption spetra of pheophytin **a**, dissolved in methanol containing a wide range of concentrations of added acid or base, were measured.

Experimental Materials and Methods

Pheophytin **a** was prepared as follows: 0.6 ml. of a 2.4 *m* solution of HCl in methanol was added to 150 ml. of a 4 × 10^{-4} *m* solution of purified chlorophyll **a**[3] in ether. After standing for about 6 hours at room temperature, the pheophytin was transferred to about 10 ml. of petroleum ether A, and was purified chromatographically on powdered sugar, using petroleum ether A containing 0.5% isopropyl alcohol as a developer. Only a single band appeared on the column. The absorption spectrum of an ethereal solution of this material agreed closely with the spectrum published by Zscheile and Harris.[4]

Methanolic hydrochloric acid was prepared by bubbling dry hydrogen chloride into purified methanol.[5] Solutions of sodium methoxide were prepared by dissolving clean sodium in purified methanol. The concentrations of these solutions were determined by titration with standard aqueous solutions of acid and base.

The spectrophotometric measurements were made (at approximately 25°) with a Beckman DU spectrophotometer, using 10.0-mm. Corex cells. A few experiments were performed, with a Carey recording spectrophotometer, to test for the possible existence of a transient, reversible form of pheophytin in basic solutions.

Results and Conclusions

Values of log I_0/I of 1.5 × 10^{-5} *m* pheophytin **a**, from λ3400 to 7000 Å., were measured at 100 Å. intervals for methanolic solutions containing the following added substances at the concentrations indicated: (1) 10^{-1} *m* HCl, (2) 10^{-2} *m* HCl, (3) 10^{-3} *m* HCl, (4) 10^{-4} *m* HCl, (5) 3 × 10^{-5} *m* HCl, (6) 10^{-5} *m* HCl, (7) 5 × 10^{-6} *m* HCl, (8) 10^{-6} *m* HCl, (9) 7.5 × 10^{-2} *m* $CH_2Cl{\cdot}COOH$ + 7.5 × 10^{-3} *m* $CH_2Cl{\cdot}COONH_4$, (10) no added substance, (11) 10^{-3} *m* CH_3CONa, and (12) 10^{-1} *m* CH_3CONa. The absorption spectra of solutions (1) and (2) correspond to curve A of Fig. 1; of solutions (8), (9) and (10) to curve N; and of solutions (11) and (12) to curve B.

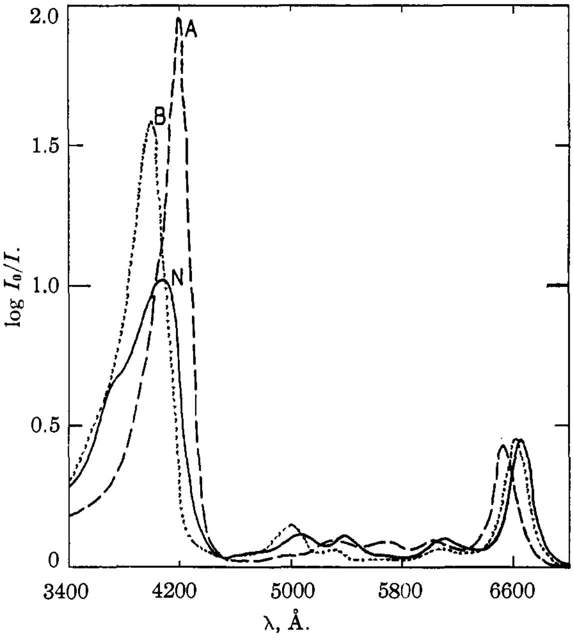

Fig. 1.—Absorption spectra of pheophytin in neutral, acidic and basic methanolic solutions: A, solutions containing HCl at concentrations of 10^{-2} *m* or greater; N, solutions in pure methanol; B, solutions formed by dissolving pheophytin in strongly basic solutions.

TABLE OF PRINCIPAL MAXIMA

Solutions	λ, Å.	log I_0/I	λ, Å.	log I_0/I
A	4180	1.95	6525	0.43
N	4080	1.04	6670	0.45
B	4000	1.57	6630	0.44

The spectra of solutions (3) to (7) exhibit (principal) isobestic points at λ4030 and 6600 Å. Spectra

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[1] This work was made possible by the support of the Office of Naval Research (NR 059,028, Contract N6ori-212, T.O.I) to which the authors are indebted. R. Pariser, Ph.D. Thesis, Univ. of Minnesota, 1950.

[2] Compare, however, W. Broser and W. Lautsch, *Naturwissenschaften*, **38**, 209 (1951).

[3] R. Livingston, D. Sickle and A. Uchiyama, *J. Phys. Chem.*, **51**, 775 (1947).

[4] F. Zscheile and D. Harris, *Bot. Gaz.*, **104**, 515 (1943).

[5] R. Livingston and R. Pariser, THIS JOURNAL, **70**, 1510 (1948).

identical with those observed for these solutions can be obtained by linear combination of curves A and N. The acid form (A) is stable in acid solutions and exists in (rapidly reversible) equilibrium with the neutral form (N) in solutions of intermediate acidity.

In basic solutions pheophytin undergoes an irreversible reaction producing a single substance whose absorption spectrum is represented by curve B. If a basic solution containing this reaction product is neutralized with acid, the absorption spectrum of the resulting solution has its principal maxima at λ4120 and 6480 Å. In dilute solutions of strong base (or of moderate concentrations of aliphatic amines), the irreversible reaction of pheophytin to form the product (B) is measurably slow. There is no evidence for the transient existence, in any of these solutions, of a reversible, intermediate basic form of pheophytin.

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N-Phenylpyrrolidine[1]

By Carl J. Olsen and Arthur Furst[2]

Received February 2, 1953

By passing tetrahydrofuran and aniline over activated alumina at 400°, Yur'ev and Minkina[3] obtained N-phenylpyrrolidine in 45.5% yield. Bourns, Embleton and Hansuld,[4] by carefully controlling feed rate, molar ratios and temperature conditions, increased the yield to 88%.

A study was made to see if the desired product could be obtained by merely heating tetrahydrofuran and aniline in an autoclave with a Lewis acid. When aluminum chloride was used as a catalyst N-phenylpyrrolidine was obtained in 42% yield. It was subsequently found possible to obtain a 20% yield in the presence of aluminum chloride at atmospheric pressure.

Experimental

Pressure Reaction.—A mixture of 4.0 g. (0.043 mole) of aniline, 5.7 g. (0.054 mole) of anhydrous aluminum chloride and 4.0 g. (0.056 mole) of tetrahydrofuran was placed in an autoclave, and the pressure was brought up to 1000 lb./sq. in. with nitrogen gas. The mixture was heated to 240° and rocked for 24 hours. The amber colored semi-solid reaction product was made basic with sodium hydroxide solution and extracted with ether. The ether was removed and N-phenylpyrrolidine was recovered by distillation under reduced pressure; b.p. 106–109° (6 mm.), yield 2.7 g. (0.018 mole) or 42.6%, m.p. *ca.* 13°, picrate, m.p. 116–118°, lit. value[3] 116°. No depression of melting point was noted when authentic picrate was mixed with product above.

Other catalysts used and yields were: hydrogen chloride (3.2%), sulfuric acid (no yield), phosphorus pentoxide (31.6%), activated alumina (no yield).

Atmospheric Pressure.—Anhydrous aluminum chloride, 28.5 g. (0.210 mole), was added in portions to 20.0 g. (0.215 mole) of aniline. The temperature rose to *ca.* 150°. With constant stirring, 20.0 g. (0.276 mole) of tetrahydrofuran was added drop by drop. The solution darkened. The temperature was maintained at 150–160° by heating. After one-third of the tetrahydrofuran was added the temperature dropped. The reaction mixture was heated to reflux and the remainder of the tetrahydrofuran added. Refluxing was continued two more hours.

On cooling, the solution was made basic, steam distilled, and the distillate extracted with ether. A yield of 6.1 g. (0.042 mole), 19.8%, N-phenylpyrrolidine was obtained.

Acknowledgment.—This investigation was supported by a grant-in-aid from the Research Corporation. Tetrahydrofuran was kindly supplied by E. I. du Pont de Nemours and Co.

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[1] Taken in part from the Master of Science Thesis of Carl J. Olsen, June, 1952.

[2] Department of Pharmacology and Therapeutics, Stanford University School of Medicine, San Francisco, California.

[3] Yu. K. Yur'ev and G. A. Minkina, *J. Gen. Chem.* (*USSR*), **1**, 2945 (1937); *C. A.*, **32**, 5399 (1938).

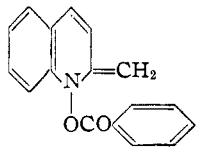
[4] A. N. Bourns, H. W. Embleton and M. K. Hansuld, *Can. J. Chem.*, **30**, 1 (1952).

The Benzoylation of Quinaldine Oxide

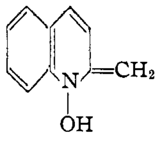
By Irwin J. Pachter

Received February 27, 1953

The reaction of quinaldine oxide (I) with benzoyl chloride and sodium hydroxide was investigated by Henze[1] who obtained a compound, $C_{17}H_{13}NO_2$, which was formulated as IIa. Upon treatment with either acid or alkali the compound was converted to a new substance, $C_{10}H_9NO$, isomeric with quinaldine oxide. This substance reacted with Fehling solution and Tollens reagent, but not with phenylhydrazine or hydroxylamine. Structure IIIa was suggested for the debenzoylated product.[1]



IIa



IIIa

A substance of structure IIIa would undergo facile tautomerism to quinaldine oxide, particularly under the conditions employed in effecting debenzoylation. It may therefore be discounted as a possibility. A more likely product would be 2-quinolinemethanol (IIIb) which, being analogous to an α-ketol, would be expected to undergo oxidation in Fehling solution and Tollens reagent. A reaction scheme for the formation of IIIb, involving attack of hydroxyl ion or water on the methylene group of IIa with concurrent elimination of benzoate ion or benzoic acid, can readily be formulated.

The syntheses described by Henze were repeated. The identity of the debenzoylated product with a sample of 2-quinolinemethanol prepared from methyl quinaldate by reduction with lithium aluminum hydride[2,3] was established by mixture melting point determination and infrared spectroscopy.

The infrared spectrum of the compound formulated as IIa was examined. The absence of bands indicative of a terminal methylene group suggested that the product might be 2-quinolinemethyl benzoate (IIb). To test this possibility, IIIb was rebenzoylated. The compound thus obtained was

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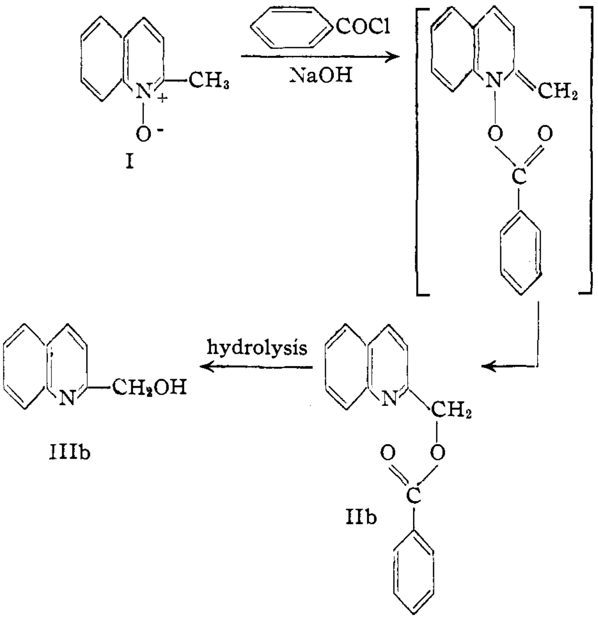
[1] M. Henze, *Ber.*, **69**, 534 (1936).

[2] C. E. Kaslow and W. R. Clark, *J. Org. Chem.*, **18**, 55 (1953).

[3] The author is grateful to Professor C. E. Kaslow for supplying this authentic sample.

found to be identical with that formed directly from quinaldine oxide and benzoyl chloride. Reaction with rearrangement thus occurs when quinaldine oxide is treated with benzoyl chloride. The subsequent formation of IIIb from IIb is the result of simple hydrolysis.



In isolating IIb, Henze acidified the benzoylation product with hydrochloric acid, purified the hydrochloride, and then liberated IIb with alkali. It was possible that the acidification transformed initially-formed IIa to IIb. An experiment avoiding acidification was therefore performed. The product isolated directly from the alkaline benzoylation mixture proved to be identical with that obtained *via* the hydrochloride.

A simplified method for the preparation and purification of quinaldine oxide hydrate is described.

Experimental[4]

Quinaldine Oxide Hydrate.—To 20 g. of freshly distilled quinaldine was added 22 g. of 30% aqueous hydrogen peroxide and 60 ml. of acetic acid. The solution was heated at 55° for 20 hours. It was then cooled in ice and slowly treated with a solution of 80 g. of potassium hydroxide in 100 ml. of water. Quinaldine oxide hydrate separated as a dark oil and soon solidified. It was filtered and the filtrate was extracted with 30 ml. of chloroform. The chloroform was evaporated from the extract and the residue was combined with the main product and added to 300 ml. of benzene. The mixture was distilled until water no longer came over with the benzene. The light yellow benzene solution was then decanted from dark brown insoluble materials, cooled, and stirred with a few ml. of water. The quinaldine oxide hydrate, which separated as almost colorless needles, was filtered and dried to give 16.2 g. of product, m.p. 75–76°. Recrystallization from water raised the m.p. to 77–78°.

2-Quinolinemethyl Benzoate.—To 0.5 g. of 2-quinolinemethanol was added 20 ml. of water, 2 ml. of 10% aqueous sodium hydroxide and 0.5 g. of benzoyl chloride. The mixture was stirred until the pale yellow oil solidified. The product was filtered and recrystallized from aqueous methanol to form clusters of almost colorless plates, m.p. 52–53°. The infrared spectrum and m.p. of the compound were identical with those of the product obtained from the reaction of quinaldine oxide hydrate with benzoyl chloride. There was no depression of m.p. upon admixture of the two samples.

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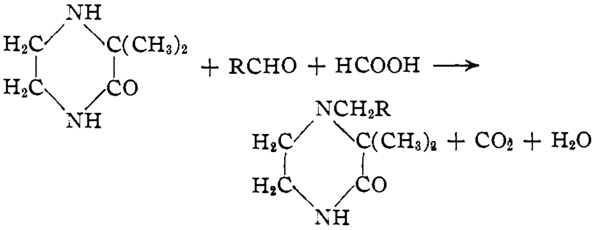
Leuckart Alkylation of 2-Piperazinones[1]

BY PHILIP RUBY AND PETER L. DEBENNEVILLE

RECEIVED FEBRUARY 20, 1953

The availability of 2-piperazinones by a new method developed in these laboratories,[2] suggested the possibility of alkylation on the amine nitrogens under Leuckart conditions. In this way, the amide nitrogen could be the site for a desired methylolation reaction without the complication of resin formation from the secondary amino group.

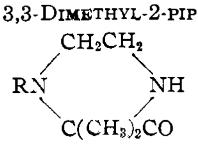
The alkylation may be illustrated by the series of compounds prepared from 3,3-dimethyl-2-piperazinone.[3]



Data for these reactions are given in Table I. Reaction proceeded smoothly at temperatures of 100–130°, resulting in good yields when aldehydes were used. Ketones failed to react even at high temperatures, and in all three cases tried, 4-formyl-2-piperazinone was the only product. The failure of ketones to react can probably be ascribed to the methyl groups in the 3-position, as well as to the fact that the piperazinone is a secondary amine. It has been noted that in the sequence ammonia, methylamine and dimethylamine, yields of 78,

TABLE I

ALKYLATED 3,3-DIMETHYL-2-PIPERAZINONES



R	Yield, %	M.p., °C.[a]	Empirical formula	Nitrogen,[b] % Calcd.	Found
Methyl	72	131–132	$C_7H_{14}N_2O$	19.7	19.2
Ethyl	27	164–165	$C_8H_{16}N_2O$	17.9	17.6
Isobutyl	60	136–138	$C_{10}H_{20}N_2O$	15.2	15.1
p-Chlorobenzyl	56	201–203	$C_{13}H_{17}N_2OCl$	11.1[c]	11.0[c]
3,4-Methylene-dioxybenzyl[d]	35	190–193	$C_{14}H_{18}N_2O_3$	10.6	10.5
3,5,5-Trimethylhexyl	73	99–100	$C_{15}H_{30}N_2O$	11.1	11.2

[a] Uncorrected. [b] Kjeldahl method. [c] Calcd. for $C_{13}H_{17}N_2OCl$: Cl, 14.0. Found: Cl, 13.7. [d] From piperonal.

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(4) It was reported[1] that the debenzoylated compound, now formulated as IIIb, gives a red color with ferric chloride in the alcoholic solution. In the present work, a yellow precipitate, but no red color, was observed. In other experiments, the results reported by Henze were obtained.

(1) Communications should be directed to Peter L. deBenneville, Rohm & Haas Co., 5000 Richmond St., Philadelphia, Pa.

(2) V. T. Elkind, J. S. Strong and W. E. Craig, private communication.

(3) S. R. Aspinall, THIS JOURNAL, 62, 1203 (1940).

53 and 0% are obtained in the Leuckart reaction with laurophenone.[4]

Experimental

Formaldehyde and paraldehyde were used in the form of their revertible polymers as described below. Other aldehydes were commercial products, used without purification. The yields, given in Table I, are crude yields. The preparation of 4-*p*-chlorobenzyl-2-piperazinone described below is typical.

3,3-Dimethyl-2-piperazinone[3] was prepared by the method of Elkind, Strong and Craig.[2] Formic acid was 98% commercial grade.

3,3,4-Trimethyl-2-piperazinone.—To a mixture of 3,3-dimethyl-2-piperazinone (128 g., 1 mole) and paraformaldehyde (35 g., 1.1 moles), heated with stirring on the steam-bath under reflux, formic acid (57.5 g., 1.25 moles) was added dropwise. The paraformaldehyde went into solution and CO$_2$ was evolved copiously. After further heating for 2.5 hours on the steam-bath, reaction was complete. The solid product distilled from a Claisen flask at 160–170° at 26 mm. to yield 131 g. of colorless crystals, melting at 100–110°. After recrystallization from isopropyl alcohol, a yield of 102 g. (72%) melting at 128–130° was obtained. Further recrystallization raised the melting point to 131–132°.

3,3-Dimethyl-4-ethyl-2-piperazinone.—A mixture of paraldehyde (9.7 g., 0.22 mole), 3,3-dimethyl-2-piperazinone (25.6 g., 0.2 mole), formic acid (11.5 g., 0.25 mole), and 0.7 ml. of 37% HCl was heated at 125–130° for 29 hours. The solid obtained on cooling was recrystallized twice from isopropyl alcohol and then from benzene to give 6.9 g. (22%) of alkylated product melting at 164–165°. A small amount of product (5%) was recovered from the mother liquors.

3,3-Dimethyl-4-*p*-chlorobenzyl-2-piperazinone.—A mixture of *p*-chlorobenzaldehyde (62 g., 0.44 mole), 3,3-dimethyl-2-piperazinone (51.2 g., 0.4 mole) and formic acid (23 g., 0.5 mole) was heated at reflux for 8 hours. The product solidified on cooling and was recrystallized from isopropyl alcohol to yield 53 g. (56%) of colorless crystals melting at 201–203°.

Failure of Ketones to React in the Leuckart Reaction.—A mixture of 3,3-dimethyl-2-piperazinone (51.2 g., 0.4 mole), cyclohexanone (43.1 g., 0.44 mole) and formic acid (23 g., 0.5 mole) was heated at reflux for 54 hr. The solid produced was recrystallized from ethanol and then from benzene. There was obtained 22.4 g. of colorless crystalline product, which melted at 170–172°. This proved on analysis to be 4-formyl-3,3-dimethyl-2-piperazinone in 36% yield. Calcd. for $C_7H_{12}N_2O_2$: N, 17.9. Found: N, 17.8.

The same product, compared by mixed melting point, was obtained from similar reactions of acetone (52% yield) and acetophenone (62.5% yield). This formyl derivative was heated for 10 hr. with acetophenone at 200°, and then for 9 hours additional in the presence of an equivalent quantity of formic acid at 200°. No CO$_2$ was evolved and the formyl derivative was recovered.

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[4] F. S. Crossley and M. L. Moore, *J. Org. Chem.*, **9**, 529 (1944).

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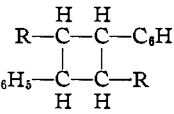
The Structure of a Photodimer of Dibenzalacetone

BY G. W. RECKTENWALD, J. N. PITTS, JR., AND R. L. LETSINGER

RECEIVED JANUARY 26, 1953

Two different dimers have been reported as irradiation products of dibenzalacetone. One of these (m.p. 245°) was obtained in 90% yield from a reaction of dibenzalacetone in glacial acetic acid which contained uranyl chloride. It was assigned structure I.[1] The other substance, formed by the action of sunlight on dibenzalacetone in ethanol, was obtained in a crude state only (m.p. 125–135°). It was shown to be a dimer but was not further characterized.[2]

By irradiating dibenzalacetone in an isopropyl alcohol–benzene solution with ultraviolet light, we obtained in 30% yield a dimeric product which melted at 139.5–140°. The dimer precipitated from this particular solvent system during the course of the reaction in a relatively pure state. It seems likely that the substance previously reported to melt at 125–135° was principally this substance. As the dimer was an unsaturated ketone which yielded δ-truxinic acid (III) on oxidation with neutral potassium permanganate, it must have structure II. The configuration probably also corresponds to that of δ-truxinic acid; however, since the possibility of izomerization among the different truxinic acid type compounds under the conditions of the oxidation has not been eliminated, such an assignment cannot be made unequivocally.



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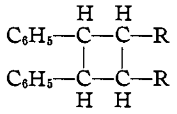
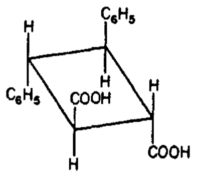


II

R is $C_6H_5CH{=}CHCO-$



III

In only a few cases have dimers been isolated from reactions in which α,β-unsaturated acids or carbonyl compounds are irradiated in solution in an organic solvent. Generally, under these conditions, the compounds either are only isomerized or else form resins.[3] In the other cases where dimerization in solution did occur and the structures of the products were investigated (methyl benzalpyruvate,[4] benzalacetophenone[5] and benzal-*p*-methylacetophenone[5]) the dimers were also found to be of the truxinic type. On the other hand, the photodimer obtained from an acetic acid solution of 2-cinnamylidene-2-phenylacetonitrile[6] was a truxillic type compound.

Experimental

A mixture of 20 g. of dibenzalacetone, 30 cc. of thiophene-free benzene and 90 cc. of isopropyl alcohol was irradiated for 90 hours with the light from a Hanovia type SH quartz-mercury arc. A Pyrex plate was used as a filter to absorb short wave length radiations. Throughout this period a nitrogen atmosphere was maintained above the reactants, which were mixed by a magnetic stirrer. The mixture was allowed to warm up from the heat of the lamp until all of the benzalacetone had dissolved (eight hours); thereafter the temperature was maintained at about 25° by cooling the solution with a cold finger condenser. A white precipitate began to form after approximately 60 hours of irradiation. At the completion of the reaction the precipitate was filtered and washed with cold ethyl ether; yield 6.1

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[1] P. Praetorius and F. Korn, *Ber.*, **43**, 2744 (1910).

[2] G. Ciamician and P. Silber, *ibid.*, **42**, 1386 (1909).

[3] C. Ellis and A. B. Wells, "The Chemical Action of Ultraviolet Rays," Reinhold Publ. Corp., New York, N. Y., 1941, pp. 482–493. A. Mustafa, *Chem. Revs.*, **51**, 1 (1952). Most of the photodimers which have been isolated were obtained from reactions in which the dry solid or aqueous suspensions of the solids were irradiated. Both truxinic and truxillic type compounds are formed under these conditions.

[4] M. Reimer, THIS JOURNAL, **46**, 783 (1924).

[5] H. Stobbe and K. Bremer, *J. prakt. Chem.*, **123**, 1 (1929).

[6] H. Stobbe and F. Kuhrman, *Ber.*, **58**, 85 (1925).

g. (30%), m.p. 139.5–140°. A sample was recrystallized from ethyl alcohol for analysis. The compound was unsaturated (it decolorized cold, neutral permanganate solution and a solution of bromine in carbon tetrachloride) and gave a positive carbonyl test with 2,4-dinitrophenylhydrazine. The molecular weight was found by the Rast camphor method to be about 450.

Anal. Calcd. for $C_{34}H_{28}O_2$: C, 87.15; H, 6.02. Found: C, 86.92; H, 5.96.

A hot solution of 10 g. of potassium permanganate in 50 cc. of water was slowly added to 5 g. of the photodimer of dibenzalacetone. After this mixture had been refluxed for three hours it was treated with sufficient sodium bisulfite to dissolve the manganese dioxide, acidified and extracted with 200 cc. of ether to remove the benzoic acid produced during the oxidation. The mixture was then made basic with sodium hydroxide, filtered and reacidified. The acid which precipitated melted at 174–175°. δ-Truxinic acid is reported to melt at 175°.[7] The melting points of the other truxinic acids are: β, 209–210°; ξ, 239°; nev, 209–210°; μ, 196°; ω, 245°; and the melting points of the isomeric truxillic acids are: α, 274°; γ, 228–230°; ε, 192°; η, 266°; and epi, 285–287°.

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 73.00; H, 5.42; neut. equiv., 151.0. Found: C, 72.92; H, 5.23; neut. equiv., 148.5.

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(7) R. Stoermer and F. Bacher, *Ber.*, **55**, 1882 (1922).

DEPARTMENT OF CHEMISTRY
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

The Reaction of Amine Oxides with Aqueous Potassium Dichromate

BY PAUL J. SCHEUER, WALTER I. KIMOTO AND KIICHI OHINATA

RECEIVED JANUARY 14, 1953

When Freund and Speyer[1] treated the N-oxide of codeine-sulfonic acid with potassium chromate in aqueous solution, they obtained formaldehyde and a substance which upon desulfonation was believed to be isomeric with morphine. Diels and Fischer[2] repeated this work and recognized Freund and Speyer's product to be norcodeine. They further showed that the reaction could be applied to codeine-N-oxide itself.

Bailey and Robinson[3] recently realized that this little-known method might be applied to prepare pseudo-strychnine from strychnine-N-oxide, a tertiary amine which cannot be demethylated. This proved to be the case.

Neither Brehm[4] nor Scheuer[5] were able to isolate pseudostrychnine or any other product from this reaction. Brehm,[6] however, succeeded in preparing pseudo-strychnine by treating strychnine-N-oxide with potassium *dichromate* instead of *chromate*. He also isolated a neutral by-product, oxostrychnine, which was shown by Scheuer[5] to be 18-oxostrychnine.[7]

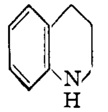
This research was undertaken to determine whether the production of a lactam from an amine oxide might be of general applicability. For an initial approach kairoline-N-oxide (N-methyl-1,2,3,4-tetrahydroquinoline-N-oxide) was chosen as the starting material, for it is readily accessible and all of the expected reaction products are easily characterized.

After considerable experimentation with other routes of approach it was found that kairoline could best be prepared by the methylation of commercial tetrahydroquinoline with dimethyl sulfate according to the general procedure of Gilman and Banner[8,9] in about 50% yield. The colorless oil formed a yellow picrate, m.p. 121°.

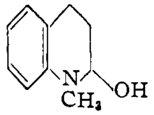
Preparation of kairoline-N-oxide by the elegant method used by Brehm[6] in the strychnine series proved unsatisfactory. Considerable amounts of starting material remained unreacted. This may be explained by the difference in basic strength between strychnine and alkyl-substituted anilines.[10] For the relatively weak base kairoline longer reaction times proved necessary as, *e.g.*, in the earlier work of Meisenheimer and Dodonow.[13] No attempt was made to isolate the hygroscopic solid which was identified by its yellow picrate melting at 122–123° into a green liquid.

The crude kairoline-N-oxide was immediately subjected to the reaction with potassium dichromate. In a series of experiments the best conditions were found to be brief reaction times and catalytic amounts (one mole per cent.) of dichromate at 65°. Ether extraction of the reaction mixture at acidic, basic and neutral *p*H values yielded, beside intractable tars, only one product, a colorless crystalline solid, m.p. 163–164°. This compound was shown to be identical with hydrocarbostyril (2-oxo-1,2,3,4-tetrahydroquinoline), m.p. 167–167.5°, which was prepared from aniline.[14,15] The two compounds when mixed melted at 164–167° and had identical infrared spectra.

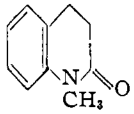
Reasoning from the results obtained by earlier workers, one may conclude that the following structures represent possible reaction products.



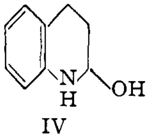
I



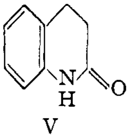
II



III



IV



V

If the reaction had followed the course of the original Freund and Speyer[1] reaction with *chromate*, compound I would have been the product. Compound II should have resulted by analogy with the work of Bailey and Robinson[3] and compound IV if

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(1) M. Freund and E. Speyer, *Ber.*, **44**, 2339 (1911).

(2) O. Diels and E. Fischer, *ibid.*, **47**, 2043 (1914); **49**, 1721 (1916).

(3) A. S. Bailey and R. Robinson, *J. Chem. Soc.*, 703 (1948).

(4) W. J. Brehm, private communication.

(5) P. J. Scheuer, Ph.D. thesis, Harvard, 1950.

(6) W. J. Brehm, Ph.D. thesis, Harvard, 1948.

(7) (a) The numbering system suggested by Woodward and Brehm[7b] is used; (b) R. B. Woodward and W. J. Brehm, THIS JOURNAL, **70**, 2107 (1948).

(8) H. Gilman and I. Banner, *ibid.*, **62**, 345 (1940).

(9) After completion of this work another report (S. Hünig, *Ber.*, **85**, 1056 (1952)) on successful N-methylation of aromatic amines with dimethyl sulfate was received.

(10) Strychnine, pK_b = 6.63[11]; dimethylaniline, pK_b = 9.62.[12]

(11) V. Prelog and O. Häfliger, *Helv. Chim. Acta*, **32**, 1851 (1949).

(12) L. F. Fieser and M. Fieser, "Organic Chemistry," Second Edition, D. C. Heath and Co., Inc., Boston, Mass., 1950, p. 635.

(13) J. Meisenheimer and J. Dodonow, *Ann.*, **385**, 134 (1911).

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

(15) F. Mayer, L. van Zuetphen and H. Phillips, *Ber.*, **60**, 858 (1927).

both demethylation (*cf.* compound I) and isomerization (*cf.* compound II) had taken place. Both these compounds are carbinolamines in equilibrium with their open chain aldehydic tautomers and are undoubtedly difficult to isolate. It is likely that the resinous material in the reaction mixture contained some of these compounds. Compound III should have arisen if the reaction had followed the course which led to oxostrychnine (*vide supra*) and, finally, compound V if this mode of reaction were coupled with demethylation. The latter reaction actually took place. It constitutes a greater structural change than was observed previously. This may well be due to the fact that substituted anilines are more sensitive to oxidizing agents than is strychnine or codeine. It is nevertheless remarkable that the action of aqueous dichromate on an amine oxide has once again led to a lactam as in the case of oxostrychnine.[5]

Experimental Part[16,17]

Kairoline from 1,2,3,4-Tetrahydroquinoline.—Following the procedure of Gilman and Banner[8] kairoline was prepared from freshly distilled 1,2,3,4-tetrahydroquinoline (Eastman Kodak Co., White Label) and freshly distilled dimethyl sulfate. The product immediately upon distillation was a colorless oil, b.p. 128–129° (25 mm.) (52% yield).

The picrate melted at 121° (recorded 123–124°[18] and 136–137°[19]).

Anal. Calcd. for $C_{16}H_{16}N_4O_7$: C, 51.06; H, 4.29; N, 14.9. Found: C, 51.09; H, 4.20; N, 14.7.

Kairoline-N-oxide.—The successful procedure which was finally adopted was fashioned after that of Meisenheimer and Dodonow.[13] In occasional runs the oxide crystallized spontaneously in colorless chunky needles after the solvent had been removed *in vacuo*. In general, no attempt was made to obtain the substance crystalline.

A picrate was prepared: fragile yellow needles from EtOH, m.p. 122–123°, turning green on melting (recorded m.p. 122°[13]).

Anal. Calcd. for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.11; N, 14.3. Found: C, 48.72; H, 4.00; N, 14.3.

Dichromate Reaction with Kairoline-N-oxide.—The crude N-oxide was subjected to this reaction in 7-g. batches. The oxide was dissolved in 60 ml. of water and warmed to 65°. One mole per cent. of $K_2Cr_2O_7$ dissolved in 20 ml. of water also at 65° was added slowly with stirring. The dichromate color was discharged immediately and although there was considerable frothing, no odor of formaldehyde could be detected. Stirring was continued for 10 minutes. The brown solution was separated from considerable amounts of tarry material and extracted thoroughly with ether at *p*H's of 3, 7 and 12. All three extracts upon drying over Na_2SO_4 and concentration on the steam-bath furnished small amounts of light brown needles, totaling 1 g., m.p. 145–150°. After 6 recrystallizations from MeOH-H_2O the colorless needles melted at 163-164°.

Anal. Calcd. for C_9H_9NO: C, 73.45; H, 6.16; N, 9.5. Found: C, 73.15, 73.61; H, 6.21, 6.00; N, 8.9, 9.4.

Infrared spectrum,[20] six-membered lactam band at 5.98 μ.

The tarry residue was dissolved in 1 *M* HCl and on cooling was made basic with 6 *M* NH_4OH. Several ether extractions furnished only films of brown oil which could not be identified.

Anilide of β-Chloropropionic Acid.—Prepared from freshly distilled aniline (J. T. Baker Analyzed) and β-chloropropionyl chloride (Eastman Kodak Co., White Label); m.p. of product recrystallized from MeOH 117–119° (reported[15] 119).

Hydrocarbostyril.—The anilide was cyclized with $AlCl_3$ without solvent as described by Mayer, *et al.*,[15] and obtained as gray needles, m.p. 140–155°. After 5 recrystallizations from dilute MeOH, m.p. 167.0–167.5° (reported[15] 163°). Mixed m.p. with the product from the dichromate reaction was 164–167°.

Anal. Calcd. for C_9H_9NO: C, 73.45; H, 6.16; N, 9.5. Found: C, 73.15; H, 6.38; N, 9.7.

Infrared spectrum, identical with degradation product; six-membered lactam band at 5.98 μ.

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[16] Microanalyses by Drs. G. Weiler and F. B. Strauss, Oxford, England.

[17] Melting points were taken on a Kofler micro hot stage. Melting points and boiling points are uncorrected.

[18] F. H. Beilstein, "Handbuch der Organischen Chemie," Erstes Ergänzungswerk, Vol. 20, Vierte Auflage, Julius Springer, Berlin, 1935, pp. 94-95.

[19] J. F. Thorpe and A. S. Wood, *J. Chem. Soc.*, 1611 (1913).

[20] Taken in chloroform solution with a Baird double-beam recording instrument.

Cleavage of 3-Bromo-2,2-dimethyl-1-propanol by Base[1]

BY S. SEARLES[2] AND M. J. GORTATOWSKI

RECEIVED DECEMBER 19, 1952

In the course of a study of substituted trimethylene oxides, the compound 2,2-dimethyltrimethylene oxide (I) was desired. This compound has been reported by Bennett and Philip[3] and by Fonteyne and Ticket[4] who prepared it by heating 3-bromo-2,2-dimethyl-1-propanol (II) with solid and aqueous potassium hydroxide. Although no information was given regarding the yield, several factors would appear to be favorable: (1) impossibility of 1,2-elimination, (2) steric hindrance of intermolecular substitution, and (3) gem-dialkyl structure, which generally favors ring closure. Related intramolecular Williamson reactions generally give good yields—for example, 1,1-diethyltrimethylene oxide (90% from 1-chloro-3-ethyl-3-pentanol),[5] 1,1-dimethyltrimethylene oxide (43% from 4-chloro-2-methyl-2-butanol)[3] and 2,2-bis-(bromomethyl)-trimethylene oxide (79% from pentaerythrityl tribromide).[6]

The reaction of II with powdered and aqueous potassium hydroxide gave only 10–25% yields of I in this Laboratory, however, and it was of interest that a substantial amount of isobutylene was found to be a gaseous product. This compound, which apparently was overlooked previously, was identified by its boiling point, its 2,4-dinitrobenzenesulfenyl chloride adduct, and its bromination products. The yield of isobutylene was about 20% in the Bennett and Philip procedure, but became 60% when 15% aqueous potassium hydroxide is the base and 75% when the bromoalcohol is added to a melted NaOH–KOH mixture at 200°.

The other primary cleavage product appears to be formaldehyde, which was isolated in small yield as its dimedone derivative from the reaction mixture obtained with 15% potassium hydroxide. The Cannizzaro products of formaldehyde, methanol and formic acid, were identified in all the reaction mixtures.

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[1] Abstracted from the B.S. Thesis of Melvin J. Gortatowski, University of Illinois, February, 1950.

[2] Department of Chemistry, Kansas State College, Manhattan, Kansas.

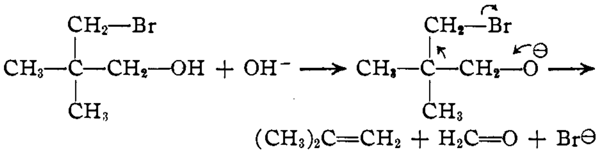
[3] G. M. Bennett and W. G. Philip, *J. Chem. Soc.*, 1938 (1928).

[4] R. Fonteyne and M. Ticket, *Natuurw. Tijdschr.*, **25**, 49 (1943).

[5] C. Moureu and G. Barrett, *Bull. soc. chim.*, [4] **29**, 994 (1921).

[6] F. Govaert and M. Beyaert, *Natuurw. Tijdschr.*, **22**, 73 (1940).

Pyrolysis of I would be expected to give isobutylene and formaldehyde,[7] but this possible source seems untenable in view of the observation that even at 250° I is stable in the presence of potassium hydroxide. Furthermore, the cleavage in 15% potassium hydroxide occurs at a temperature of 100° or less, which is much too low for a pyrolysis. It would appear reasonable, however, that isobutylene and formaldehyde result from a rearrangement of the same alkoxide ion which is the intermediate for the cyclization reaction



$$CH_3-\overset{\displaystyle CH_2-Br}{\underset{\displaystyle CH_3}{C}}-CH_2-OH + OH^- \longrightarrow CH_3-\overset{\displaystyle CH_2-Br}{\underset{\displaystyle CH_3}{C}}-CH_2-O^{\ominus} \longrightarrow (CH_3)_2C=CH_2 + H_2C=O + Br^{\ominus}$$

Thus, this cleavage reaction is an extended chain analog of the usual elimination reaction which generally accompanies substitution, but which is impossible here because of the lack of β-hydrogen atoms. A few other examples of this type of elimination have been reported, as in the cases of β-dimethylpivalophenone methiodide[8] and α-tosyloxy-β,β-dimethyl-γ-butyrolactone,[9] and the reverse aldol reaction is, of course, closely related. The alkali-instability of the bromoalcohol considered here was observed in 1913 by Franke,[10] who reported its decomposition by boiling sodium carbonate solution to an unknown steam volatile oil which reduced Tollens reagent. The nature of the decomposition was not recognized but the latter observation indicated that some cleavage had occurred, since I does not reduce Tollens reagent. On repeating the experiment it was observed that the cleavage reaction proceeds so slowly under these conditions that the steam distillate is principally unreacted bromoalcohol, contaminated with small amounts of I and formaldehyde.

Experimental

Reaction of 3-Bromo-2,2-dimethyl-1-propanol (II) with Alkali. (A).—An intimate mixture of 110 g. of powdered sodium hydroxide and 21.5 g. of II (prepared by the method of Fonteyne and Ticket[4] in 55% yield) was immersed in an oil-bath maintained at 200°. The distillate was collected in two traps kept at 0 and −70°, respectively, and after drying over potassium carbonate was fractionally distilled.

Isobutylene, b.p. −6.5 to −6° (lit. −6°[11]), was obtained in the amount of 1.5 g. (23% yield); m.p. of 2,4-dinitrobenzenesulfenyl chloride adduct,[12] 85–86° (lit. 86–87°[13]). Addition of bromine dissolved in methylene dichloride to a solution of the olefin in methylene dichloride, cooled by an ice–salt bath, gave a 41% yield of 1,2-dibromo-2-methylpropane, b.p. 143–145° (750 mm.), $n^{21.5}_{D}$ 1.5072 and a 12% yield of 1,2,3-tribromo-2-methylpropane, b.p. 111–114° (22 mm.), $n^{21.5}_{D}$ 1.5644, in agreement with the results of Hurd and Spence.[14]

2,2-Dimethyltrimethylene oxide, b.p. 77–79° (752 mm.) was obtained in the amount of 1.3 g. (13% yield) and from a low boiling (66–70°) fraction was obtained 0.5 g. of methyl 3,5-dinitrobenzoate, m.p. 106–107° (lit. 108°[15]). Evidence for the formation of potassium formate was obtained by dissolving the reaction residue in water, acidifying with phosphoric acid and distilling. The distillate was acidic, decolorized potassium permanganate and reduced mercuric oxide to a dark gray precipitate of elemental mercury.

(B).—Dropwise addition of 40 g. of II to a stirred molten mixture of 60 g. of potassium hydroxide and 40 g. of sodium hydroxide at 200°, which is a good reagent for preparing trimethylene oxide from 3-chloropropyl acetate, gave 10 g. of isobutylene (77% yield) and 2.5 g. of 2,2-dimethyltrimethylene oxide (12% yield).

(C).[12]—To 100 g. of 15% potassium hydroxide at 90°, 25 g. of I was added dropwise with stirring over a period of 50 minutes; the bath temperature was then slowly raised to 150° over a period of two hours. The products which distilled off were collected as described in (A), but a water layer in the 0° trap was separated before the remainder was dried over potassium carbonate. Acidification of this water layer with acetic acid and addition of dimedone gave a few milligrams of formaldehyde dimedone, fine needles melting at 187° (lit. 189°[16]). Distillation of the non-aqueous products gave 5 g. (60% yield) of isobutylene and 1.3 g. (10% yield) of 2,2-dimethyltrimethylene oxide.

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(7) A. Barbot, *Ann. chim.*, **11**, 519 (1939).

(8) H. R. Snyder and J. H. Brewster, THIS JOURNAL, **71**, 1061 (1949).

(9) H. Bretschneider and H. Hass, *Monatsh.*, **81**, 945 (1950).

(10) A. Franke, *ibid.*, **34**, 1893 (1913).

(11) C. C. Coffin and O. Maass, THIS JOURNAL, **50**, 1433 (1928).

(12) Unpublished work of W. K. Witsiepe, Northwestern University, 1950, which is acknowledged with thanks.

(13) N. Kharasch and C. M. Buess, THIS JOURNAL, **71**, 2724 (1949).

(14) C. D. Hurd and L. U. Spence, *ibid.*, **51**, 3361, 3569 (1929).

(15) W. M. D. Bryant, *ibid.*, **54**, 3760 (1932).

(16) D. Vorlander, *Z. anal. Chem.*, **77**, 247 (1929).

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Condensations of α-Carbethoxy-α-methyl-γ-butyrolactone

BY GLENN S. SKINNER AND R. E. HERBENER

RECEIVED JANUARY 5, 1953

In continuation of the study of the reaction of α-alkyl-α-carbethoxy-γ-butyrolactones[1] with urea and related compounds the methyl homolog has been prepared and condensed with urea, thiourea, guanidine and benzamidine.

The reactions proceeded in the expected manner in all cases. However, the following comparisons should be noted. The condensation of this lactone ester with thiourea required milder temperature conditions to obtain good yields. It was necessary to modify the procedures also on account of the marked differences in the solubilities of the barbituric acid derivatives. The intermediate sodium salt obtained from the condensation with urea is much more insoluble in alcohol and the free acid is so much more soluble in water as to require very specific conditions for its isolation.

This lactone ester was condensed with benzamidine to test the validity of the proposal[2] that the active hydrogen of the unalkylated lactone ester participates in the reaction leading to the tetrahydropyrimidine derivative.

Another possible explanation is that the nonformation of the tetrahydropyrimidine derivative from the alkylated lactone esters is due to steric hindrance. Actually, the substitution of the smaller methyl radical for the active hydrogen led only to the lactone amidine. Within the limits of the possibilities of decreasing the size of the alkyl group it would therefore appear that the hindrance to the cleavage of the lactone ring is not steric in nature.

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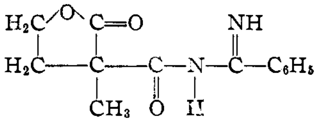
(1) Last previous report of this series: G. S. Skinner and W. H. Waitz, Jr., THIS JOURNAL, **74**, 498 (1952).

(2) G. S. Skinner, Ethel Anderson and R. F. Bogart, *ibid.*, **71**, 1482 (1949).



Lactone amidine

By mouth in rats (I) at 400 mg./kg., (V) at 400–900 mg./kg., and (VII) at 400–900 mg./kg. gave no hypnosis. When orally administered to rats (III) at 400 mg./kg. gave no protection by either the metrazol or electroshock method, (VI) at 400 mg./kg. gave no protection by electroshock and 40% protection by the metrazol method, and (VII) at 400 mg./kg. gave no protection[3] against either metrazol or electroshock.

BARBITURIC ACID DERIVATIVES $RCH_3C(CONH)_2C{=}X$

	R	X	Yield, %	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
I	$HOCH_2CH_2-$	O	72	202–203	15.0	14.9
II	$HOCH_2CH_2-$	S	55	194.5–195.5	13.9	13.7
III	$HOCH_2CH_2-$	NH	58	202–203	22.7	22.5
IV	$BrCH_2CH_2-$	O	72	166–167	11.2	11,2
V	$(H_2N\underset{\underset{NH_2}{\|}}{C}-SCH_2CH_2-)^+Br^-$	O	88	265–265.5[a]	17.2	17.1
VI	$H_2N-\underset{\underset{NH}{\|}}{C}-SCH_2CH_2-$	O	94	197[a]	22.9	22.5
VII	$EtO-\underset{\underset{S}{\|}}{C}-S-CH_2CH_2-$	O	64	161.5–162.5	9.6	9.5
VIII	$HSCH_2CH_2-$	O	66	145–146	13.9	14.4

[a] Decomposition.

Experimental

α-Carbethoxy-α-methyl-γ-butyrolactone.—This ester was prepared in the usual way from 2.0 moles of powdered sodium, 4.0 moles of diethyl methylmalonate and 4.0 moles of ethylene bromide in one liter of dry benzene. The mixture was heated 13 hours at 75–80°. Conversion of the bromo compound to the lactone ester was effected after removal of the solvent by refluxing 8 hours at 135° (120 mm.); yield 66% (based on sodium), b.p. 146–149° (18 mm.), $n^{20}D$ 1.4430, $d^{20}/^4$ 1.1386.

Anal. Calcd. for $C_8H_{12}O_4$: M_R, 40.25; C, 55.8; H, 7.0. Found: M_R, 40.07; C, 55.1; H, 6.9.

Condensations of the Lactone Ester: (a) With Urea.—The previously described general procedure for condensation with urea was employed.[4] The product was isolated as the very insoluble sodium salt by filtration and washing with absolute alcohol. A rubber dam was used for protection against moisture; yield 97%.

Anal. Calcd. for $C_9H_{14}O_5N_2Na_2$: Na, 16.65. Found: Na, 16.47.

After a number of attempts to isolate the acid the following satisfactory procedure was adopted. A mixture of 50 g. of crushed ice and 20 cc. of hydrochloric acid (d. 1.19) was cooled in a freezing bath. With good stirring 27 g. of the salt was added. After one-half hour the product was filtered with suction, washed with ice-cold dilute hydrochloric acid and then sparingly with ice-cold water; yield of crude product 17 g. (91%), m.p. 191–194°. After two recrystallizations from absolute alcohol the melting point was constant at 202–203°.

(b) With Thiourea.—The best result for the reaction with thiourea was obtained by adding to a stirred solution of sodium ethoxide prepared from 4.6 g. of sodium and 92 cc. of absolute alcohol at 2° first 11.4 g. (0.15 mole) of thiourea and then 17.2 g. (0.10 mole) of the lactone ester. After several hours when the temperature had risen to 15° a precipitate began to form. The amount of precipitate reached a maximum after standing 24 hours at 19–24°. The yield of this intermediate was 26 g. but it could not be obtained pure for analysis.

By applying the above treatment with hydrochloric acid this salt yielded 13 g. (65%) of the 2-thiobarbituric acid, m.p. 186–189°. Five recrystallizations from absolute alcohol were necessary to give a pure product, m.p. 194.5–195.5°.

(c) With Guanidine.—By an adaptation of the previously described procedure[2] 18.0 g. (0.10 mole) of guanidine carbonate was added to a solution of sodium ethoxide prepared from 8.0 g. (0.347 mole) of sodium and 125 cc. of absolute alcohol. The lactone ester (8.6 g., 0.050 mole) was added with stirring at 5°. The mixture was allowed to stand 3 hours at 5° and then 24 hours at room temperature. The precipitate was dissolved by stirring with 100 cc. of ice and water. The solution, while cooled in ice, was made just acid to litmus with acetic acid and then cooled in an ice–salt bath. The precipitate was filtered, washed with dilute acetic acid and then with ice-cold water; yield 8.8 g. (95%), m.p. 200–203°. When recrystallized from the minimum amount (500 cc.) of 64% alcohol it had m.p. 202–203°.

To a solution of sodium ethoxide prepared from 5.6 g. (0.243 mole) of sodium and 100 cc. of absolute alcohol there were added with stirring at 22° 13.56 g. (0.0866 mole) of benzamidine hydrochloride and then immediately 11.9 g. (0.0693 mole) of the lactone ester. The temperature was brought rapidly to 45° where it was maintained for 24 hours and then at 70° for 3 hrs. The stirred ice-cold mixture was carefully neutralized to litmus by the addition of hydrochloric acid (1.19) and the salt was filtered with suction. Concentration of the filtrate gave 0.5 g. of product, m.p. 136–138°. Extraction of the precipitate with alcohol gave 4.8 g., m.p. 136.5–138.5°. Recrystallization from absolute alcohol gave a product free from chlorine, m.p. 138–139°.

Anal. Calcd. for $C_{13}H_{14}O_3N_2$: N, 11.4. Found: N, 11.2.

The above lactone amidine (1.0 g.) was converted to the inner salt by dissolving it in the minimum amount (6 cc.) of cold 5% sodium hydroxide and allowing it to stand at room temperature for two hours. The solution was cooled in an ice-bath and made just acid to litmus with hydrochloric acid (d. 1.19). The product did not precipitate at once when cooled in an ice–salt bath, but after standing 36 hours a white crystalline precipitate had formed. This was filtered, washed sparingly with water and dried on porous plate in a desiccator; m.p. 153–155° (dec.). Careful decomposition gave ammonia, and the residue gave the characteristic odor of benzonitrile. It is therefore the expected inner salt.

Anal. Calcd. for $C_{13}H_{16}O_4N_2$: N, 10.6. Found: N, 10.1.

Compounds from 5-(β-Hydroxyethyl)-5-methylbarbituric Acid.—To avoid cleavage of the ring the following modification of the previously described procedure[5] was employed to convert I to IV. Thirty-seven and two-tenths grams (0.20 mole) of I was mixed with 60 cc. of hydrobromic acid (60%), first at 0° and then at room temperature in a bottle capped with a rubber disc, until dissolved. After standing 24 hours at room temperature the solution had set to a solid mass; yield of crude product 43.7 g. (88%), m.p. 164–166°.

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(3) Pharmacological tests by Eli Lilly and Co.

(4) G. S. Skinner, Arthur Stokes and George Spiller, THIS JOURNAL, **69**, 3083 (1947).

(5) G. S. Skinner, *ibid.*, **59**, 322 (1937).

Crystallization from ethyl alcohol gave 36 g., m.p. 166–167°.

The bromide IV was converted successively to V, VI and VIII by procedures that require no further description.[1]

The xanthoethyl derivative VII was also made by an unmodified procedure.[6]

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(6) G. S. Skinner and J. B. Bicking, THIS JOURNAL, **72**, 1140 (1950).

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Alkylene Bis-(2-thenylquaternaryammonium) Salts[1]

BY D. RICHARD SMITH[2a] AND CHESTER J. CAVALLITO[2b]

RECEIVED JANUARY 24, 1952

During the past few years, bis-quaternary-ammonium salts of a wide variety of types have been prepared and studied for curarimimetic and autonomic drug activity. Peak curarimimetic activity usually is associated with bis-quaternary salts in which ten carbon atoms or equivalent distance separates the quaternary nitrogen atoms and autonomic blockade is maximal in homologs with a five or six carbon atom separation. In the present series of compounds, 2-thenyl substituted quaternary salts of various size were prepared for comparison with one another and with some corresponding isosteric phenyl substituted analogs.

Muscle paralytic activity, as measured in mice according to published procedures,[3] followed the expected sequence. In the bis-thenyldimethylammonium series, activity increased in the following sequence with ED_{50} values of approximately 8 mg. per kg. for the C_6, 2 for C_9 and 1 for the C_{10} homologs; corresponding bis-benzyldimethylammonium derivatives were of the same order of activity as the thenyl analogs. In the C_{10} bis-thenylammonium series, activity decreased with degree of steric hindrance about the nitrogen atoms in the order: dimethyl (1 mg. per kg.), diethyl (2 mg. per kg.) and cyclohexamethylene (10 mg. per kg.). Tests for autonomic activity (in anesthetized dogs) revealed that all of the compounds markedly reduced blood pressure, but for only from five to thirty minutes after intravenous administration of 2 mg. per kg. Mechanism of action varied within the series.[4]

Experimental[5]

2-Thenylamines.—Tertiary 2-thenylamines were prepared by the Leuckart reaction from 2-thienylaldehyde[6] (0.1 mole), formic acid (0.25 mole) and appropriate secondary amine (0.2 mole). The procedure was similar to that of Smith and Macdonald[7]; refluxing was for ten hours or with volatile amines, heating was carried out in a pressure bomb. From dimethylamine, N,N-dimethyl-2-thenylamine[8] was obtained in better than 70% yield and its physical properties agreed with those published. Treatment with methyl iodide yielded a crystalline methiodide, m.p. 167–168°.

Anal. Calcd. for $C_8H_{14}INS$: C, 33.93; H, 4.98; I, 44.82. Found: C, 34.09; H, 5.09; I, 44.20.

N,N-Diethylthenylamine was prepared in similar manner in 65% yield; b.p. 40° at 1.5 mm., $n^{20}D$ 1.5095.

Anal. Calcd. for $C_9H_{15}NS$: N, 8.27. Found: N, 8.18.

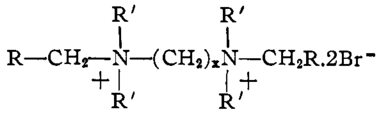
Methiodide, m.p. 156°. *Anal.* Calcd. for $C_{10}H_{18}INS$: C, 38.59; H, 5.79. Found: C, 38.64; H, 5.89.

From hexamethyleneimine there was obtained a 44% yield of N-(2-thenyl)-hexamethyleneimine, b.p., 72–73° at 1.5 mm., $n^{23}D$ 1.5375.

Anal. Calcd. for $C_{11}H_{17}NS$: N, 7.17. Found: N, 6.77.

TABLE I

α,ω-ALKYLENE BIS-QUATERNARYAMMONIUM SALTS



$$R{-}CH_2{-}\overset{R'}{\underset{R'}{\overset{|}{\underset{+|}{N}}}}{-}(CH_2)_x\overset{R'}{\underset{R'}{\overset{|}{\underset{|+}{N}}}}{-}CH_2R.2Br^-$$

R	R′	x	M.p., °C. (cor.)	Reflux, hr.	Yield, %	Analyses, % Calcd. Carbon	Calcd. Hydrogen	Calcd. Bromine	Found Carbon	Found Hydrogen	Found Bromine
2-C_4H_3S	CH_3	3	219	23	60	42.15	5.83	33.33	42.42	5.98	32.75
2-C_4H_3S	CH_3	4	223	8	85	43.37	6.07	32.07	43.71	6.28	31.65
2-C_4H_3S	CH_3	5	111–114	8	75	44.53	5.70	31.19	44.65	6.26	30.65
2-C_4H_3S	CH_3	6	218–220	3[a]	70	S, 12.18		30.36	S, 11.75		29.90
2-C_4H_3S	CH_3	9	226	35	50	48.59	7.09	28.11	48.40	7.14	28.29
2-C_4H_3S	CH_3	10	200	7[a]	60	49.47	7.26	27.47	49.56	7.23	26.96
2-C_4H_3S	C_2H_5	10	176–180	50	40	52.65	7.87	25.03	52.85	8.04	24.45
2-C_4H_3S	Cyclo(—CH_2—)$_6$[b]	10	201–204	24	45	55.64	7.88	23.14	55.76	8.08	23.36
C_4H_6	CH_3	5	218–220	8	85	55.20	7.25	31.94	55.27	7.26	31.64
C_6H_5	CH_3	6	226	8	90	56.03	7.45	31.07	56.20	7.43	30.72
C_6H_5	CH_3	10	208	8	70	58.94	8.14	28.01	59.08	8.08	27.75

[a] 90 lb. pressure in bomb. [b] Hexamethyleneimonium derivative.

Reaction of Thenylamines with Alkylene Dibromides.—The bis-quaternaryammonium bromide salts were prepared by heating the reagents in *n*-propanol solution in the proportions: 0.05 mole of α,ω-alkylene dibromide, 0.15 mole of tertiary thenylamine, 50 ml. of propanol. Heating time, yields and analyses are summarized in Table I. The bis-quaternary salts were recrystallized from *n*-propanol.

Reaction of Benzyldimethylamine with Alkylene Dibromides.—Benzyldimethylamine (15 g. or 0.11 mole) was re-

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(1) Contribution from the Department of Chemistry, James Millikin University, and from the Research Laboratories of Irwin, Neisler & Company.

(2) (a) Phillips Petroleum Co., Waco, Texas; (b) Irwin, Neisler & Company.

(3) C. J. Cavallito, A. E. Soria and J. O. Hoppe, THIS JOURNAL, **72**, 2661 (1950).

(4) Curarimimetic tests by Dr. T. B. O'Dell, autonomic activity measurements by Dr. F. J. Macri, of Irwin, Neisler & Company.

(5) Halogen analyses by Mr. C. F. Duewer of Irwin, Neisler & Company. Microanalyses by Clark Microanalytical Laboratory, Urbana, Illinois.

(6) W. J. King and F. F. Nord, *J. Org. Chem.*, **13**, 635 (1948).

(7) P. A. S. Smith and A. J. Macdonald, THIS JOURNAL, **72**, 1037 (1950).

(8) L. P. Kyrides, F. C. Meyer, F. B. Zienty, J. Harvey and L. W. Bannister, *ibid.*, **72**, 745 (1950).

TABLE I

REPLACEMENT OF AMINO GROUP BY HYDROGEN

Compound deaminated	Product				Yield, %	
	Structure	B.p., °C.	n^{25}_D	d^{25}_4	Using C_2H_5OH	Using H_3PO_2
3-H_2N-$C_6H_4CF_3$	$C_6H_5CF_3$	98–101			37	47.4
3-H_2N-4-Br–$C_6H_3CF_3$	4-Br–$C_6H_4CF_3$	154–155	1.4705	1.607	40	67
5-H_2N2-Br–$C_6H_3CF_3$	2-Br–$C_6H_4CF_3$	165–168			60	
3-H_2N-2,4-Br–$C_6H_2CF_3$ or 5-H_2N-2,4-Br–$C_6H_2CF_3$	2,4-Br–$C_6H_3CF_3$[a]	97–102.5[b]	1.5279	2.006		53
Unfractionated reaction mixture	............[c]				49.3	65.7

[a] Calcd. for $C_7H_3Br_2F_3$: Br, 52.56. Found: Br, 52.51. [b] At 20.5 mm. [c] The products consisted of benzotrifluoride, *p*-bromo-, *o*-bromo- and 2,4-dibromobenzotrifluoride. They were obtained in 4.8, 21, 12 and 11.5% yield, respectively, using ethanol; in 12.5, 20, 22 and 11.2% yield using H_3PO_2.

fluxed for 8 hours in 100 ml. of *n*-propanol with 0.04 mole of alkylene dibromide. The solution was cooled, diluted with ethyl ether, the precipitate filtered off and recrystallized from hot *n*-propanol–benzene solution.

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The Formation and Deamination of Brominated *m*-Aminobenzotrifluorides[1]

BY PAUL TARRANT AND MARVIN R. LILYQUIST

RECEIVED JANUARY 26, 1953

m-Bromobenzotrifluoride is a useful starting material for the synthesis of a number of compounds since it readily forms a Grignard reagent.[2] Although *m*-bromobenzotrifluoride can be made in a straightforward reaction from benzotrifluoride, the ortho and para isomers must be made indirectly. Jones[3] has prepared *p*-bromobenzotrifluoride in an over-all yield of about 40% from *p*-nitrotoluene; however, the process required the use of two bromination steps, a fluorination, a reduction and, finally, the replacement of the amino group by bromine. Jones was also able to prepare *o*-bromobenzotrifluoride, but again a lengthy procedure was used. Since the completion of this research, Benkeser and Severson[4] have described a two-step synthesis of *o*-bromobenzotrifluoride involving the metallation and subsequent bromination of benzotrifluoride with 28% yields.

Since *m*-aminobenzotrifluoride is commercially available, it seemed probable that it might serve as a starting point for a convenient synthesis of *o*- and *p*-bromobenzotrifluoride. This paper reports a study of the bromination of *m*-aminobenzotrifluoride and the deamination of the resulting aminobromo compounds to form various bromobenzotrifluorides.

m-Aminobenzotrifluoride was brominated under a variety of conditions. The best yields of monobromobenzotrifluorides resulted when the reaction was carried out at 5–10° in an excess of the amine when no catalyst was employed. Both 3-amino-4-bromo- and 5-amino-2-bromobenzotrifluoride were obtained under these conditions but no 3-amino-2-bromobenzotrifluoride was isolated during any experiments. When larger amounts of bromine were used, a compound believed to be 5-amino-2,4-dibromobenzotrifluoride was formed. When the brominations were conducted at 50° or when *m*-acetaminobenzotrifluoride served as the starting material, a considerable amount of unidentified high boiling material resulted.

The structure of the 3-amino-4-bromobenzotrifluoride was established by deamination to a bromobenzotrifluoride which, when hydrolyzed with sulfuric acid, was converted to *p*-bromobenzoic acid. The amine was also diazotized and treated with hydrobromic acid to give the known 3,4-dibromobenzotrifluoride. The 5-amino-2-bromobenzotrifluoride was diazotized and reduced to *o*-bromobenzotrifluoride thus establishing the position of the bromine as being adjacent to the trifluoromethyl group. Final confirmation resulted when the replacement of the amino group by chlorine gave the known 2-bromo-5-chlorobenzotrifluoride.[5]

The aminodibromobenzotrifluoride was deaminated and hydrolyzed to 2,4-dibromobenzoic acid indicating that its structure was either 3-amino-2,4-dibromo- or 5-amino-2,4-dibromobenzotrifluoride. Since no 3-amino-2-bromobenzotrifluoride was ever isolated, it seems likely that 5-amino-2,4-dibromobenzotrifluoride was formed.

Deaminations were carried out using either hypophosphorus acid or ethanol as the reducing agent. Better yields were obtained with hypophosphorus acid as indicated in Table I.

Experimental

The Bromination of *m*-Aminobenzotrifluoride.—The bromination of *m*-aminobenzotrifluoride and the corresponding acetamino compound were carried out under a variety of conditions. The latter compound was treated with bromine at 100° without catalyst and at 50° with a small amount of iron powder but most of the starting material was recovered. Essentially these same results have recently been reported.[6] The bromination of *m*-aminobenzotrifluoride at 10° without catalyst produced 21% conversions each of 3-amino-4-bromo- and 5-amino-2-bromobenzotrifluoride. At 5–10° using iron a 40% conversion to 3-amino-4-bromobenzotrifluoride was obtained but no other isomeric products were isolated; at 50°, a 31% yield was obtained with no other monobromo compound isolated.

A typical procedure follows. *m*-Aminobenzotrifluoride (1 mole) was added to 300 ml. of glacial acetic acid in a one-liter flask equipped with stirrer, addition funnel and thermometer. The contents were cooled to 10° and bromine (1 mole) added dropwise; about 2.5 hours were required for the addition. After another hour of stirring, 500 ml. of concentrated ammonia solution was added slowly and the

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[1] Presented at the 118th Meeting of the American Chemical Society, Chicago, 1950.

[2] J. H. Simons and E. O. Ramler, THIS JOURNAL, **65**, 389 (1943).

[3] R. G. Jones, *ibid.*, **69**, 2346 (1947).

[4] R. A. Benkeser and R. G. Severson, *ibid.*, **73**, [illegible] (1951).

[5] E. T. McBee, R. A. Sanford and P. J. Graham, *ibid.*, **72**, 1651 (1950).

[6] E. T. McBee, O. R. Pierce, R. D. Lowry and B. Rapkin, *ibid.*, **73**, [illegible] (1951).

heavy organic layer separated and steam distilled. The product was distilled through a Lecky–Ewell column 72 cm. long and of 20 mm. diameter.

The distillation curve had plateaus at three temperatures at 5 mm.: 20 g. of unreacted *m*-aminobenzotrifluoride was obtained at 60–65°; 79 g. of 3-amino-4-bromobenzotrifluoride at 80–85°; 23.5 g. of 5-amino-2-bromobenzotrifluoride at 104–108°. A considerable amount of residue was left which was undoubtedly identical with the 5-amino-2,4-dibromo- or 3-amino-2,4-dibromobenzotrifluoride found in later experiments. The formation of the dibromide could be prevented by doubling the quantity of *m*-aminobenzotrifluoride.

In some cases the crude brominated mixture was deaminated. The relative amounts of the various products under these conditions are given in Table I.

3-Amino-4-bromobenzotrifluoride.—A center fraction of the 80–85° fraction had the following properties: b.p. 81–82° at 5 mm., $n^{25}\text{D}$ 1.5197, d^{25}_4 1.694.

Anal. Calcd. for $C_7H_5BrF_3N$: Br, 33.29; N, 5.83. Found: Br, 33.28; N, 5.61.

The structure of the compound was established by deamination followed by hydrolysis of the $-CF_3$ group according to the method employed by Le Fave.[7] The melting point of 254–256° for the resulting *p*-bromobenzoic acid agrees with the reported value.[8]

5-Amino-2-bromobenzotrifluoride.[6]—Although this compound was formed in the experiment described above, larger amounts were obtained when two moles of *m*-aminobenzotrifluoride was treated with one mole of bromine. The properties of this substance are as follows: b.p. 104–108° at 5 mm., 81–84° at 0.5 mm., m.p. 55–56°.

Anal. Calcd. for $C_7H_5BrF_3N$: Br, 33.29; N, 5.83. Found: Br, 33.06; N, 5.78.

Deamination of this material gave *o*-bromobenzotrifluoride. Final identification was made by converting the amine by the Sandmeyer reaction to a bromochlorobenzotrifluoride which had the following physical properties: b.p. 198°, $n^{25}\text{D}$ 1.5056, m.p. 14.9–16.2°. The values compare with those reported for 2-bromo-5-chlorobenzotrifluoride.[5]

5-Amino-2,4-dibromo- or 3-Amino-2,4-dibromobenzotrifluoride.—Bromination of *m*-aminobenzotrifluoride at 50° in the presence of iron filings gave a relatively large amount (13% conversion) of aminodibromobenzotrifluoride, b.p. 113–115° at 3 mm., m.p. 45–47°.

Anal. Calcd. for $C_7H_4Br_2F_3N$: Br, 50.11; N, 4.39. Found: Br, 50.08; N, 4.35.

The compound was deaminated and hydrolyzed to 2,4-dibromobenzoic acid.[9]

Deamination Reactions with Ethanol.—The procedure was adapted from that of Clarke and Taylor.[10] To 300 ml. of 95% ethanol in a one-liter flask equipped with a stirrer, thermometer and addition funnel were added 0.5 mole of the amine and 55 ml. of 96% sulfuric acid. The solution was cooled to −5° and 0.58 mole of sodium nitrite dissolved in the minimum amount of water slowly added. The temperature was maintained between 0 and 5° during the reaction and for one hour afterwards. The addition funnel was replaced by a reflux condenser and the temperature of the solution slowly raised to 30° where it was maintained for an hour, finally being raised slowly until reflux began and the evolution of nitrogen ceased. The reaction mixture was then distilled through a 12-inch column packed with Berl saddles until the temperature reached 80°. The distillate was added to 1500 ml. of water and the lower layer separated. The residue from the fractionation was steam distilled and the oil obtained added to the water-insoluble layer. The combined products were dried and distilled through an 18-inch column packed with $^1/_8$ inch glass helices.

Deamination Reactions with Hypophosphorus Acid.—The procedure was adapted from that of Kornblum.[11] About 125 ml. of concentrated hydrochloric acid was added to a 500-ml. flask equipped as for the ethanol deaminations. One-quarter mole of the amine was added slowly, the mixture cooled to −5° and 0.36 mole of sodium nitrite dissolved in a small amount of water added while the temperature was held below 10°. The resulting solution was stirred for half an hour and a precooled 50% solution containing one mole of hypophosphorus acid slowly added. Stirring was continued for two hours after all the acid had been added and the flask stored at 10° for 18 hours. The heavy, red liquid which separated was dried and distilled.

2-Bromo-5-chlorobenzotrifluoride.—A solution of 98 g. of 5-amino-2-bromobenzotrifluoride dissolved in 100 ml. of concentrated hydrochloric acid was treated at 0–5° with a solution containing 140 g. of sodium nitrite. After the diazotization was complete, 1.5 g. of copper powder was added and the solution heated gently. When the evolution of nitrogen had ceased, the mixture was steam distilled and the resulting oil dried and distilled. 2-Bromo-5-chlorobenzotrifluoride (45 g.), b.p. 197–202°, was obtained. A center fraction had a boiling point of 198°, m.p. 14.9–16.2° and $n^{25}\text{D}$ 1.5056.

3,4-Dibromobenzotrifluoride.—By essentially the method described above, 0.2 mole of 3-amino-4-bromobenzotrifluoride was treated with 202 g. of 40% hydrobromic acid solution, 69 g. of sodium nitrite and, subsequently, copper powder to give a 71% yield of 3,4-dibromobenzotrifluoride, b.p. 101–102° at 25 mm., $n^{25}\text{D}$ 1.5189, d^{25}_4 1.973, AR_F 1.19.

Anal. Calcd. for $C_7H_3Br_2F_3$: Br, 52.56. Found: Br, 52.54.

Hydrolysis with 100% sulfuric acid gave 3,4-dibromobenzoic acid, m.p. 235–236.5°. 3,4-Dibromobenzotrifluoride has previously been prepared by the direct bromination of benzotrifluoride.[2]

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[7] G. M. Le Fave, THIS JOURNAL, **71**, 4148 (1949).

[8] H. Hübner, J. Ohly and O. Philipp, *Ann.*, **143**, 247 (1867).

[9] R. H. C. Nevile and O. Winther, *Ber.*, **13**, 972 (1880).

[10] H, T. Clarke and E. R. Taylor, "Organic Syntheses," Coll, Vol. I, John Wiley and Sons, Inc,, New York, N. Y., 1941, p. 415.

[11] N. Kornblum, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 294.

Heat Capacities at Low Temperatures and Entropies at 298.16°K. of Hafnium Dioxide and Hafnium Tetrachloride

BY S. S. TODD

RECEIVED MARCH 7, 1953

Thermodynamic values of hafnium compounds have been lacking because of unavailability of adequately pure materials. Recently, substantially pure hafnium and some of its compounds have been produced in considerable amounts. This paper reports low-temperature heat capacity data and entropy values at 298.16°K. for hafnium dioxide and hafnium tetrachloride. No previous, similar data exist for either substance.

Materials.—The hafnium dioxide and hafnium tetrachloride were furnished by the Northwest Electrodevelopment Laboratory of the Bureau of Mines at Albany, Ore., along with the results of chemical and spectrographic analyses, which were reported in the recent paper of Orr,[1] who measured high-temperature heat contents of identical materials. The hafnium dioxide contained 1.66% zirconium dioxide and a 0.37% total of minor impurities. The hafnium tetrachloride contained 3.31% zirconium tetrachloride and 0.08% of minor impurities.

Heat Capacities.—The heat capacities were determined with previously described apparatus.[2] The results are expressed in defined calories (1 cal. = 4.1840 abs. joules), molecular weights accord with the 1951 International Atomic Weights,[3] and all weighings were reduced to vacuum. The measurements employed 339.96 g. of the dioxide and 277.65 g. of the tetrachloride.

The experimental heat capacity values are listed

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[1] R. L. Orr, THIS JOURNAL, **75**, 1231 (1953).

[2] K. K. Kelley, B. F. Naylor and C. H. Shomate, U. S. Bur. Mines Tech. Paper 686 (1946).

[3] E. Wichers, THIS JOURNAL, **74**, 2447 (1952).

in Table I. The results for hafnium dioxide were corrected for the zirconium dioxide content by means of data of Kelley,[4] and those for hafnium tetrachloride were corrected for the zirconium tetrachloride content by means of data of the author.[5] The corrections ranged from 0.09 to 0.99% for the dioxide and from 1.11 to 1.23% for the tetrachloride, depending upon the temperature.

The substances exhibit normal types of heat capacity curves over the temperature range 51–298°K., analogous in shape to those of the corresponding zirconium compounds.

TABLE I

HEAT CAPACITIES

T, °K.	C_p, cal./deg. mole	T, °K.	C_p, cal./deg. mole	T, °K.	C_p, cal./deg. mole
		HfO_2 (mol. wt., 210.60)			
52.47	2.216	114.60	6.507	216.37	11.82
56.55	2.499	124.63	7.153	226.34	12.21
60.70	2.818	136.02	7.843	236.13	12.53
65.29	3.177	146.13	8.435	245.94	12.89
70.13	3.525	156.02	9.000	256.36	13.21
74.90	3.853	166.07	9.523	266.38	13.51
80.36	4.237	176.11	10.04	276.25	13.81
85.12	4.562	187.91	10.61	286.50	14.11
94.99	5.220	196.35	10.98	296.34	14.33
104.57	5.845	206.35	11.42	(298.16)	(14.40)
		$HfCl_4$ (mol. wt., 320.43)			
52.26	11.48	114.45	20.54	216.53	26.81
56.24	12.17	124.48	21.54	226.22	27.18
60.51	13.00	135.90	22.55	236.15	27.47
64.93	13.85	146.16	23.34	245.86	27.71
69.42	14.63	155.96	23.98	256.37	27.93
73.99	15.34	166.15	24.60	266.41	28.16
79.91	16.25	176.19	25.15	276.27	28.40
84.01	16.86	186.15	25.64	286.53	28.62
94.88	18.30	196.10	26.07	296.55	28.73
104.44	19.42	206.33	26.42	(298.16)	28.80

Entropies.—The entropy increments between 51 and 298.16°K. (the measured range) were obtained by Simpson-rule integrations of C_p against log T plots. Extrapolations from 51 to 0°K. were made by means of the empirical Debye and Einstein function sums given below. The function sum for hafnium dioxide fits the measured data to within 1.0% up to 200°K. and to within 3.2% up to 298.16°K. Similarly, that for hafnium tetrachloride fits the measured data to within 1.0% up to 167°K. and to within 3.3% up to 298.16°K.

$$HfO_2\text{: } D(266/T) + E(479/T) + E(794/T)$$
$$HfCl_4\text{: } D(69.0/T) + 2E(161/T) + 2E(402/T)$$

The entropy results appear in Table II. They may be compared with values for zirconium dioxide and zirconium tetrachloride, which are, respectively, $S°_{298.16}$ = 12.12 ± 0.08[4b] and $S°_{298.16}$ = 44.5 ± 0.5.[5]

TABLE II

ENTROPIES AT 298.16 °K. (CAL./DEG. MOLE)

	HfO_2	$HfCl_4$
0–51 °K. (extrap.)	0.89	8.64
51–298.16 °K (meas.)	13.29	36.93
$S°_{298.16}$	14.18 ± 0.10	45.6 ± 0.6

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[4] K. K. Kelley, (a) *Ind. Eng. Chem.*, **36**, 377 (1944); (b) U. S. Bur. Mines Bulletin 477 (1950).

[5] S. S. Todd, THIS JOURNAL, **72**, 2914 (1950).

Dehydration Products of 1,1,4,4-Tetraphenyl-1,4-butanediol[1]

BY WILLIAM J. WASSERMAN AND MILTON C. KLOETZEL

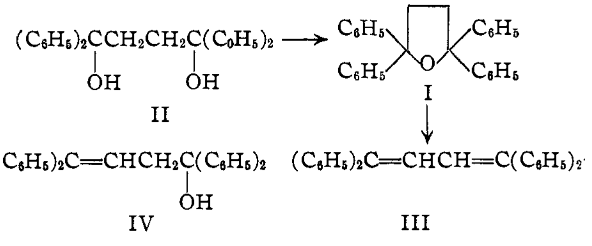
RECEIVED JANUARY 17, 1953

A compound melting at 182° and described as 2,2,5,5-tetraphenyltetrahydrofuran (I) was reported by Valeur[2] and again by Salkind and Teterin[3] to result from the dehydration of 1,1,4,4-tetraphenyl-1,4-butanediol (II) with boiling acetic acid. However, Acree[4] designated I as one of three possible structures for a substance, m.p. 163–165°, isolated from the reaction of phenylmagnesium bromide with diethyl succinate and also from the dehydration of the aforementioned diol.

In the course of certain investigations of the hydrogenated furan nucleus we had occasion to prepare I and therefore found it necessary to establish the identities of the materials melting at 182° and at 163–165°.

The reaction of phenylmagnesium bromide with methyl β-benzoylpropionate was found to yield diol II in 54% yield when effected at room temperature,[5] 49% at the temperature of refluxing ether, and 41% at 0°. In the latter instance there was also produced a 10% yield of 1,4-diphenyl-1,4-butanedione.

Dehydration of diol II with boiling acetic acid or with bromine yielded a compound melting at 180.5–181.5° as reported by Valeur[2] and by Salkind and Teterin.[3] This substance showed the proper analysis for a monodehydration product of diol II and did not react with cold permanganate solution. Zerewitinoff analysis indicated that the compound contained no active hydrogen. With anhydrous formic acid the compound was dehydrated to 1,1,4,4-tetraphenyl-1,3-butadiene (III). This compound is therefore 2,2,5,5-tetraphenyltetrahydrofuran (I) as originally designated by Valeur.[2]



Valeur[6] and Dilthey and Last[7] have reported excellent yields of diol II from the slow addition of diethyl succinate to phenylmagnesium bromide at

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[1] Abstracted from the M.S. thesis of William J. Wasserman. Presented at the 123rd National Meeting of the American Chemical Society, Los Angeles, March, 1953.

[2] A. Valeur, *Compt. rend.*, **136**, 694 (1903).

[3] J. Salkind and V. Teterin, *Ber.*, **62**, 1746 (1929).

[4] S. F. Acree, *Am. Chem. J.*, **33**, 180 (1905).

[5] M. C. Kloetzel, THIS JOURNAL, **62**, 3405 (1940).

[6] A. Valeur, *Bull. soc. chim. France*, **29**, 683 (1903).

[7] W. Dilthey and E. Last, *Ber.*, **37**, 2639 (1904).

room temperature. In our hands this reaction, effected in gently refluxing ether, yielded 64% of diol II and 11% of 1,4-diphenyl-1,4-butanedione when the reaction mixture was hydrolyzed with ammonium chloride solution. When dilute hydrochloric acid was employed for hydrolysis the yield of diol was reduced to 54% and a small quantity (6%) of 1,1,4,4-tetraphenyl-3-buten-1-ol (IV), m.p. 122.5–123.5°, was isolated.

Zerewitinoff analysis of the unsaturated alcohol showed the presence of one hydroxyl group. The compound rapidly decolorized cold permanganate solution. Structure IV was confirmed when ozonolysis yielded benzophenone and 3-hydroxy-3,3-diphenylpropanoic acid.

It is obvious that the substance reported by Acree[4] to melt at 163–165° is neither I nor IV. In an effort to obtain a sample of the material reported by Acree, diethyl succinate was added rapidly to phenylmagnesium bromide so that the reaction was effected in vigorously refluxing ether, and sulfuric acid was employed for hydrolysis. Under these conditions, which approximate as closely as possible those described by Acree, the products were obtained in the form of a mixture which was difficult to separate and which had a relatively narrow m. p. range in the vicinity of 160°. Upon careful fractional crystallization from carbon disulfide and nitromethane, this mixture finally yielded 2,2,5,5-tetraphenyltetrahydrofuran (I) and 1,1,4,4-tetraphenyl-1,3-butadiene (III).

It appears likely that the substance reported by Acree to melt at 163–165° was actually a mixture of I and III.

Experimental[8]

The reaction of methyl β-benzoylpropionate with phenylmagnesium bromide was effected as previously described[5] except that the ester was added to the mechanically stirred Grignard reagent, kept at ice-bath temperature, over a period of 35 minutes, and the temperature of the reaction mixture was subsequently allowed to rise to 20° during the course of one hour. Fractional crystallization of the product from acetone yielded 4.9 g. (41%) of **1,1,4,4-tetraphenyl-1,4-butanediol** (II), m.p. 203.5–204.5°, and 0.73 g. (10%) of **1,4-diphenyl-1,4-butanedione**, m.p. 145–146°. The latter showed no m.p. depression when mixed with an authentic sample of the diketone prepared by the method of Fritz.[9]

When the ethereal solution of methyl β-benzoylpropionate was added over a period of one hour to the Grignard reagent kept at constant reflux, the yield of diol II was 49%.

2,2,5,5-Tetraphenyltetrahydrofuran (I).—When 2.03 g. of diol II was added to 50 cc. of boiling glacial acetic acid and the solution was boiled for 5 minutes, 1.32 g. (68%) of I separated from the solution upon cooling; m.p. 180.5–181.5° after two recrystallizations from acetone.

The tetrahydrofuran was also obtained when 4.7 g. of a 13% solution of bromine in chloroform was added dropwise to a solution of 1.00 g. of the diol in 100 cc. of chloroform. After standing at 20° for 6.5 hours the solution was evaporated under reduced pressure. The residue was crystallized once from acetone to yield 0.58 g. (61%) of I.

Anal. Calcd. for $C_{28}H_{24}O$: C, 89.32; H, 6.42. Found: C, 89.30; H, 6.19.

The tetrahydrofuran did not decolorize a 2% aqueous solution of potassium permanganate at 20°. A Zerewitinoff determination[10] showed the absence of active hydrogen.

A mixture of 180 mg. of 2,2,5,5-tetraphenyltetrahydrofuran and 5 cc. of anhydrous formic acid was refluxed for 3 hours. After dilution with 5 cc. of water the mixture was extracted with 30 cc. of benzene and the extract was washed with 5% potassium hydroxide solution. Evaporation of the dried benzene extract yielded 0.13 g. (76%) of crude 1,1,4,4-tetraphenyl-1,3-butadiene (III) which melted at 202.5–203.5° after two recrystallizations from acetone and one from benzene. Valeur[2] reported a m.p. of 202°.

Reaction of Diethyl Succinate with Phenylmagnesium Bromide. (a) **Slow Addition of Ester.**—A solution of 17.6 g. of diethyl succinate in 70 cc. of ether was added, over a period of 2.5 hours, to the gently refluxing Grignard reagent prepared from 13.7 g. of magnesium, 82.2 g. of bromobenzene, 110 cc. of ether and a small crystal of iodine. The mixture was then refluxed for an additional period of 0.5 hour and allowed to stand at 20° for 3 hours.

Sixty per cent. of the reaction solution was poured over a mixture of ice and ammonium chloride solution and the resulting suspension was filtered. The crystalline solid was combined with an additional quantity obtained by evaporation of the ether layer. Fractional crystallization from acetone yielded 15.2 g. (64%) of **1,1,4,4-tetraphenyl-1,4-butanediol** (II) and 1.6 g. (11%) of **1,4-diphenyl-1,4-butanedione**. No 1,1,4,4-tetraphenyl-3-buten-1-ol (IV) was found.

The remaining 40% of the original Grignard reaction solution was hydrolyzed by pouring onto a mixture of 300 g. of ice and 5 cc. of concentrated hydrochloric acid. Filtration yielded some solid which was added to that obtained by evaporation of the ether layer. Fractional crystallization from acetone yielded 8.5 g. (54%) of **1,1,4,4-tetraphenyl-1,4-butanediol**, 1.0 g. (11%) of **1,4-diphenyl-1,4-butanedione**, and 0.9 g. (6%) of **1,1,4,4-tetraphenyl-3-buten-1-ol** (IV), m.p. 117–118°. Two recrystallizations from acetone raised the m.p. of IV to 122.5–123.5°.

The unsaturated alcohol decolorized cold 2% permanganate solution practically instantaneously. Reaction with methylmagnesium iodide at 90° in a Zerewitinoff analysis yielded 0.89 mole of methane per mole of IV.

Anal. Calcd. for $C_{28}H_{24}O$: C, 89.32; H, 6.42. Found: C, 89.37; H, 6.56.

A 200-mg. sample of 1,1,4,4-tetraphenyl-3-buten-1-ol dissolved in 70 cc. of reagent ethyl acetate was treated with a stream of oxygen containing 2% ozone for 0.5 hour at 20°. The ozonide solution was then allowed to stand for 3 days in contact with a solution of 5 cc. of 3% hydrogen peroxide in 70 cc. of water. The ethyl acetate layer was then extracted with 50 cc. of 10% aqueous sodium bicarbonate and evaporated to dryness. When the residue was heated with 10 cc. of ethanol and 150 mg. of 2,4-dinitrophenylhydrazine, and 0.2 cc. of concentrated hydrochloric acid was added, a clear solution resulted. Continued refluxing for 5 minutes resulted in the separation of an orange crystalline precipitate. This was washed with cold ethanol and upon crystallization from 25 cc. of acetic acid yielded 50 mg. of **benzophenone 2,4-dinitrophenylhydrazone**, m.p. 234–235°. This material produced no m.p. depression when mixed with authentic benzophenone 2,4-dinitrophenylhydrazone.

The sodium bicarbonate extract of the ethyl acetate solution was acidified with hydrochloric acid and then extracted with five 20-cc. portions of ether. Evaporation of the ether and crystallization of the residue from Skellysolve F yielded 50 mg. of **3-hydroxy-3,3-diphenylpropanoic acid** in colorless needles, m.p. 211–212°, which gave no depression of m.p. when mixed with authentic acid prepared by the method of Rupe and Busolt.[11]

(b) **Rapid Addition of Ester.**—A solution of 35.2 g. of diethyl succinate in 140 cc. of ether was added, over a period of 70 minutes, to the vigorously refluxing Grignard reagent prepared from 27.4 g. of magnesium, 164.4 g. of bromobenzene, 220 cc. of ether, and a small crystal of iodine. After being allowed to stand at 20° for 3.5 hours the reaction mixture was poured onto a large quantity of ice and then treated with 10 cc. of 5% sulfuric acid. When the ether had evaporated the suspended solid was filtered and recrystallized from ethanol or acetone. Separation of pure compounds could not be effected by successive recrystallizations from these solvents, but mixtures melting over such ranges as 147–158°, 156–163°, 157–161° and 159.5–163.5° were obtained easily.

Separation of a typical mixture finally was effected in the

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[8] All melting points are uncorrected. Analyses are by Dr. Adalbert Elek, Elek Microanalytical Laboratory, Los Angeles, California.

[9] V. Fritz, *Ber.*, **28**, 3028 (1895); *ibid.*, **29**, 1750 (1896).

[10] H. E. Zaugg and W. M. Lauer, *Anal. Chem.*, **20**, 1022 (1948).

[11] H. Rupe and E. Busolt, *Ber.*, **40**, 4537 (1907).

following manner. A 5.3-g. sample, m.p. 156–163°, was treated with a mixture of 15 cc. of carbon disulfide and 5 cc. of nitromethane, whereupon all but 1.92 g. of solid dissolved. The insoluble portion was crystallized twice from acetone to yield 0.70 g. of **2,2,5,5-tetraphenyltetrahydrofuran** (I). Recrystallizations of the soluble portion of the original mixture eventually yielded 0.12 g. of **1,1,4,4-tetraphenyl-1,3-butadiene** (III) as the only other compound which could be isolated in pure condition.

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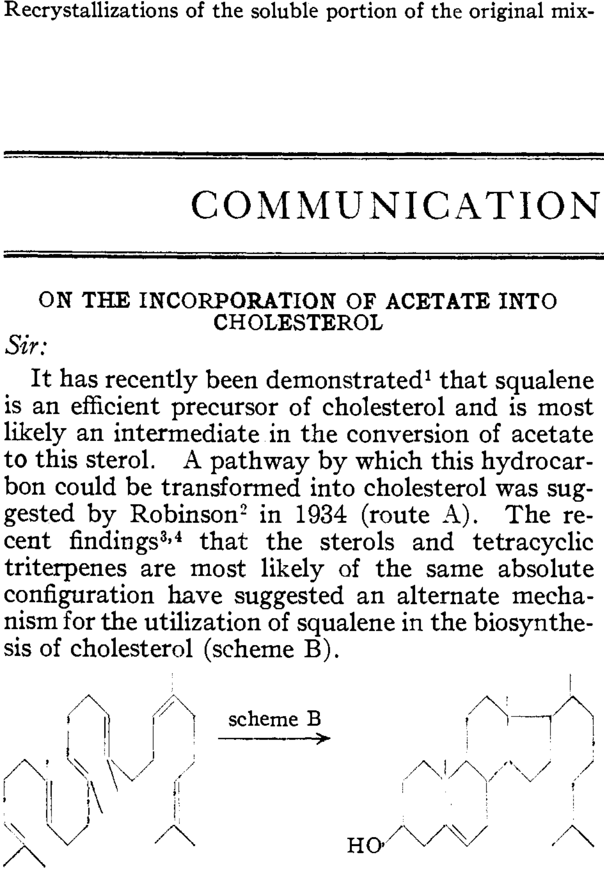
COMMUNICATIONS TO THE EDITOR

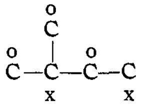
ON THE INCORPORATION OF ACETATE INTO CHOLESTEROL

Sir:

It has recently been demonstrated[1] that squalene is an efficient precursor of cholesterol and is most likely an intermediate in the conversion of acetate to this sterol. A pathway by which this hydrocarbon could be transformed into cholesterol was suggested by Robinson[2] in 1934 (route A). The recent findings[3,4] that the sterols and tetracyclic triterpenes are most likely of the same absolute configuration have suggested an alternate mechanism for the utilization of squalene in the biosynthesis of cholesterol (scheme B).



Degradation of the side-chain[5] and of ring A[6] of cholesterol formed from C^{14}-labeled acetate in biological experiments has indicated that such a biosynthesis might proceed by condensation of isoprenoid units labeled as shown in (I).[7] Therefore, if route A was followed



$$\begin{array}{cccc} & \overset{\circ}{C} & & \\ & | & & \\ \overset{\circ}{C} - & \underset{x}{C} - & \overset{\circ}{C} - & \underset{x}{C} \end{array}$$

I

carbon atoms 10, 13, 20 and 25 of cholesterol would be derived from a carboxyl carbon of acetate and carbon atoms 18, 19, 21 and 26 from the methyl carbon. Such would not be the case if the tetracyclic triterpenoid type of scheme (B) was followed since a migration of a carbon atom would be involved. Thus in route B, carbon atoms 10, 20 and 25 would be from carboxyl carbons and carbon atoms 13, 18, 19, 21 and 26 from methyl carbons. Hence, the acetic acid derived from a Kuhn–Roth oxidation of cholesterol which had been formed biosynthetically from C^{14}-methyl-labeled acetic acid should contain C^{14} in the carboxyl group if route B was followed and not if route A was utilized.

Such an experiment was performed and the acetic acid so obtained was degraded by a Schmidt reaction. It was found that the acetic acid had a specific activity of 55,[8] the carboxyl carbon had 35 and the methyl carbon had 74. It is seen that the carboxyl carbon atom of acetic acid derived from cholesterol possessed C^{14} as would be predicted by route B and thus would rule against the Robinson postulate (route A).

If one assumes that the ratio of methyl carbons to carboxyl carbons in cholesterol derived from acetate[9] is 15/12 and that 5 of the 8 carbon atoms of the 4 molecules of acetic acid (from the angular positions as discussed above) obtained from the Kuhn–Roth oxidation of such a labeled cholesterol are, in turn, derived from the methyl carbons, then the specific activity of the carbon dioxide obtained by decarboxylation of acetic acid should have a value of only 22. The higher value, 35, can be reconciled by consideration of the involvement of the progenitor, methyl-labeled acetate, in the tricarboxylic acid cycle which would lead to some doubly-labeled acetate. This degree of randomization is of the same order of magnitude as recently reported by Cornforth, Hunter and Popják.[6]

These results strongly indicate that if squalene is directly utilized in the synthesis of cholesterol, a reaction scheme of type B is strongly suggested.[10]

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(1) R. G. Langdon and K. Bloch, *J. Biol. Chem.*, **200**, 135 (1953).

(2) R. Robinson, *J. Soc. Chem. Ind.*, **53**, 1062 (1934).

(3) W. Klyne, *J. Chem. Soc.*, 2916 (1952).

(4) W. G. Dauben, D. F. Dickel, O. Jeger and V. Prelog, *Helv. Chim. Acta*, **36**, 325 (1953).

(5) J. Wüersch, R. L. Huang and K. Bloch, *J. Biol. Chem.*, **195**, 439 (1952).

(6) J. W. Cornforth, G. D. Hunter and G. Popják, *Biochem. J.*, **53**, xxiv (1953).

(7) The methyl carbon of acetate is denoted by o and the carboxyl carbon by x.

(8) All specific activities are expressed as dis./min./mg. $BaCO_3$

(9) H. N. Little and K. Bloch, *J. Biol. Chem.*, **183**, 33 (1950).

(10) A recent report by Woodward and Bloch (THIS JOURNAL, **75**, 2023 (1953)) has suggested the same reaction scheme.

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RECEIVED MAY 1, 1953

POSSIBLE SIGNIFICANCE OF LACTONES AS INTERMEDIATES IN OXIDATION OF CARBONACEOUS MATERIALS

Sir:

Controlled oxidation of aqueous, alkaline suspensions of bituminous coals results in the conversion of about 50% of the carbon to a mixture of