Related Thermal Data.—Table III lists the heats, entropies and free energies of formation at 298.16° K. of the two silicates from the elements and from the oxides. The entropy values are derived from the compilation of Kelley[13] and the work of Humphrey, King and Kelley,[14] and Todd and Bonnickson.[15]

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[13] K. K. Kelley, U. S. Bureau of Mines Bull. 477 (1950).

[14] G. L. Humphrey, E. G. King and K. K. Kelley, U. S. Bureau of Mines, Report of Investigations 4870 (June, 1952).

[15] S. S. Todd and K. R. Bonnickson, This Journal, **73**, 3894 (1951).

BERKELEY 4, CALIFORNIA

NOTES

The Effect of Sodium Oxide on the Chromium Oxide Catalyzed Conversion of Aldehydes to Ketones[1]

BY J. R. COLEY[2] AND V. I. KOMAREWSKY

RECEIVED MARCH 1, 1952

In the course of a study[3] of the action of metallic oxide catalysts on alcohols, it was found that alcohols and aldehydes of "n" carbon atoms undergo a complex dehydrogenation–condensation reaction when passed over a chromia catalyst at 400° to form ketones of "$2n - 1$" carbon atoms. It was noted that a sodium hydroxide precipitated catalyst was quite active in contrast to a comparatively inactive ammonia precipitated catalyst.

It has therefore been of interest to determine the effect of sodium content in a chromia catalyst upon this reaction.

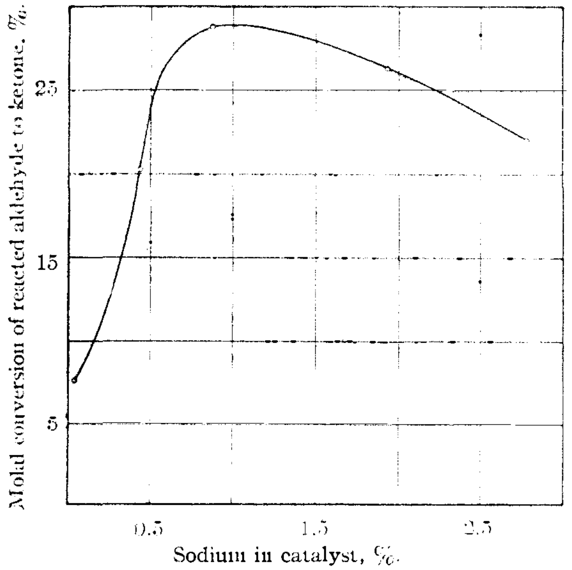

Fig. 1.—The effect of sodium oxide on the conversion of n-butyraldehyde to di-n-propyl ketone.

Experimental Part

Procedure.—The catalysts were prepared by redissolving a cold slurry of chromium hydroxide precipitate in cold excess sodium hydroxide. The chromite solution on standing overnight formed a chromium hydroxide gel. The gel was washed anion free, dried at 110°, screened to 8 mesh and heated in an atmosphere of hydrogen at gradually increased temperatures up to 500°. To vary the sodium content, portions of the catalyst, after washing but prior to drying, were agitated in sodium carbonate solutions of varying concentrations, filtered and dried. The method of sodium analysis was a modification of the triple acetate procedure devised by Kahane.[4]

The catalytic reaction procedure consisted of passing a three to one mixture of nitrogen and vaporized n-butyraldehyde over a granular (8–10 mesh) catalyst bed (volume 50 cc.), maintained at a temperature of 400° by an electrically heated furnace. A constant liquid space velocity of 0.1 was used for all runs. All products were distilled in a 20-inch super-cal Heli Grid Podbielniak Column.

Discussion of Results

The results obtained are given in Table I and Fig. 1.

TABLE I

DATA ON SODIUM CONTENT OF CHROMIA CATALYSTS *versus* YIELD OF KETONE

Weight % sodium	Molal conversion of reacted aldehyde to ketone,[a] %
0.01	7.6
.45	20.3
.88	28.8
1.93	26.3
2.79	22.1

[a] Dipropyl ketone, b.p. 144.18°.

These results indicate that the sodium content of a chromia catalyst has a definite effect on the catalytic activity for the dehydrogenation–condensation reaction discussed. This is consistent with the aldol mechanism proposed[3] for this ketone synthesis. The optimum sodium content was found to be approximately 1.0%.

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[1] From the Senior Problems of B. M. Joseph and S. C. Mikszta.

[2] Research Dept., Standard Oil Co. (Indiana), Whiting, Indiana.

[3] V. I. Komarewsky and J. R. Coley, This Journal, **63**, 700 3269 (1941).

[4] E. Kahane, *Bull. soc. chim.*, **47**, 382 (1930).

DEPARTMENT OF CHEMICAL ENGINEERING
ILLINOIS INSTITUTE OF TECHNOLOGY
CHICAGO, ILLINOIS

Preparation and Some Reactions of Indenyllithium

BY NORMAN H. CROMWELL AND DAVID B. CAPPS

RECEIVED MARCH 24, 1952

In connection with a general project in this Laboratory concerned with the synthesis and reactions of cyclic ketones, methods of preparing β-(1-indanyl)-propionic acid have been under investigation. This acid had previously been prepared by v. Braun and co-workers[1] in a several step, side-chain building process starting with 1-indanone. It seemed desirable to develop a synthesis involving a readily prepared metallic derivative of the inexpensive indene. Although indenyllithium had been prepared previously[2] from indene using ethyllithium and diethylmercury, it seemed advisable to avoid this latter expensive and poisonous reagent.

Using a procedure similar to that employed in the synthesis of 9-fluorenyllithium and fluorene-9-carboxylic acid,[3] we have obtained indenyllithium and indene-1-(or 3)-carboxylic acid in good yields from the reaction of butyllithium with indene, followed by treatment with solid carbon dioxide.

Indenyllithium was found to react with ethyl β-bromopropionate to give a low (14%) yield of ethyl β-[1(or 3)-indenyl]-propionate. The major reaction probably involved the loss of hydrogen bromide from the β-bromo ester. The ester product on hydrolysis gave β-[1(or 3)-indenyl]-propionic acid which was readily hydrogenated to the β-[1-indanyl]-propionic acid.

Experimental

Indenyllithium and Indene-1(or 3)-carboxylic Acid.—Approximately 0.2 mole of *n*-butyllithium was prepared in 150 ml. of dry ether by the procedure of Gilman, *et al.*[4] To this solution 21.8 g. (0.188 mole) of indene (Eastman Kodak Co. Practical grade) was added over a period of 30 minutes with the evolution of butane. The rust colored mixture was refluxed for two hours and then poured in a thin stream onto solid carbon dioxide. One liter of water was cautiously added to the lithium-free ether mixture. The basic aqueous layer was acidified with hydrochloric acid to give 20.1 g. of indene-1(or 3)-carboxylic acid which was recrystallized from benzene, m.p. 159–160°; neut. equiv., calcd. 160.2, found 160 and 158.7.[5]

This experiment indicated that at least 67% of the indene had been converted into its lithium derivative.

β-[1(or 3)-Indenyl]-propionic Acid.—A solution of indenyllithium, prepared as in the previous experiment, was transferred through a glass wool filter into a nitrogen swept separatory funnel and added slowly in 30 minutes to a 160 ml. of dry ether solution of 34 g. (0.187 mole) of ethyl β-bromopropionate cooled to 3–5°. After the addition was complete the reaction mixture was allowed to stand at room temperature for 12 hours. The cooled solution was mixed with ice and ammonium chloride and the ether layer distilled to give 7.6 g. of the crude ethyl β-[1(or 3)-indenyl]-propionate, b.p. 155–163° (15 mm.). Hydrolysis of this ester with 20% sodium hydroxide produced 5.3 g. (14.7% yield based on the bromo ester) of β-[1(or 3)-indenyl]-propionic acid. Recrystallization from aqueous alcohol and then benzene gave colorless crystals, m.p. 129–130°.[6] Aqueous alkaline solutions of this unsaturated acid decolorized potassium permanganate instantly while aqueous acetone solutions gave a slower decolorization at 25°.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43; neut. equiv., 188.2. Found: C, 76.84; H, 6.38; neut. equiv., 188.5 and 190.2.

β-[1-Indanyl]-propionic Acid.—A sample of β-[1(or 3)-indenyl]-propionic acid (1.95 g.) in absolute alcohol was hydrogenated in the presence of palladinized charcoal under three atmospheres of hydrogen for seven hours. Isolation produced 1.45 g. of the crude acid, m.p. 45–48.5°. Recrystallization from petroleum ether gave a purer product, m.p. 49.5–51°.[1]

AVERY LABORATORY
UNIVERSITY OF NEBRASKA
LINCOLN, NEBRASKA

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[1] (a) J. v. Braun and J. Reutter, *Ber.*, **59B**, 1922 (1926); (b) J. v. Braun and E. Danzinger and Z. Koehler, *ibid.*, **50**, 56 (1917).

[2] (a) W. Schlenk and E. Bergmann, *Ann.*, **463**, 227 (1928); (b) O. Blum-Bergmann, *ibid.*, **484**, 28 (1931).

[3] R. R. Burtner and J. W. Cusic, THIS JOURNAL, **65**, 264 (1943).

[4] H. Gilman, *et al.*, *ibid.*, **71**, 1499 (1949).

[5] W. S. Knowles, J. A. Kuck and R. C. Elderfield, *J. Org. Chem.*, **7**, 377 (1942). No evidence seems to be available to establish the location of the carboxy group with respect to the five-ring double bond. It seems probable that the correct structure is indene-3-carboxylic acid with C=O conjugated with the C=C bond.

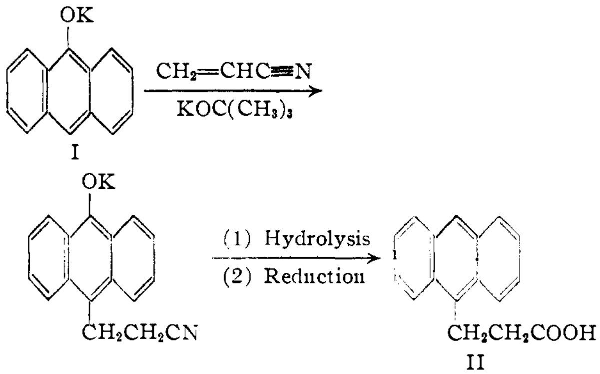
[6] Since completing our work we have noticed that G. R. Clemo *et al.*, *J. Chem. Soc.*, 863 (1951), have reported the preparation of β-[3-indenyl]-propionic acid, m.p. 120.5–121.5°, by four methods two of which start with indene and two starting with 1-indanone, all of which gave rather low yields. In spite of the difference in melting points we believe that our acid is essentially the same as that of Professor Clemo.

The Monocyanoethylation of Anthrone. An Improved Synthesis of β-(9-Anthranyl)-propionic Acid and β-(9,10-Dihydro-9-anthranyl)-propionic Acid[1]

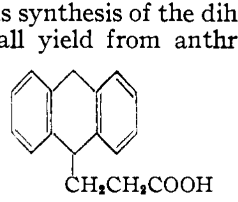
BY GUIDO H. DAUB AND W. CARTER DOYLE

RECEIVED APRIL 21, 1952

The cyanoethylation of anthrone as previously carried out by Bruson[2] gave 9,9-di-(β-cyanoethyl)-anthrone in 88% yield. Since it has been shown that certain phenols can be monocyanoethylated in excellent yield on a ring carbon[3] it was thought that anthrone as its potassium enolate salt could be monocyanoethylated in the 10-position. This has been carried out in excellent yield by allowing potassium anthranolate (I) to react with acrylonitrile in *t*-butyl alcohol using potassium *t*-butoxide as the condensing agent. The product was not isolated but was hydrolyzed and reduced with zinc dust in ammonium hydroxide to β-(9-anthranyl)-propionic acid (II) which was obtained in over-all yield of 90–95% from anthrone.



Reduction of the β-(9-anthranyl)-propionic acid (II) with sodium in *n*-amyl alcohol gave an 86% yield of β-(9,10-dihydro-9-anthranyl)-propionic acid (III). This synthesis of the dihydro acid (III) in 77.6% over-all yield from anthrone represents considerable improvement over its three-step syn-



III

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[1] This work was supported in part by a grant from the National Cancer Institute, U. S. Public Health Service.

[2] H. A. Bruson, THIS JOURNAL, **64**, 2457 (1942).

[3] H. A. Bruson, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 94.

thesis from 9-anthraldehyde described by Cook, Ludwiczak and Schoental.[4]

Experimental[5]

β-(9-Anthranyl)-propionic Acid (II).—A 1-l., three-necked flask with ground glass joints was fitted with a dropping funnel, condenser and mercury-sealed stirrer. The air in the system was replaced by dry nitrogen and 200 ml. of *t*-butyl alcohol[6] was added. After 4.88 g. (0.125 mole) of potassium was dissolved in the alcohol, 19.4 g. (0.1 mole) of anthrone,[7] m.p. 154–155°, was added with the aid of 10 ml. of *t*-butyl alcohol and the solution was stirred for one hour at room temperature. To this reddish-brown solution of potassium anthranolate was added dropwise over a period of one hour a solution of 7.3 ml. (0.11 mole) of acrylonitrile (Eastman Kodak Co.) in 40 ml. of anhydrous *t*-butyl alcohol. During the addition of the nitrile a bright red precipitate separated. The solution was refluxed for two hours and a clear deep red colored solution was obtained. After the addition of 11 ml. of concentrated hydrochloric acid (sp. gr. 1.18) in 225 ml. of water the *t*-butyl alcohol was removed by distillation during which time an additional 100 ml. of water was added. After the removal of 350 ml. of distillate the contents remaining in the flask were cooled and the aqueous layer was separated from a brown oil by decantation. The oily nitrile was refluxed for two hours with 100 ml. of concentrated hydrochloric acid during which time a solid acid separated. After cooling, the hydrochloric acid was removed with the aid of a sintered glass filter stick and the solid remaining in the flask was washed with 100 ml. of water. The solid acid was dissolved in 360 ml. of concentrated ammonium hydroxide and 240 ml. of water and the resulting solution was heated at 90–95° in an oil-bath for four hours with 60 g. of zinc dust (activated with copper sulfate). During the reduction the solution changed in color from reddish-orange to pale yellow. The cooled reaction mixture was filtered to remove excess zinc and the filtrate was extracted once with ether. The aqueous layer was acidified with hydrochloric acid and a tan oil separated which solidified on standing. The solid was filtered, washed with water and dried to give 22.5 g. (90% yield) of β-(9-anthranyl)-propionic acid (II), m.p. 190–193° (reported[4] m.p. 191–192°), as pale yellow crystals. Recrystallization of a small sample of the crude acid from glacial acetic acid gave pale yellow prisms, m.p. 194–195°.

In a larger run using 0.3 mole of anthrone and *t*-butyl alcohol (Eastman Kodak Co.) which had not been dried over sodium the yield of crude acid obtained was 71.3 g. (95% yield), m.p. 188–193°. When methyl acrylate was substituted for the nitrile in the condensation the yield of β-(9-anthranyl)-propionic acid (II) was lowered to 60%.

β-(9,10-Dihydro-9-anthranyl)-propionic Acid (III).—Twenty grams (0.08 mole) of crude β-(9-anthranyl)-propionic acid (II), m.p. 190–193°, was dissolved in 500 ml. of *n*-amyl alcohol (Eastman Kodak Co., practical grade) in a 1-l. round-bottomed flask equipped with a reflux condenser. To this refluxing solution was added 16.6 g. (0.72 mole) of sodium in small pieces over a period of five hours. The *n*-amyl alcohol was removed by steam distillation and the aqueous solution remaining in the flask was filtered and allowed to cool. The sodium salt of the dihydro acid crystallized in glistening plates and was filtered, washed with water, and redissolved in hot water. The resulting solution was acidified with hydrochloric acid to give 15.07 g. (74.5% yield) of almost colorless β-(9,10-dihydro-9-anthranyl)-propionic acid (III), m.p. 137–140° (reported[4] m.p. 139–140°). Acidification of the mother liquor from the crystallization of the sodium salt gave 5.9 g. of a yellow solid, m.p. 120–130°, which upon recrystallization from benzene gave an additional 2.32 g. (11.5% yield) of almost colorless dihydro acid (III), m.p. 134–140°. Recrystallization of a sample of the acid from benzene gave colorless crystals, m.p. 139–140°.

LABORATORY OF ORGANIC CHEMISTRY
UNIVERSITY OF NEW MEXICO
ALBUQUERQUE, NEW MEXICO

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(4) J. W. Cook, R. S. Ludwiczak and R. Schoental, *J. Chem. Soc.*, 1112 (1950).

(5) All melting points are uncorrected.

(6) Dried by refluxing over and distilling from sodium.

(7) K. H. Meyer, "Organic Syntheses," Coll. Vol. 1, John Wiley & Sons, Inc., New York, N. Y., 1941, p. 60.

5-Ethoxyquinoxaline[1]

BY WILLIAM K. EASLEY[2] AND MICHAEL X. SULLIVAN

RECEIVED JANUARY 19, 1952

The recent synthesis of 5-hydroxyquinoxaline[3,4] prompts us to report the synthesis of 5-ethoxyquinoxaline which had been prepared as an intermediate in this Laboratory. It was prepared from the known 2,3-dinitrophenetole[5] by catalytic reduction to the intermediate 2,3-diaminophenetole, which was not isolated but condensed with sodium glyoxal bisulfite to form 5-ethoxyquinoxaline. Both 5-ethoxyquinoxaline and copper-5-quinoxalinate have been found to produce 100% inhibition of the standard organism, *Aspergillus niger*, in 250 parts per million concentrations. Further investigation of the fungistatic properties of these compounds is in progress.

Experimental

2,3-Dinitrophenetole.—The method of Blanksma[5] as modified by Verkade and Witjens[6] was not found satisfactory for preparing the desired quantity of product. However, the following procedure was employed to obtain the 2,3-dinitrophenetole in reasonable yield and in a good state of purity. Twenty grams (0.088 mole) of 1-ethoxy-2,3-dinitro-4-aminobenzene[6] was dissolved in 200 ml. of concentrated sulfuric acid; 70 g. of water was added dropwise to the acid solution with mechanical stirring in an ice-bath. The suspension of the sulfate was diazotized at 0–5° with a solution of 6.07 g. (0.088 mole) of sodium nitrite in 25 g. of water, which was added dropwise in about 35 minutes. The diazonium solution was stirred for another hour at the same temperature and poured into a liter of boiling 95% ethanol. The mixture was boiled for 45 minutes, then diluted with enough water to give a final volume of about 4 liters. A dark brown precipitate formed during the dilution and was removed by filtration on a buchner funnel. The yield of the crude product was 13.6 g., m.p. 96–99°. The average yield from seven similar runs was 14.0 g. If further purification is desired, the product can be crystallized from 95% ethanol. For our use the product was not further purified.

5-Ethoxyquinoxaline.—Forty-eight grams (0.226 mole) of 2,3-dinitrophenetole was dissolved in 1800 ml. of 95% ethanol and reduced with hydrogen in the presence of 6 g. of 5% palladium-on-charcoal catalyst. During filtration from catalyst, the solution darkened considerably. To the filtrate was added 100 ml. of 2 *M* acetic acid and 50 ml. of 4 *M* sodium acetate solution. The resulting solution was heated to 60° and poured rapidly into a solution of 67.11 g. (0.226 mole) of sodium glyoxal bisulfite (Carbide and Carbon Chemicals Corp.) in 2 liters of water which had previously been heated to 60° and the mixture was stirred for one hour. It was then cooled in an ice-bath and made strongly alkaline by the addition of 120 g. of sodium hydroxide pellets and 500 g. of sodium carbonate. The mixture separated into two layers, a clear aqueous layer and a dark alcohol–water layer. The layers were separated, and the dark alcohol layer was reduced to less than half its volume at the water-pump. This dark mixture was then recombined with the clear layer, and a dark oil separated which was extracted with a pound of benzene. The benzene extract was dried over anhydrous calcium sulfate. The benzene was then removed at the water-pump, and the residual dark oil was vacuum distilled. The fraction that distilled from 106–117° at 0.5 to 2 mm. was collected. It was brownish-yellow in color and solidified in the receiving flask. Recrystallization from petroleum ether gave a white prod-

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(1) Taken from the thesis submitted by William K. Easley in partial fulfillment of the requirements for the Ph.D. degree at The Division of Chemistry, Graduate School, Georgetown University, Washington, D. C.

(2) The Chemstrand Corporation, Marcus Hook, Pennsylvania.

(3) F. E. King, N. G. Clark and P. M. H. Davis, *J. Chem. Soc.*, 3012 (1949).

(4) S. K. Freeman and P. E. Spoerri, *J. Org. Chem.*, **16**, 438 (1951).

(5) J. J. Blanksma, *Rec. trav. chim.*, **27**, 49 (1908).

(6) P. E. Verkade and P. H. Witjens, *ibid.*, **65**, 361 (1946).

uct, m.p. 63–64°. Yield of crude product was 16.9 g., 41.9% of the theoretical yield.

Anal. Calcd. for $C_{10}H_{10}ON_2$: C, 68.94; H, 5.79; N, 16.08. Found: C, 69.11; H, 5.88; N, 16.24.

The reddish-orange salt of 5-ethoxyquinoxaline and methyl iodide was prepared by the procedure of Easley and Bahner,[7] m.p. 214–215° uncor. (with dec.).

Anal. Calcd. for $C_{11}H_{13}ION_2$: N, 8.85. Found: N, 8.60.

The scarlet salt with ethyl iodide was prepared in the same manner, m.p. 146–148° uncor. (with dec.).

Anal. Calcd. for $C_{12}H_{14}ION_2$: N, 8.50. Found: N, 8.22.

Acknowledgments.—The authors wish to thank Dr. E. Mosettig for use of his reduction apparatus and Miss Rita McCollum and Mr. T. S. Barker for microanalyses.

[7] W. K. Easley and C. T. Bahner, This Journal, **72**, 3803 (1950).

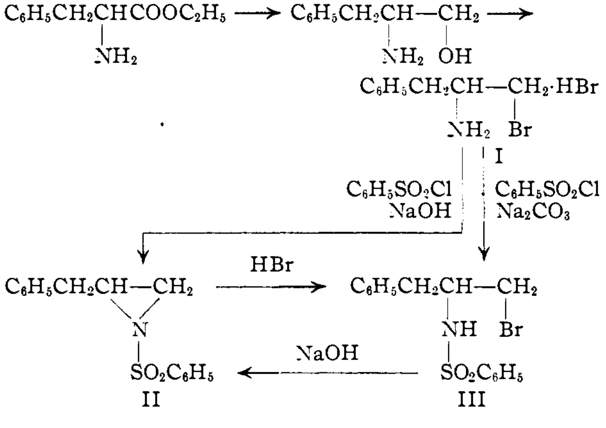
Chemo-Medical Research Institute
Georgetown University
Washington, D. C.

Ring Cleavage of 1-Benzenesulfonyl-2-benzylethylenimine with Hydrogen Bromide[1]

By Walter J. Gensler and John C. Rockett

Received March 5, 1952

When 1-benzenesulfonyl-2-bromomethylethylenimine reacts with hydrobromic acid, ring cleavage occurs to form 1,3-dibromo-2-benzenesulfonamidopropane. In this process attack of the bromide ion occurs preferentially at the unsubstituted rather than at the substituted carbon of the three-membered ring.[2] We wish to record another example of this mode of cleavage in the production of 1-phenyl-2-benzenesulfonamido-3-bromopropane (III) from the action of hydrobromic acid on 1-benzenesulfonyl-2-benzylethylenimine (II). The structure of the cleavage product was established by its identity with the product (III) obtained on treating 1-phenyl-2-amino-3-bromopropane hydrobromide (I) with benzenesulfonyl chloride and aqueous sodium carbonate. The ethylenimine compound (II) was prepared by treating the hydrobromide (I) with benzenesulfonyl chloride and aqueous alkali, or by treating 1-phenyl-2-benzenesulfonamido-3-propane (III) with alkali.



Experimental[3]

1-Phenyl-2-amino-3-bromopropane Hydrobromide (I).—*dl*-Phenylalanine ethyl ester was converted to *dl*-phenylalaninol, m.p. 67–68°, by reduction with lithium aluminum hydride.[4]

A sealed tube containing 1.0 g. (0.006 mole) of *dl*-phenylalaninol and 25 ml. of 48% hydrobromic acid was heated at 170–175° for five hours. The dark colored reaction mixture, in which some carbonized material was present, was diluted with 100 ml. of water and was decolorized with charcoal (Nuchar). The resulting water-white, strongly acid solution was taken to dryness under reduced pressure on the steam-bath. The dry residue after crystallization from absolute alcohol weighed 1.27 g. (65%) and melted at 173–176°. A second crystallization (from 3 ml. of absolute alcohol) afforded 0.97 g. (49%) of pure 1-phenyl-2-amino-3-bromopropane hydrobromide, m.p. 174–175°.

Anal. Calcd. for $C_9H_{13}NBr_2$: C, 36.8; H, 4.4. Found: C, 36.7; H, 4.4.

When the reaction was carried out at 100° instead of at 170°, the hydrobromide of *dl*-phenylalaninol was the only material isolated. This salt was prepared in a separate experiment by evaporating a mixture of 1.0 g. (0.0066 mole) of *dl*-phenylalaninol and 25 ml. of 48% hydrobromic acid under reduced pressure, and crystallizing the dry residual solids from ethyl alcohol. The hydrobromide obtained in this way (1.21 g. or 79%) melted at 148–149°, and showed no change in melting point after admixture with the material (m.p. 148–149°) obtained from the reaction at 100°.

Anal. Calcd. for $C_9H_{14}NOBr$: C, 46.5; H, 5.6. Found: C, 46.3; H, 5.3.

1-Benzenesulfonyl-2-benzylethylenimine (II) from 1-Phenyl-2-amino-3-bromopropane Hydrobromide (I).—To a vigorously stirred solution of 1.5 g. (0.0050 mole) of the hydrobromide (I) in 10 ml. of water was added 0.78 ml. (0.0060 mole) of benzenesulfonyl chloride followed immediately by a solution of 1.0 g. (0.0025 mole) of sodium hydroxide in 10 ml. of water. The mixture was stirred for 40 minutes at room temperature. The solids were collected by filtration, washed on the funnel with water and air-dried. The dry material (1.22 g. or 89%; m.p. 54–56°) was taken up in ether, the ether solution was washed with several portions of water, and was dried over sodium sulfate. On crystallizing the oil remaining after the ether solvent had been removed from ethyl alcohol, there was obtained 1.03 g. (75%) of 1-benzenesulfonyl-2-benzylethylenimine, m.p. 55–56°.

Anal. Calcd. for $C_{15}H_{15}NSO_2$: C, 65.9; H, 5.5. Found: C, 65.7; H, 5.6; ash, 0.3.

1-Benzenesulfonyl-2-benzylethylenimine (II) from 1-Phenyl-2-benzenesulfonamido-3-bromopropane (III).—A mixture of 0.5 g. (0.0014 mole) of compound III, 0.4 g. (0.010 mole) of sodium hydroxide and 10 ml. of water was shaken for 15 minutes. The crystalline solids (0.36 g. or 95%; m.p. 53–55°) were collected and crystallized from 5 ml. of ethyl alcohol. The product obtained weighed 0.31 g. (81%), and melted both before and after admixture with the 1-benzenesulfonyl-2-benzylethylenimine prepared as indicated above at 55–56°.

1-Phenyl-2-benzenesulfonamido-3-bromopropane (III) from 1-Benzenesulfonyl-2-benzylethylenimine (II).—A mixture of 10 ml. of 48% hydrobromic acid and 0.40 g. (0.00146 mole) of ethylenimine II was heated on the steam-bath for one hour. Twenty milliliters of water was added, and the cold mixture was thoroughly extracted with ether. The ether extract, after washing with water, was dried over anhydrous sodium sulfate. Removal of the solvent left a residual oil (0.44 g.) which, after crystallization from ethyl alcohol, furnished 0.34 g. (65%) of white crystalline 1-phenyl-2-benzenesulfonamido-3-bromopropane, m.p. 22–23°.

Anal. Calcd. for $C_{15}H_{16}NSO_2Br$: C, 50.8; H, 4.5. Found: C, 50.6; H, 4.6.

The mixed melting point with the same material prepared as described below was 22–23°.

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[1] Abstracted from a portion of the Thesis submitted by John C. Rockett to the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Master of Arts.

[2] W. J. Gensler, This Journal, **70**, 1843 (1948).

[3] Melting points are uncorrected. The elementary analyses were carried out by Carol K. Fitz, 115 Lexington Avenue, Needham Heights 94, Mass.

[4] P. Karrer, P. Portmann and M. Suter, *Helv. Chim. Acta*, **31**, 1617 (1948); M. C. Rebstock, *et al.*, This Journal, **73**, 3666 (1951).

1-Phenyl-2-benzenesulfonamido-3-bromopropane (III) **from 1-Phenyl-2-amino-3-bromopropane Hydrobromide** (I).—To a vigorously stirred solution of 1.5 g. (0.0051 mole) of compound I in 10 ml. of water was added 0.78 ml. (0.0060 mole) of benzenesulfonyl chloride followed immediately by a solution of 0.83 g. (0.010 mole) of sodium carbonate in 10 ml. of water. After the reaction mixture had been stirred for one hour at room temperature, the oily product was extracted with ether. The ether solution was washed thoroughly with water, and dried over magnesium sulfate. Crystallization of the oil obtained on removal of the ether solvent from ethyl alcohol afforded 1.03 g. (57%) of 1-benzene-2-benzenesulfonamido-3-bromopropane, m.p. 22-23°.

CHEMISTRY DEPARTMENT
BOSTON UNIVERSITY
BOSTON, MASSACHUSETTS

Some Alkyl and Heterocyclic Sulfides and Sulfones

BY HENRY GILMAN, ROBERT K. INGHAM AND T. C. WU

RECEIVED APRIL 19, 1952

In connection with some studies on the pharmacological activity of certain sulfur-containing compounds, a series of alkyl and heterocyclic sulfides and sulfones has been prepared. The germicidal properties of some sulfides[1] have been demonstrated. The antistreptococcal activity of 4,4′-diaminodiphenyl sulfone,[2] the antitubercular effect of this and similar compounds,[3-5] and the indicated antimalarial activity[6] of its derivatives suggested the preparation of some quinolyl or other heterocyclic sulfones.

Of interest was the effect of incorporating a fat-soluble group into the molecule with a view toward increased absorption of the drug by the animal body.[7] Also, introduction of the physiologically active dialkylaminoalkyl grouping[8] was considered worthy of investigation.

The unsymmetrical sulfides were prepared by treatment of the sodium mercaptide with the proper organic halide. The sodium mercaptide was best prepared by addition of the mercaptan to a sodium ethoxide–ethanol solution. The sulfones were prepared from the corresponding sulfides by treatment with 30% hydrogen peroxide, with glacial acetic acid as a solvent. Additional derivatives of certain of these compounds have been prepared. Physical constants and analytical data of these sulfides and their derivatives are given in Tables I and II.

Of interest is the observation that quinine is oxidized in animals to 2-hydroxyquinine, thus the 2-substituted quinoline nucleus might be rendered more stable in the animal body.[9]

Results of pharmacological tests of these compounds will be reported elsewhere.

Experimental

Preparation of the Sulfides.—The sodium mercaptide was prepared by reaction of the theoretical amount of sodium with an excess of absolute ethanol; to the resulting sodium ethoxide solution was added an equivalent amount of mercaptan. Subsequently, the resulting mercaptide was refluxed with an organic halide and the sulfide thus obtained was extracted with ether. Following drying of the ethereal solution over sodium sulfate and removal of the solvent, purification of the sulfide was effected by vacuum distillation, recrystallization from an appropriate solvent, or in some cases both. Recrystallization solvents for the solid sulfides are given in Table I. In the preparation of the heterocyclic alkyl sulfides, the heterocyclic chlorides were employed; and with the dodecyl sulfides, the dodecyl group was introduced *via* the mercaptan. The dialkylaminoalkyl chlorides were prepared in accordance with a previously reported procedure.[10] The preparation of two typical sulfides follows. All melting points in Tables I and II are uncorrected.

2-[*n*-Octadecylmercapto]-quinoline.—To 100 ml. of absolute ethanol was added 0.7 g. (0.03 g. atom) of sodium. After completion of the reaction, 8.6 g. (0.03 mole) of *n*-octadecylmercaptan was added dropwise. After 30 minutes, 5.0 g. (0.03 mole) of 2-chloroquinoline was added dropwise and the resulting solution refluxed for 10 hours. The solvent was then removed by distillation and the residue extracted with an ether-dilute sodium hydroxide mixture. Following separation of the ethereal solution and drying over sodium sulfate, the ether was distilled off. Vacuum distillation of the residue gave a yellow liquid, b.p. 234-240° (0.2 mm.) which solidified on standing. Recrystallization from petroleum ether (b.p. 60-70°) gave 10.7 g. (85%) of white crystals, melting at 53-54°.

Preparation of *n*-Dodecyl γ-Hydroxypropyl Sulfide.—Sodium metal, 34.5 g. (1.5 g. atoms), was cut into small pieces and added slowly to 600 ml. of absolute ethanol until all of the sodium had dissolved (1.5 hours). To this solution was added 303.6 g. (1.5 moles) of *n*-dodecyl mercaptan; then 146 g. (1.54 moles) of trimethylene chlorohydrin was added over a period of one hour to the refluxing sodium mercaptide solution. The reaction mixture was refluxed for 12 hours and then filtered to remove the white precipitate formed. The solvent was distilled from the filtrate to give 413 g. of a solid residue. This solid was then vacuum distilled; there was thus obtained 336.8 g. (86%) of distillate, b.p. 157-159° (0.5 mm.). The product solidified on standing yielding a white solid, m.p. 34-35°.

Preparation of the Sulfones.—The sulfide was dissolved in a minimum amount of glacial acetic acid. An excess of 30% hydrogen peroxide was slowly added and the resulting solution refluxed for 1-4 hours. The sulfone which separated on cooling was filtered and recrystallized from an appropriate solvent (see Table II).

Carbonation of γ-*n*-Dodecylmercaptopropyllithium.—γ-*n*-Dodecylmercaptopropyl chloride (22.4 g., 0.08 mole) was added dropwise, in a dry nitrogen atmosphere, to a vigorously stirred mixture of 1.2 g. (0.17 g. atom) of lithium in 100 ml. of anhydrous ether. This addition required 30 minutes, during which period the ether was gently refluxing. The milky-white mixture was then stirred for 4 hours at room temperature. The mixture was filtered, in a nitrogen atmosphere, through glass wool into a dropping funnel and then added to a Dry Ice-ether slurry,[11] with the tip of the dropping funnel immersed in the slurry. Following return to room temperature, the carbonation mixture was carefully neutralized with dilute hydrochloric acid. The ethereal solution was separated and extracted twice with 5% sodium hydroxide. Removal of the solvent by distillation gave 8.8 g. (43%) of impure di-γ-*n*-dodecylmercaptopropyl ketone, melting at 50-57°. Three recrystallizations from absolute ethanol raised the m.p. to 67-68°. The pure product weighed 6.5 g. (32%). The alkali extract was acidified and shaken with dry ether. From the ethereal solution was obtained 6.2 g. (27%) of γ-*n*-dodecylmercaptobutanoic acid, melting at 51-54°. Two recrystallizations from petroleum ether (b.p. 28-40°) raised the m.p. to 57.5-58.5°. The pure product weighed 4.7 g. (20%).

In another experiment the corresponding Grignard reagent was prepared according to the entrainment method[12]

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TABLE I

PROPERTIES OF SOME ALKYL AND HETEROCYCLIC SULFIDES

No.	Sulfide	Formula	M.p., °C.	B.p., °C.	Yield, %	Sulfur, % Found	Sulfur, % Calcd.	Recrystallization solvent
1	*n*-Dodecyl-*n*-propyl sulfide	n-$C_{12}H_{25}SC_3H_7$-n	....	124–125 (0.25 mm.)[a]	62	13.19	13.11	....
2	*n*-Dodecyl-β-diethylaminoethyl sulfide	n-$C_{12}H_{25}SCH_2CH_2N(C_2H_5)_2$	....	132–133 (0.1 mm.)[b]	69	10.58	10.63	....
3	*n*-Dodecyl-β-diethylaminoethyl sulfide·HCl	n-$C_{12}H_{25}SCH_2CH_2N(C_2H_5)_2 \cdot HCl$	101–102	....	64	9.45	9.48	Diss. in EtOH, pptd. with ether
4	*n*-Dodecyl-γ-diethylaminopropyl sulfide	n-$C_{12}H_{25}SCH_2CH_2CH_2N(C_2H_5)_2$	....	156–157 (0.1 mm.)[c]	80	10.07	10.16	....
5	*n*-Dodecyl-γ-diethylaminopropyl sulfide·HCl	n-$C_{12}H_{25}SCH_2CH_2CH_2N(C_2H_5)_2 \cdot HCl$	106–108	....	73	9.09	9.11	EtOH–ether
6	*n*-Dodecyl-γ-chloropropyl sulfide	n-$C_{12}H_{25}SCH_2CH_2CH_2Cl$	....	153–155 (0.6 mm.)[d]	74	11.21[e]	11.45	....
7	*n*-Dodecyl-γ-hydroxypropyl sulfide	n-$C_{12}H_{25}SCH_2CH_2CH_2OH$	34–35	157–159 (0.5 mm.)	86	12.24	12.30	....
8	1,6-Di-*n*-dodecylmercaptohexane	$(n$-$C_{12}H_{25}SCH_2CH_2CH_2)_2$	51–53	....	93	13.03	13.17	Acetone
9	Bis-(γ-*n*-dodecylmercaptopropyl) ketone	$(n$-$C_{12}H_{25}SCH_2CH_2CH_2)_2CO$	67–68	....	32	12.73	12.46	EtOH
10	γ-*n*-Dodecylmercaptobutanoic acid	n-$C_{12}H_{25}SCH_2CH_2CH_3COOH$	57.5–58.5	....	20	11.04[f]	11.11	Pet. ether, b.p. 28–38°
11	2-γ-*n*-Dodecylmercaptopropylquinoline	$C_9H_6NCH_2CH_2CH_2SC_{12}H_{25}$-$n$	34–36	....	67	8.76	8.63	EtOH
12	2-γ-*n*-Dodecylmercaptopropylquinoline picrate	$C_9H_6NCH_2CH_2CH_2SC_{12}H_{25} \cdot C_6H_3O_7N_3$	96–98	....	42	5.61[g]	5.34	EtOH
13	2-[Benzylmercapto]-quinoline[h]	$C_6H_5CH_2SC_9H_6N$	44–44.5	....	74	12.45	12.76	Pet. ether, b.p. 60–70°
14	2-[Benzylmercapto]-quinoline hydrochloride	$C_6H_5CH_2SC_9H_6N \cdot HCl$	187–190	....	86	11.34	11.16	EtOH
15	2-[*n*-Dodecylmercapto]-quinoline	n-$C_{12}H_{25}SC_9H_5N$	....	185–188 (2 mm.)[i]	78	9.82	9.73	....
16	2-[*n*-Hexadecylmercapto]-quinoline[h]	n-$C_{16}H_{33}SC_9H_6N$	43–44	....	62	8.50	8.31	Pet. ether, b.p. 60–70°
17	2-[*n*-Octadecylmercapto]-quinoline[h]	n-$C_{18}H_{37}SC_9H_6N$	53–54	....	85	7.64	7.75	Pet. ether, b.p. 60–70°
18	2-Benzothiazolyl-2'-quinolyl sulfide[h]	$C_7H_4SNSC_9H_5N$	[illegible]		78	21.69	21.78	Dil. EtOH
19	2-[4-Phenylthiazoyl]-2'-quinolyl sulfide[h]	$C_9H_6SNSC_9H_6N$	[illegible]	....	50	19.72	19.05	Pet. ether, b.p. 60–70°
20	2-Benzimidazolyl-2'-quinolyl sulfide[h]	$C_7H_5N_2SC_9H_6N$	32.5–34	....	60	11.61	11.57	Pet. ether, b.p. 77–115°
21	4-[7-Chloroquinolyl]-2'-benzothiazolyl sulfide[j]	$C_7H_4SNSC_9H_5NCl$	138–140[k]	....	44	19.39	19.49	Pet. ether, b.p. 77–115°

[a] n^{20}_D 1.4608. [b] n^{20}_D 1.4680. [c] n^{20}_D 1.4680. [d] n^{20}_D 1.4742. [e] *Anal.* Calcd. for $C_{15}H_{31}SCl$: Cl, 12.67. Found: Cl, 13.02. [f] *Anal.* Calcd. for $C_{16}H_{32}O_2S$: neut. equiv., 289. Found: neut. equiv., 292. [g] *Anal.* Calcd. for $C_{30}H_{40}O_7N_4S$: N, 9.33. Found: N, 9.59. [h] Prepared from 2-chloroquinoline and the appropriate mercaptans. [i] n^{20}_D 1.5508. [j] Prepared from 2-mercaptobenzothiazole and the appropriate halide. [k] With decomposition.

TABLE II

PROPERTIES OF SOME ALKYL AND HETEROCYCLIC SULFONES

No.	Sulfone	Formula	M.p., °C.	Yield, %	Sulfur, % Found	Sulfur, % Calcd.	Recryst. solvent
1	*n*-Dodecylmethyl sulfone	n-$C_{12}H_{25}SO_2CH_3$	83–84	59	12.76	12.90	EtOH
2	*n*-Dodecyl-*n*-propyl sulfone	n-$C_{12}H_{25}SO_2C_3H_7$-n	66.5–67	48	11.79	11.60	EtOH
3	*n*-Dodecyl-*n*-butyl sulfone	n-$C_{12}H_{25}SO_2C_4H_9$-n	63–64	53	10.90	11.04	EtOH
4	*n*-Dodecyl-γ-chloropropyl sulfone	n-$C_{12}H_{25}SO_2CH_2CH_2CH_2Cl$	78–79	59	10.22[a]	10.31	Et_2O
5	*n*-Dodecyl-γ-hydroxypropyl sulfone	n-$C_{12}H_{25}SO_2CH_2CH_2CH_2OH$	87–88	36	10.84	10.96	Et_2O
6	1,6-Di-*n*-dodecylsulfonylhexane	$(n$-$C_{12}H_{25}SO_2CH_2CH_2CH_2)_2$	140–141	75	11.58	11.63	$CHCl_3$
7	Bis-(γ-*n*-dodecylsulfonylpropyl) ketone	$(n$-$C_{12}H_{25}SO_2CH_2CH_2CH_2)_2CO$	153–154	66	11.30	11.08	Pyridine
8	γ-*n*-Dodecylsulfonylbutanoic acid	n-$C_{12}H_{25}SO_2CH_2CH_2CH_2COOH$	130–130.5	80	10.04[b]	10.00	Acetone
9	2-Quinolyl benzyl sulfone	$C_6H_5CH_2SO_2C_9H_6N$	187–190	54	11.42	11.33	MeOH

[a] *Anal.* Calcd. for $C_{15}H_{31}O_2SCl$: Cl, 11.40. Found: Cl, 11.39. [b] *Anal.* Calcd. for $C_{16}H_{32}O_4S$: neut. equiv., 321. Found: neut. equiv., 320.

and then carbonated to give a 72% yield of γ-*n*-dodecylmercaptobutanoic acid. The above yields are based on the amount of γ-*n*-dodecylmercaptopropyl chloride employed.

Preparation of 2-γ-*n*-Dodecylmercaptopropylquinoline.—An ethereal solution of γ-*n*-dodecylmercaptopropyllithium was prepared from 28 g. (0.10 mole) of γ-*n*-dodecylmercaptopropyl chloride and 1.5 g. of lithium in a manner similar to that described above. To this organolithium compound in ether was added over a period of 3 minutes, 6.5 g. (0.05 mole) of redistilled quinoline. The reaction mixture turned yellow, later red and heat was evolved. Thirty minutes later the reaction was hydrolyzed with ice-water. Following drying of the light yellow ethereal solution over sodium sulfate and distillation of the solvent, 26.6 g. of yellow oil was obtained. This was heated with 6 ml. of nitrobenzene for 20 minutes at 180°. The resulting deep red oil was vacuum distilled. The brown oily residue (16.6 g.) was dissolved in 50 ml. of hot absolute ethanol and was boiled with a solution containing 20 g. of picric acid and 50 ml. of 95% ethanol for 15 minutes. Thus, 18.6 g. of yellow crystals was obtained. Three crystallizations from absolute ethanol gave 12.6 g. (42%) of crystals melting at 96–98°.

A mixture of 15 g. of the picrate and 100 ml. of 5% sodium hydroxide was refluxed for 5 hours. The mixture was cooled and extracted with ether. A brown oil (7.8 g., 84% based on the amount of picrate used) was obtained, which solidified on standing (m.p. 32–38°). One recrystallization from absolute ethanol gave 6.2 g. (67%) of product, m.p. 34–36°. Further recrystallization did not improve the melting point.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

The Solubility and Transition Point of Lithium Chromate

BY WINSLOW H. HARTFORD, RAYMOND L. COSTA AND PAUL E. MOORE

RECEIVED MARCH 26, 1952

Data reported by earlier workers for the solubility of lithium chromate at 18,[1] 20[2] and 30°[3] are not consistent. Further, while the usual composition of the salt is the dihydrate, our observations confirm the findings of Retgers[4] that an anhydrous salt separates from the aqueous solution on boiling. It therefore seemed desirable to determine the solubility over the range 0 to 100°, and the temperature of transition between the dihydrate and the anhydrous salt.

Experimental

The material used for the solubility experiments was recrystallized $Li_2CrO_4 \cdot 2H_2O$, prepared from lithium hydroxide monohydrate and chromic anhydride. It was found to contain 99.85% $Li_2CrO_4 \cdot 2H_2O$ based on its hexavalent chromium content, 0.006% Cl and 0.021% SO_4. It was necessary to remove traces of trivalent chromium and insoluble matter from the solutions before the final crystallization; this was done by oxidation with a small amount of sodium hypochlorite and filtrations. The final product consisted of bright yellow crystals. Solubility[5] and transition point[6] were determined by previously described methods. The following results were obtained:

Temp., °C.	Solubility, wt. % Li_2CrO_4	Solid phase
0.7	47.27	$Li_2CrO_4 \cdot 2H_2O$
7.2	47.74	$Li_2CrO_4 \cdot 2H_2O$
10.4	47.89	$Li_2CrO_4 \cdot 2H_2O$
20.0	48.60	$Li_2CrO_4 \cdot 2H_2O$
29.8	49.62	$Li_2CrO_4 \cdot 2H_2O$
40.2	50.66	$Li_2CrO_4 \cdot 2H_2O$
50.1	52.10	$Li_2CrO_4 \cdot 2H_2O$
60.0	53.52	$Li_2CrO_4 \cdot 2H_2O$
70.0	55.27	$Li_2CrO_4 \cdot 2H_2O$
74.6		$Li_2CrO_4 \cdot 2H_2O + Li_2CrO_4$
75.1	56.17	Li_2CrO_4
80.0	56.34	Li_2CrO_4
90.0	56.57	Li_2CrO_4
100.0	56.82	Li_2CrO_4

The values when plotted yield smooth curves. For the dihydrate, the equation

$$S = 47.25 + 0.05037T + 0.0009143T^2$$

fits the observed data with an average deviation of 0.05% and a maximum deviation of 0.09%. For the anhydrous salt, the equation

$$S = 52.646 + 0.06265T - 0.0002096T^2$$

fits the data with an average deviation of 0.01% and a maximum deviation of 0.02%. Calculation of the concentration at the transition temperature gives: from the dihydrate equation, 56.10% Li_2CrO_4; from the anhydrous salt equation, 56.15% Li_2CrO_4.

A value of 56.12% Li_2CrO_4 is therefore reported for the solution concentration in equilibrium with the two solid phases at the transition temperature of 74.6°.

As might be expected from the relatively slight change of solubility of both phases with temperature and the oblique angle of intersection of the two solubility curves, the heat effect on transition is very small, and is estimated to be of the order of 1–2 kcal./mole, as contrasted with 15 kcal./mole reported[7] for the $Na_2CrO_4 \cdot 10H_2O$–$Na_2CrO_4 \cdot 6H_2O$ transition. It was necessary to heat and cool at rates in the order of 0.01°/minute to detect the thermal breaks, which were obtained at 74.6° on both heating and cooling.

Of the previous solubility determinations, only that of Schreinemakers,[3] who reported 49.94% Li_2CrO_4 at 30°, is in agreement with the present work.

An attempt was made to determine the temperature of the ice-dihydrate eutectic. This proved to be below −60°; equipment and measuring facilities were not available to investigate lower temperatures.

An unusual characteristic of the anhydrous salt is its ready solubility in the lower alcohols. Sodium chromate is soluble to the extent of only 0.35%[8] in methanol and even less in ethanol at room temperature. Other anhydrous chromates are virtually insoluble in alcohols. Anhydrous lithium chromate was prepared for study by slowly boiling a saturated solution of the dihydrate. The yellow crystals were 99.83% Li_2CrO_4. An approximate determination of the solubility of the salt in commercial absolute methanol and ethanol was made by rotating sealed containers containing these compounds with an excess of lithium chromate in a constant temperature bath for eight hours. The bottles were protected from light by a covering of black tape, since alcoholic solutions of lithium chromate, although stable for more than two months in the dark, were found to undergo decomposition fairly rapidly, with deposition of hydrous chromic chromate, when exposed to light. The following results were obtained:

Temp., °C.	Solubility, wt. % Li_2CrO_4 Methanol	Ethanol
0.5	13.4	1.6
24.4	15.7	1.8

The dihydrate is somewhat more soluble than the anhydrous salt, but its true solubility in alcohols cannot be determined, since the salt is dehydrated by these solvents.

Anhydrous lithium chromate was found to be insoluble in ether, and soluble only to the extent of about 25 p.p.m., as judged by color, in acetone. The low solubility in acetone explains the previously reported[5] decomposition of lithium dichromate to lithium chromate in acetone solution.

Density of the dihydrate and the anhydrous salt was determined by immersion in toluene in a pycnometer: Li_2CrO_4, $d^{25}{}_4$ 2.426; $Li_2CrO_4 \cdot 2H_2O$, $d^{25}{}_4$ 2.149.

PUBLICATION NO. 95, RESEARCH LABORATORIES
MUTUAL CHEMICAL COMPANY OF AMERICA
BALTIMORE, MD.

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The Reaction of Silver *n*-Perfluorobutyrate with *n*-Perfluoropropyl Iodide and with 1,2-Dibromo-1-chlorotrifluoroethane

BY MURRAY HAUPTSCHEIN AND ARISTID V. GROSSE

RECEIVED MARCH 10, 1952

Several attempts were made to synthesize perfluorinated esters by the reaction of silver salts of perfluoro-fatty acids with perfluoroalkyl iodides, but without success.[1] In contrast to the ease of formation of esters by treating perfluoro-silver salts with *n*-alkyl iodides and diiodides,[2] the attempted preparation of *n*-perfluoropropyl-*n*-perfluorobutyrate by the reaction of silver *n*-perfluorobutyrate with *n*-perfluoropropyl iodide at 275–335°, in the absence of solvents, resulted in the formation of *n*-perfluorohexane, carbon dioxide and silver iodide according to the equation

$$CF_3CF_2CF_2I + CF_3CF_2CF_2CO_2Ag \longrightarrow n\text{-}C_6F_{14} + CO_2 + AgI \quad (1)$$

These results suggest a free radical mechanism with formation of $C_3F_7\cdot$ and $C_3F_7COO\cdot$. At the high temperature of the reaction, direct combination does not take place. The latter radical loses carbon dioxide, and the coupling product, C_3F_7–C_3F_7, is formed exclusively.

Experimental

The Reaction of *n*-Perfluoropropyl Iodide with Silver *n*-Perfluorobutyrate.—The reaction of perfluoropropyl iodide[1] and silver perfluorobutyrate[1] was carried out in nickel and silver pressure reactors at 275 and 335°, respectively. In both cases the only reaction products isolated were *n*-perfluorohexane, carbon dioxide and silver iodide in agreement with equation (1). Only possible traces of unreacted perfluoropropyl iodide were detected. *n*-Perfluorohexane boiled at 56°; mol. wt. found (Victor Meyer), 336; calcd., 338; known, b.p. 55.9–56.7°.[3]

The nickel reactor (100-cc. capacity) was of the rotating type and was partially filled with stainless steel balls. The silver reactor (16-cc. capacity) was filled with silver Raschig rings. Both vessels were equipped with Hoke valves. In a typical reaction, 7.5 g. (0.053 mole) of perfluoropropyl iodide was transferred *in vacuo* to the nickel reactor containing 8.4 g. (0.0262 mole) of finely powdered silver perfluorobutyrate. After heating this mixture at 275° for 10 hours, the Dry Ice-cooled reactor was opened to a similarly cooled glass collecting trap, and the temperature of the reactor was allowed to warm up slowly to *ca.* 25°. A large quantity of uncondensed carbon dioxide gas was collected in a barium hydroxide scrubber attached to the system. Finally all volatile products were transferred *in vacuo* to the collecting trap. This material (6.46 g.) was rectified in a micro fractionating column, and 5.65 g. (66% yield) of *n*-perfluorohexane, was collected. The yield of silver iodide was quantitative. A small scale run in the silver reactor at 335° for one hour, gave an almost quantitative yield of perfluorohexane.

At temperatures below 220° only a very slight reaction occurred in sealed Pyrex tubes. When anhydrous ethyl ether was used as a solvent, there were formed some *n*-perfluoropropyl hydride and a sizable fraction boiling at 70–100° which had a distinct ester odor and was only slightly soluble in water and dilute alkali (density < 1). No pure compound, however, could be isolated under these conditions.

The Reaction of 1,2-Dibromo-1-chlorotrifluoroethane with Silver *n*-Perfluorobutyrate.—The reaction of silver perfluorobutyrate with 1,2-dibromo-1-chlorotrifluoroethane (prepared by the photochemical bromination of chlorotrifluoroethylene) was carried out in glass and metal pressure reactors at temperatures of 100–200° and higher under a variety of conditions. The desired perfluorochloroester, trifluorochloroglycol diheptafluorobutyrate, was not obtained. When ethyl ether or dioxane was used as solvent, an insignificant amount of reaction occurred with some decomposition and loss of carbon dioxide. When an ethyl ether–heptafluorobutyric acid solvent mixture was employed, despite the formation of 50% silver bromide, evidence was found only for the formation of carbon dioxide, the olefin chlorotrifluoroethylene, and only possible traces of a higher boiling ester. Despite its reactivity, methanol was tried as a solvent because of its high solubilizing effect for the reactants. In this case the theoretical amount of silver bromide was isolated as well as a high yield of methyl *n*-heptafluorobutyrate,[4] b.p. 80–80.8° at 760 mm., $n^{20}D$ 1.293, formed by reaction with the solvent.

In the latter case, 15.0 g. of the dibromide, 36.5 g. of the silver salt and 70 ml. of methanol were heated together at 100° for 5 hours in a sealed Pyrex bulb. There were formed 20.2 g. of silver bromide, traces of chlorotrifluoroethylene, and after washing and drying with calcium chloride, 18.18 g. of pure methyl *n*-heptafluorobutyrate.

Acknowledgment.—The authors wish to express their appreciation to the U. S. Air Force, Wright Air Development Center, for their financial support of this work.

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[1] The perfluorinated inner ester, perfluorobutyrolactone, is the only completely fluorinated ester to be described to date. See M. Hauptschein and A. V. Grosse, This Journal, **73**, 2461 (1951); M. Hauptschein, C. S. Stokes and A. V. Grosse, *ibid.*, **74**, 1974 (1952).

[2] M. Hauptschein and A. V. Grosse, *ibid.*, **73**, 5139 (1951); also M. Hauptschein, unpublished results.

[3] T. J. Brice in J. H. Simons, "Fluorine Chemistry," Vol. I, Academic Press, Inc., New York, N. Y., 1950, p. 453. Also, J. H. Simons and W. H. Pearlson, 112th Meeting American Chemical Society, September, 1947.

[4] Minnesota Mining and Manufacturing Co. Brochure on Heptafluorobutyric Acid.

THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY
PHILADELPHIA, PENNSYLVANIA

Molecular Order in *n*-Heptane and *n*-Perfluoroheptane

BY J. H. HILDEBRAND AND G. J. ROTARIU

RECEIVED APRIL 7, 1952

Molecules of *n*-perfluoroheptane are undoubtedly far less flexible than those of *n*-heptane by reason of the size of the fluorine atoms, hence they can be expected to pack in a somewhat more orderly, parallel array in the liquid state, especially at lower temperatures. The liquids should differ like dry and cooked spaghetti. We sought evidence for this in a difference between their entropies of vaporization like the differences previously found between liquids with differing order due to molecular geometry.[1] According to the "Hildebrand Rule" liquids composed of highly symmetrical molecules all have the same entropy of vaporization per mole, Δs^v, when compared at temperatures where they have the same gas volume, v^g, but any degree of order in the liquid, whether the result of molecular association or simply of geometrical shape, leads to a higher entropy of vaporization as this order is destroyed.

We have reliable vapor pressure equations for *n*-heptane[2] and for *n*-perfluoroheptane.[3] Instead of obtaining their entropies of vaporization graphically from the slope of log p *vs.* log T plots, as heretofore, we differentiated the vapor pressure equations to obtain $\Delta s^v = R(\mathrm{d}\ln p/\mathrm{d}\ln T)$. Selecting 25° as the temperature of comparison for the heptane, we calculated 15° as the temperature at which the perfluoroheptane would vaporize to the same volume, 403 liters, assuming ideal gases, which introduces no significant discrepancy. Table I gives the resulting figures for Δs^v, and shows an excess of 1.6 entropy units for the perfluoroheptane. This seems reasonable when compared with the

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[1] J. H. Hildebrand, *J. Chem. Phys.*, **7**, 233 (1939).

[2] "Selected Values of Hydrocarbons," Circular of the National Bureau of Standards, C 461, 1947, p. 123.

[3] G. D. Oliver and J. W. Grisard, This Journal, **73**, 1688 (1951).

excess of 1.2 e.u. for *n*-hexane over diisopropyl at 49.5 liters.[1]

TABLE I

ENTROPY OF VAPORIZATION

	v_g = 403 lit.	t, °C.	v^g/v^l = 2703	t, °C.
C_7H_{16}	29.5	25	29.5	25
C_7F_{16}	31.1	15	32.4	7
Diff.	1.6		2.9	

Pitzer[4] has shown that in the case of molecules having radial intermolecular potentials of the same form, such as the rare gases, the entropies of vaporization are equal not at equal vapor volumes, v^g, but at equal ratios of vapor to liquid volume, v^g/v^l, but Hildebrand and Gilman[5] showed that in the case of polyatomic molecules with different liquid volumes the agreement is considerably better at equal v^g. The molal volume of perfluoroheptane is so much larger than that of heptane that a much lower temperature must be taken to make the comparison at equal v^g/v^l, 7° if the heptane is at 25°. Table I gives the comparison under these conditions. The difference in this case, 2.9 e.u., is, in our opinion, greater than is reasonable to expect from difference in order alone, and it furnishes another instance of the inferiority of the corresponding states rule as a basis for comparing polyatomic molecular species with potential fields so far from radial.

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[4] K. S. Pitzer, *J. Chem. Phys.*, **7**, 583 (1939).

[5] J. H. Hildebrand and T. S. Gilman, *ibid.*, **15**, 229 (1947).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIFORNIA

Correction Concerning Some Reported Derivatives of D-Talitol

BY C. S. HUDSON, M. L. WOLFROM AND T. Y. SHEN

RECEIVED APRIL 10, 1952

Barker and Bourne[1] have recently shown that data of the literature justify a belief that a dimethylene acetal which Hann, Haskins and Hudson[2] reported as 2,4:3,5-dimethylene-D-talitol is in reality the 2,4:3,5-dimethylene-allitol that Wolfrom, Lew and Goepp[3] prepared from authentic allitol. Upon receipt of this information from Messrs. Barker and Bourne by early letter, for which we express our appreciation, we examined the original samples from the two researches[2,3] by mixed melting point measurements and by X-ray diffraction diagrams. In like manner the respective original samples of two derivatives,[2,3] namely, the 1,6-diacetate and the 1,6-ditosylate, were also compared. In all cases the results show unequivocally that the reported "D-talitol" acetal is 2,4:3,5-dimethylene-allitol. In one of the researches[2] three additional derivatives of the acetal were reported as belonging in the D-talitol series; since the acetal is now known to be of the allitol series the names of these derivatives are be changed to 1,6-dibenzoyl-2,4:3,5-dimethylene-allitol (m.p. 188–189°), 1,6-didesoxy-2,4:3,5-dimethylene-allitol (m.p. 165–166°) and 1,6-didesoxy-1,6-diiodo-2,4:3,5-dimethylene-allitol (m.p. 219–220°). All the substances have *meso* configurations and are to be regarded as devoid of optical rotation; the very small specific rotations that were reported[2] are near the limits of observation. The recorded melting points[2,3] are essentially correct.

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[1] S. A. Barker and E. J. Bourne, *J. Chem. Soc.*, 905 (1952).

[2] R. M. Hann, W. T. Haskins and C. S. Hudson, THIS JOURNAL, **69**, 624 (1947).

[3] M. L. Wolfrom, B. W. Lew and R. M. Goepp, Jr., *ibid.*, **68**, 1443 (1946).

3016 TILDEN ST., N. W., WASHINGTON, D. C. (C. S. H.)
THE OHIO STATE UNIVERSITY, COLUMBUS, OHIO
(M. L. W. AND T. Y. S.)

The Heat of Combustion and Resonance Energy of Tropolone

BY WARD N. HUBBARD, CHARLES KATZ, GEORGE B. GUTHRIE, JR., AND GUY WADDINGTON

RECEIVED APRIL 5, 1952

In 1945, Dewar predicted[1] that tropolone (2,4,6-cycloheptatriene-1-one-7-ol) would exhibit aromaticity and later made a theoretical estimate of its resonance energy.[2] Following its synthesis,[3] Dr. W. von E. Doering of the Hickrill Chemical Research Foundation suggested that an estimate of its resonance energy from heat of combustion data would be valuable and offered four grams of tropolone to this Laboratory. Consequently, and because of current interest in other related seven-membered cyclic compounds (*e.g.*, ref. 3b), heat of combustion measurements for tropolone[4] were included in the Bureau of Mines calorimetric program.

Material.—The sample had been prepared and purified according to ref. 3a and was then recrystallized from cyclohexane and sublimed three times. The method of purification and the carbon dioxide determinations (see table) suggest that the material (m.p. 51°) was of high purity. The material was non-hygroscopic and when compressed into briquets was not significantly volatile at room temperature.

The Apparatus and Its Calibration.—The apparatus (with the exception of the bomb) and combustion technique have been previously described.[5] The bomb used in this investigation was sealed with a pure gold gasket and had an internal volume of 0.374 l. The energy equivalent of the calorimeter was determined by combustion of benzoic acid (National Bureau of Standards Standard Sample 39g) having for its isothermal heat of combustion at 25° a value of $-\Delta U_B/M$ of 26.4338 abs. kj. g.$^{-1}$. Since the conditions in these experiments were not quite those of the standard bomb process, the N.B.S. value was corrected to 26.4306 abs. kj. g.$^{-1}$. Eight combustions of benzoic acid yielded an average value 3190.95 cal. deg.$^{-1}$ for the energy equivalent, S_B, of the system. The average deviation from the mean of these experiments was ±0.006% with a maximum spread of 0.025%.

Auxiliary Quantities.—Weights were corrected to a vacuum basis by use of a density value of 1.34 g. cc.$^{-1}$ for

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[1] M. J. S. Dewar, *Nature*, **155**, 50, 141, 451 (1945).

[2] M. J. S. Dewar, *ibid.*, **166**, 790 (1950).

[3] (a) W. von E. Doering and L. H. Knox, THIS JOURNAL, **72**, 2305 (1950); (b) **73**, 828 (1951); (c) J. W. Cook, A. R. Gibb, R. A. Raphael and A. R. Somerville, *Chemistry and Industry*, 427 (1950); (d) R. D. Haworth and J. D. Hobson, *ibid.*, 441 (1950).

[4] J. W. Cook, A. R. Gibb, R. A. Raphael and A. R. Somerville, *J. Chem. Soc.*, 503 (1951), have recently published a value of the heat of combustion of tropolone having a claimed accuracy of ±0.9 kcal./mole. This datum was obtained for them by G. R. Nicholson of Imperial Chemical Industries Limited. Because of the higher order of accuracy of the present work and because of the current great interest in tropolone, it has seemed desirable to record both the original and derived data of the combustion experiments performed in this Laboratory.

[5] W. N. Hubbard, J. W. Knowlton and H. M. Huffman, THIS JOURNAL, **70**, 3259 (1948).

tropolone estimated from the dimensions and mass of the briquets. The specific heat of tropolone, used in calculating the heat capacity of the bomb contents, was estimated to be 0.29 cal. deg.$^{-1}$. The heats of formation of water and carbon dioxide at 25° were taken to be −68,317.4[6] and −94,-051.8[7] cal. mole^{-1}, respectively. The correction for the amount of nitric acid formed during combustion was calculated using −13.82[8] kcal. mole^{-1} for the heat of reaction (1) at 25° in the bomb process. For computing the heat of

$$1/2N_2(g) + 5/4O_2(g) + 1/2H_2O(l) + aq \longrightarrow HNO_3(aq) \quad (1)$$

combustion of gaseous tropolone the heat of sublimation at 25° was taken as 20.0 ± 0.2 kcal./mole.[4]

Experimental Data and Discussion of Results.—The data of the four combustions attempted are given in Table I.

TABLE I

1 cal. = 4.1840 abs. joules; mol. wt. tropolone = 122.118

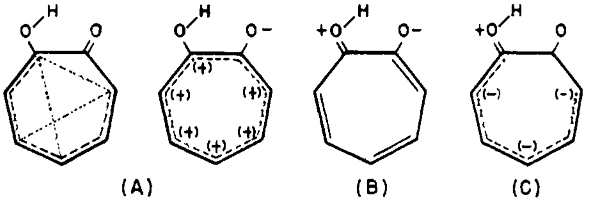
Mass of sample (vac.), g.	q_{fuse}	q_{HNO_3}	Temperature rise, °C.	CO_2 found, % theor.	$-\Delta U_B/M_{(25°)}$, cal. g.$^{-1}$	$\Delta H°_{c\,(25°)}$, kcal. mole^{-1}
0.96941	17.05	0.68	2.01155	99.98$_2$	6608.7	
.96436	16.74	1.08	2.00095	....	6607.8	−806.06
.96461	16.74	1.00	(2.00082)	99.97$_9$	(6605.9)	
.96478	15.49	0.77	2.00144	99.99$_2$	6608.1	−806.10

The columns headed q_{fuse} and q_{HNO_3} give the corrections for the combustion of the fuse and the formation of nitric acid; $-\Delta U_B/M$ is the heat evolved in the bomb process; and ΔH_c° is the heat of combustion of solid tropolone with all the reactants and products in their respective standard states. In each experiment the ignition energy was 1.28 cal.; the Washburn correction was −0.063% ΔU_B; and the heat capacities of the initial and final contents of the bomb, S_I and S_F were 3.10 and 3.34 cal. deg.$^{-1}$, respectively. The bomb gases were tested for carbon monoxide following two of the combustions. In each case the tests showed less than 0.00007% carbon monoxide present. The calorimetry of the third experiment was somewhat uncertain and the result is given no weight. The small value of q_{HNO_3} in the first experiment suggests that possibly some of the nitric acid formed was lost. Therefore $-\Delta U_B/M$ for this combustion may be 0.4 to 0.7 cal. g.$^{-1}$ too high. The average heat of combustion, ΔH_c°, of the remaining two experiments is −806.08 kcal. mole^{-1}. From this, the standard heat of formation, ΔH_f° (25°), of tropolone from graphite, hydrogen and oxygen is calculated to be −57.23 ± 0.2 kcal. mole^{-1} for the solid and −37.23 ± 0.3 kcal. mole^{-1} for the gas.

The resonance energy of tropolone has been calculated and discussed by Cook, *et al.*,[4] and by Koch.[9] These two discussions are weakened by logical inconsistency; namely, the resonance energy of tropolone calculated by Coates and Sutton's[10] bond energies has been compared with resonance energies calculated both from heat of combustion data using Pauling's bond energies and from heat of hydrogenation data. In any discussion of resonance it is desirable that all resonance energies used be calculated on a common basis so that uncertainties in the bond energies and related quantities tend to cancel.

Since most of the resonance energies based on Pauling's bond energies needed for this discussion are readily obtained, and since many chemists are more familiar with these, the resonance energy of tropolone has been recalculated. Using Pauling's table of bond energies,[11] the heat of formation calculated for the reference structure of gaseous tropolone is −1.4 kcal. mole^{-1}. Therefore, tropolone is 36 kcal. mole^{-1} more stable than the reference structure. This is 7 kcal. mole^{-1} greater than the value 29 kcal. mole^{-1}, reported by Cook, *et al.*,[9] and the difference arises from the differences between the two sets of bond energies used in the two calculations.

Koch[10] has estimated from an investigation of the infrared spectrum that a hydrogen bond between the hydroxyl and carbonyl group stabilizes tropolone by 7 kcal. mole^{-1}. This value may be a little high; a more conservative estimate would be 5–7 kcal. mole^{-1}. On the other hand, electron and X-ray diffraction studies[12] indicate that tropolone is planar. Ring strain probably destabilizes tropolone by 4–5 kcal. mole^{-1}. Thus, the resonance energy of tropolone is 33–36 kcal. mole^{-1}.



All the structures with one formal bond (or charge separation) that can be written for tropolone correspond to those which would be written for (a) tropone (cycloheptatrienone), (b) the vinylog of the carboxylic acids and (c) phenol. Since the resonance energy of tropone has not been determined, an estimate of 16–24 kcal./mole[13] will be used. The resonance energy of the carboxylic acids is 24–28 kcal./mole^{-1}. The phenol-like struc-

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(6) D. D. Wagman, J. E. Kilpatrick, W. J. Taylor, K. S. Pitzer and F. D. Rossini, *J. Research Natl. Bureau Standards*, **34**, 143 (1945).

(7) E. J. Prosen, R. S. Jessup and F. D. Rossini, *ibid.*, **33**, 447 (1944).

(8) E. J. Prosen and F. D. Rossini, *ibid.*, **33**, 255 (1944).

(9) H. P. Koch, *J. Chem. Soc.*, 513 (1951).

(10) G. E. Coates and L. E. Sutton, *ibid.*, 1187 (1948).

(11) L. Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p. 54.

(12) J. M. Robertson, *J. Chem. Soc.*, 1222 (1951); K. Hedberg and E. Heilbronner, THIS JOURNAL, **73**, 1386 (1951).

(13) This estimate is reached as follows: Two sets of structures may be written, each corresponding to a linear system of four conjugated double bonds. Pauling has estimated (as quoted in ref. 9) that four conjugated carbon–carbon double bonds have a resonance energy of 17 kcal. mole. Wheland (ref. 15) suggests 18 kcal. mole^{-1}. Since there are two sets of these structures the resonance energy may be 6 kcal. mole^{-1} greater, *i.e.*, total resonance energy 24 kcal. mole^{-1}. *o*-Benzoquinone, which has two hetero-atoms and structures analogous to tropone, has a resonance energy of 16 kcal. mole^{-1}. The resonance energy of tropone probably lies between these two limits.

tures probably do not make a significant contribution.[14]

Application of a crude method of calculating resonance energies suggested by Wheland[15] shows that the resonance energy of tropolone should be less than the sum (40–52 kcal. mole^{-1}) of the resonance energies of these two hybrid structures. This calculation gives 24 kcal. mole^{-1} for the resonance energy of tropone, 24 kcal. mole^{-1} for the carboxylic acid vinylog and 30 kcal. mole^{-1} for tropolone. Although this calculation is not intended for non-hydrocarbons, it shows clearly the effect of superimposing two resonance hybrids. The observed resonance energy (36 kcal. mole^{-1}) is quite reasonable for a hybrid of the tropone and carboxylic acid vinylog structures.

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[14] In phenol these structures account for a 7 kcal. mole^{-1} increase in the resonance energy over that of benzene. These structures (c) are certainly less important than structure (b) since the cycloheptatriene nucleus is a poorer electron acceptor than the carbonyl group or a phenyl group.

[15] G. W. Wheland, "Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, pp. 79 *ff*.

CONTRIBUTION NO. 29 FROM
THERMODYNAMICS LABORATORY
PETROLEUM EXPERIMENT STATION, BUREAU OF MINES
BARTLESVILLE, OKLAHOMA

Reactions of Pivalyl, 2-Thenoyl and 2-Furoyl Chlorides with Cyclopentene[1]

BY L. H. KLEMM[2] AND THEODORE LARGMAN

RECEIVED SEPTEMBER 17, 1951

Treatment of a mixture of pivalyl chloride and cyclopentene in carbon disulfide with anhydrous stannic chloride (as catalyst) and subsequent dehydrohalogenation of the intermediate product by means of refluxing diethylaniline yielded an impure oil which reacted further with 2,4-dinitrophenylhydrazine to give a crystalline compound assigned the structure of 1-pivalylcyclopentene 2,4-dinitrophenylhydrazone. This structure was further substantiated by observation of the ultraviolet absorption spectrum of the oil which exhibited an intense maximum at 239 mμ (*E* 1.55, *c* 150 mg./liter) and a much weaker one at *ca.* 310 mμ (*E* 0.02) characteristics of an α,β-unsaturated ketone with two alkyl substituents variously attached to the available positions on the α- and β-carbons.[3] The oil proved to be inactive as an antibiotic[4] in *in vitro* tests with Gram-negative *E. coli* and Gram-positive *B. mycoides*.

Reaction of 2-thenoyl chloride with cyclopentene according to the procedure used with pivalyl chloride or with substitution of phosphorus pentoxide for the stannic chloride gave small amounts of 2-thenoic acid as the only isolable product, while use of anhydrous aluminum chloride as the catalyst gave excessive condensation to produce a small amount of yellow non-acidic crystalline material for which elemental analyses indicated the empirical formula $C_{13}H_{14}O_2S$. Anhydrous antimony pentachloride, a Lewis acid of strength intermediate between that of aluminum chloride and stannic chloride,[5] however, produced a small yield of an unstable oil which gave a positive isatin test and formed a crystalline derivative (with 2,4-dinitrophenylhydrazine reagent) of composition corresponding to that expected for 1-(2-thenoyl)-cyclopentene 2,4-dinitrophenylhydrazone.

With 2-furoyl chloride and cyclopentene, stannic chloride gave at least termolecular condensation to a colorless crystalline product of empirical formula $C_{14}H_{16}O_3$ which showed a positive pine splinter test for the presence of the furan nucleus.

Experimental[6]

Reaction of Pivalyl Chloride.[7]—A solution of 42 g. (0.161 mole) of anhydrous stannic chloride in 100 ml. of purified[8] carbon disulfide was cooled to −15° and treated with a solution of 11 g. (0.162 mole) of cyclopentene and 21.3 g. (0.177 mole) of pivalyl chloride, added dropwise with stirring. After one additional hour of stirring and four more hours in a refrigerator the viscous mixture (which had changed from light yellow to black during the course of reaction) was poured onto crushed ice and stirred to decompose the complex present. The organic layer was separated, washed with water, dried and evaporated. The resultant residue was refluxed for five hours at 185° with 20 ml. (0.125 mole) of purified[9] diethylaniline. The cooled mixture was diluted with ether, washed successively with excess 5% hydrochloric acid and 5% aqueous sodium hydroxide, dried, evaporated and fractionally-distilled; yield 7.7 g. of faintly yellow liquid, b.p. 63–68° (7 mm.), not obtained analytically pure. Treatment of a portion of this liquid with 2,4-dinitrophenylhydrazine[10] gave **1-pivalylcyclopentene 2,4-dinitrophenylhydrazone**, crystallizing from alcohol in yellow-orange needles, m.p. 144°.

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.83; H, 6.07; N, 16.85. Found: C, 57.81; H, 6.02; N, 16.87.

The ultraviolet absorption spectrum of another portion of the yellow liquid was determined by means of a Beckman quartz spectrophotometer, model DU, using matched silica cells of 1-cm. path length and absolute methanol as a solvent. The oil obeyed Beer's law in the range 15–1500 mg./liter tested.

A third portion was used for tests on antibacterial activity by means of the agar diffusion method.[11] Solutions of 1–100 mg. of the oil in 0.3 ml. of methanol showed no apparent inhibition of growth for either *Escherichia coli* or *Bacillus mycoides*.

Reaction of 2-Thenoyl Chloride.—A mixture of 6 g. (0.088 mole) of cyclopentene, 13.5 g. (0.092 mole) of 2-thenoyl chloride, and 100 ml. of purified[8] carbon disulfide was cooled to 0° in a flask fitted with a calcium chloride drying tube and was treated slowly, with stirring, with 26.6 g. (0.089 mole) of anhydrous antimony pentachloride. The brown solution was stirred 30 minutes longer and then poured into a mixture of crushed ice and concentrated hy-

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[1] From the Ph.D. thesis of Theodore Largman.

[2] Dept. of Chemistry, University of Oregon, Eugene, Oregon.

[3] R. B. Woodward, THIS JOURNAL, **63**, 1123 (1941). Compare data for 1-acetylcyclopentene, I. Heilbron, *et al.*, *J. Chem. Soc.*, 1827 (1949).

[4] For data and theories on the antibacterial action of α,β-unsaturated ketones see W. B. Geiger and J. E. Conn, THIS JOURNAL, **67**, 112 (1945); H. Rinderknecht, *et al.*, *Biochem. J.*, **41**, 463 (1947).

[5] O. C. Dermer, *et al.*, THIS JOURNAL, **63**, 2881 (1941). See also K. Bodendorf and H. Böhme, *Ann.*, **516**, 1 (1935); N. O. Calloway, *Chem. Revs.*, **17**, 327 (1935).

[6] Microanalyses were performed by B. Jarvis and A. Rosen. Melting points were determined by means of an Eimer and Amend melting point block and are uncorrected.

[7] Preparative procedure adapted from that of R. Robinson and co-workers, *J. Chem. Soc.*, 1285 (1935); 763 (1936), for 1-acetylcyclopentene.

[8] L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Boston, Mass., 1941, p. 365.

[9] A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1948, p. 550.

[10] Procedure of R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1940, p. 143.

[11] S. A. Waksman, "Microbial Antagonisms and Antibiotic Substances," 2nd Ed., The Commonwealth Fund, New York, N. Y., 1947 p. 75.

drochloric acid. The organic layer was separated, washed, dried and evaporated. Dehydrohalogenation and further purification were conducted as mentioned before, yield 3 g. of orange viscous liquid which rapidly darkened on standing and gave a positive isatin test (blue-green like that given by thiophene but not blue-black like that for 2-acetylthiophene), b.p. 128–130° (5 mm.). Treatment with 2,4-dinitrophenylhydrazine reagent[12] produced **1-(2-thenoyl)-cyclopentene 2,4-dinitrophenylhydrazone**, crystallizing in blood-red clusters from alcohol, m.p. 148–149°.

Anal. Calcd. for $C_{16}H_{14}N_4O_4S$: N, 15.63; S, 8.94. Found: N, 15.61; S, 9.27.

Repetition of the foregoing procedure except using anhydrous aluminum chloride instead of antimony pentachloride gave a small quantity of yellow platelets on crystallization from alcohol, m.p. 121–122°. The product was insoluble in 10% aqueous sodium hydroxide, showed no halogen present by both the Beilstein and sodium fusion tests, gave a negative isatin test, and depressed the melting point of an authentic sample of 2-thenoic acid upon admixture therewith.

Anal. Calcd. for $C_{13}H_{14}O_2S$: C, 66.63; H, 6.02; S, 13.67. Found: C, 66.46, 66.70; H, 5.96, 5.86; S, 12.96.

Reaction with 2-Furoyl Chloride.—A mixture of 10 g. (0.147 mole) of cyclopentene, 20 g. (0.153 mole) of 2-furoyl chloride and 90 ml. of purified[8] carbon disulfide was cooled to 2° and treated with 40 g. (0.154 mole) of anhydrous stannic chloride added dropwise over a 20-minute period during which time the color changed from orange to dark blue. After refrigeration overnight, the mixture was hydrolyzed and the intermediate product was collected as before and dehydrohalogenated by means of diethylaniline (23 g.). Fractional distillation of the resultant mixture gave an orange-red liquid, b.p. 120–200° (4–8 mm.), which solidified on cooling. Treatment of an absolute ethanolic solution of the solid with charcoal and crystallization from this solvent produced 3 g. of colorless rhombs, m.p. 124–125°. The crystals showed a positive pine splinter test (emerald green) and negative tests for halogen by both the Beilstein and sodium fusion methods.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.50, 72.58; H, 6.43, 6.76.

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[12] Procedure of G. D. Johnson, This Journal, **73**, 5888 (1951).

DEPARTMENT OF CHEMISTRY
INDIANA UNIVERSITY
BLOOMINGTON, INDIANA

Preparation of Radioactive Iodotriphenylethylene[1]

BY D. C. MORRISON

RECEIVED APRIL 14, 1952

It was desired to prepare the iodine analog of the biologically active bromotriphenylethylene, containing radioiodine as tracer, for work on synthetic estrogens. This radioactive iodotriphenylethylene was used for uptake studies in human and animal tumors. The iodotriphenylethylene was prepared by a modification of the method of Koelsch.[2] The method was adapted to a smaller scale with some variations and radioiodine(I^{131}) was employed. An attempt to obtain the compound by iodination of triphenylethylene using iodine chloride in glacial acetic acid failed.

Experimental

Experimental work was done behind lead and Lucite shields in a hood.

Preparation of Radioiodine. (This method was suggested by Dr. Earl Hoerger).—The sodium iodide carrier (0.3 g.) was dissolved in water in a separatory funnel and the desired amount of I^{131} (as sodium iodide, Oak Ridge isotope) activity added. An equal volume of benzene was added and then 0.4 g. of sodium nitrite in concentrated aqueous solution. The mixture was treated dropwise with shaking with 6 *N* nitric acid until an excess was present. The contents were agitated vigorously behind a lead shield. If the aqueous phase (after separation of layers) was still colored by an additional drop of acid, more of the latter was added until the aqueous layer remained colorless. After standing 20 minutes, the layers were separated carefully and the organic layer washed once by extraction with water. The benzene solution of radioiodine could then be added to the Grignard reagent, with or without previous drying over sodium sulfate.

The radioiodine was also generated in some runs by the reaction of active iodide with potassium iodate and dilute sulfuric acid, but the above method was preferable. Any excess of either iodide or iodate seemed to cause retention of activity in the aqueous layer. This was probably caused, in the case of excess iodate, by an exchange reaction.

Preparation of Iodotriphenylethylene.—One gram of magnesium was treated in a nitrogen atmosphere with 0.3 ml. of ethyl bromide in 25 ml. of ether. After the reaction was well under way, 1 g. of bromotriphenylethylene (m.p. 114°) was added in a few portions during 10–15 minutes. No iodine was used as a primer as Koelsch recommends.[2] This mixture was refluxed for 2.5 hours. After cooling, the gray solution (yellow if air has been admitted) was treated with the I^{131} solution. Solid inactive iodine was then added until its color was permanent. It was thought best to use an insufficient amount of carrier iodine for the reaction, and then to destroy the remaining Grignard reagent with inactive iodine in order to utilize as much activity as possible. The mixture was now hydrolyzed by a mixture of ice and 1 *N* hydrochloric acid.

The ether-benzene layer was washed with bisulfite solution and with water and was then evaporated. The residue in ether–petroleum ether solution was decolorized with Nuchar and the solvents removed. The crystalline residue was extracted with four small portions of cold petroleum ether by grinding under this solvent. This removes a small amount of oil. The iodo compound could be used as such or recrystallized from boiling petroleum ether or from alcohol. One recrystallization from the former gave a product with m.p. 125.5–127°. Koelsch gives 126–127°. A specific activity of 23 μc./mg.was obtained. In a similar experiment using inactive iodine, 2 g. of bromotriphenylethylene gave 1.573 g. of iodo compound or 68.8%.

Acknowledgment.—The author expresses gratitude to Drs. K. G. Scott, J. G. Hamilton, W. M. Garrison and E. Hoerger for advice received during this work.

CROCKER LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

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[1] The work described in this paper was sponsored by the Atomic Energy Commission. It was supported in part by a grant from the Henry, Laura and Irene B. Dernham Fund of the American Cancer Society and the Christine Breon Fund.

[2] C. F. Koelsch, This Journal, **54**, 2045 (1932).

Polarography of 8-Quinolinol-5-sulfonic Acid

BY J. P. PHILLIPS AND QUINTUS FERNANDO

RECEIVED MARCH 18, 1952

An interpretation of the polarograms of 8-quinolinol is made difficult in acid solutions by catalytic waves that obscure the reduction waves, and in neutral solutions pronounced maxima distort the curves.[1] Since the sulfonic acid group apparently does not reduce at the dropping mercury cathode,[2] and the reduction of quinoline sulfonic acids by chemical means appears little different from the unsubstituted quinolines,[3] the polarographic behavior of 8-quinolinol-5-sulfonic acid should be very similar to that of 8-quinolinol.

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[1] J. T. Stock, *J. Chem. Soc.*, 586 (1949).

[2] S. Wawzonek, *Anal. Chem.*, **21**, 64 (1949).

[3] K. V. Bokil, *J. Indian Chem. Soc.*, **13**, 404 (1936).

It was found, however, that 8-quinolinol-5-sulfonic acid gave a catalytic wave in acid solutions at more negative potentials than did 8-quinolinol, so that at least one of the reduction waves prior to the catalytic wave could be analyzed (Fig. 1). Logarithmic analysis of this reduction wave indicated a one-electron process. Additional waves were masked by the catalytic wave.

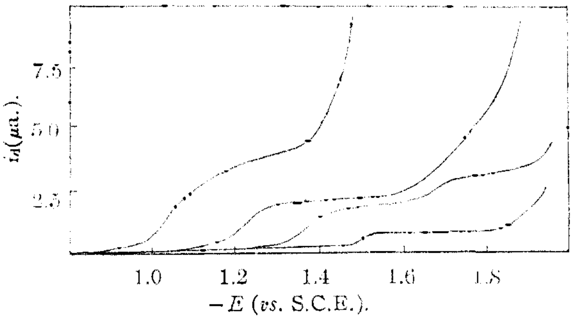


Fig. 1.—Polarograms of 8-quinolinol-5-sulfonic acid; from left to right: *p*H 3.75, 6.50, 8.90, 11.10; concentration 4.73×10^{-4} *M*.

In approximately neutral solutions 8-quinolinol-5-sulfonic acid was remarkably free from maxima, in contrast to 8-quinolinol.[1] The reduction wave found in acid solutions decreased in height with increasing *p*H. At a *p*H of 9 a well-defined double wave is obtained without indication of any following catalytic wave.

In alkaline solutions (*p*H 10–11.5) a single wave decreasing in height with increasing *p*H was obtained; the half-wave potential followed the equation $E_{1/2} = -0.77 - 0.059\ p\text{H}$. Evidently the reaction is a one-electron reduction similar to 8-quinolinol.

In stronger alkali (*p*H 12) 8-quinolinol-5-sulfonic acid was not reducible. The double negative charge on the ion in such solutions may prevent the acquisition of further electrons.

The behavior of 8-hydroxyquinaldine-5-sulfonic acid was also investigated; in most respects it resembled 8-quinolinol-5-sulfonic acid fairly closely. The half-wave potential in alkaline solutions obeyed the equation $E_{1/2} = -0.97 - 0.050\ p\text{H}$.

In view of the smoother waves obtained from these sulfonic acid derivatives in acid and neutral solutions they would seem to be better suited for analytical use than 8-quinolinol which has a usable reduction wave only in alkaline solution.

Experimental

A Sargent Model XXI Polarograph and an H-type cell kept at 25 ± 0.01° were employed for all determinations. Measurements were made against a saturated calomel electrode. The characteristics of the dropping mercury electrode, determined in 0.1 *N* potassium chloride on open circuit, were: $m = 2.30$ mg./sec., $t = 4.00$ sec.

Polarograms were run on each compound at six or more *p*H values between 2 and 12 and at concentrations ranging from 0.0001 to 0.001 *M*. Britton and Robinson buffers (consisting of acetic, phosphoric and boric acids with sodium hydroxide) were used after polarographic examination for reducible impurities. Oxygen was removed from the solutions with nitrogen. An instrument sensitivity of 0.100 was usually suitable.

Acknowledgments.—This work was supported in part by a grant from the Research Corporation. We are grateful to the Joseph E. Seagram's Distilleries for the use of their polarograph.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF LOUISVILLE
LOUISVILLE, KENTUCKY

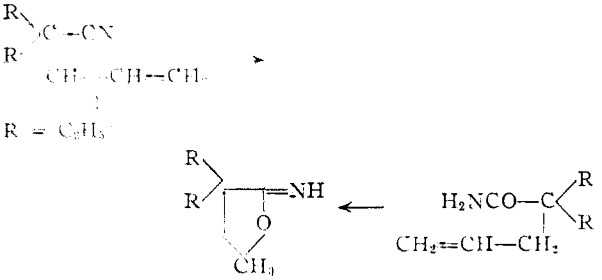
The Cyclization of Disubstituted Pentenoic Acid Derivatives

BY ROBERT F. RAFFAUF[1]

RECEIVED FEBRUARY 23, 1952

The conversion of substituted pentenoic acids to lactones, and of α-benzylpentenoic acid to a tetrahydronaphthalene derivative by means of sulfuric acid had been studied by Darzens some years ago.[2] More recent expression of interest in the cyclization of these acids[3] prompts us to record a similar series of observations with reference to the facile cyclization of 2,2-diethyl-4-pentenenitrile (I) which was carried out in these laboratories independently.

When I was dissolved in cold (0–5°) concentrated sulfuric acid and the solution was allowed to come to room temperature gradually (3–5 hr.) there was obtained, after dilution with water and neutralization with sodium hydroxide an 80% yield of a basic substance which, according to the observations of Schultz[4] and Easton,[5] we formulated as 2-imino-3,3-diethyl-5-methyltetrahydrofuran (II). The compound was surprisingly stable; it distilled with no evidence of decomposition as a colorless liquid (b.p. 80–82° (10 mm.)). *Anal.* Calcd. for $C_9H_{17}NO$: N, 9.02. Found: N, 8.80, 8.90.[6] It formed a crystalline benzenesulfonyl derivative, colorless needles from ethanol, m.p. 113–115°. *Anal.* Calcd. for $C_{15}H_{21}NO_3S$: N, 4.74; S, 10.85. Found: N, 4.68, 4.67; S, 10.80, 10.82. Hydrolysis in dilute mineral acid, or in alcoholic alkali followed by acidification, yielded a neutral, nitrogen-free product (b.p. 108–112° (19 mm.)) whose properties agreed with those expected for a lactone. *Anal.* Calcd. for $C_9H_{16}O_2$: C, 69.2; H, 10.3. Found: C, 68.8, 68.4; H, 10.2, 10.3. The same product was obtained from 2,2-diethyl-4-pentenoic amide (III); however, the solution of this compound in sulfuric acid was not strongly exothermic and could be conducted without external cooling. Craig's proposed mechanism[3] offers, in this case, a plausible description of the course of the reaction. In the case of the nitrile, however, this course is not as obvious; clearly an atom of oxygen must be introduced into the molecule to account for the product. Whether this is accomplished by initial and rapid hydrolytic attack of the CN-group followed by cyclization, or by preliminary addition of sulfuric acid to the allylic double bond followed by cyclic



II III

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[1] Research Associate, National Cancer Institute; present address: Smith, Kline and French Laboratories, Philadelphia 1, Pa.

[2] G. Darzens, *Compt. rend.*, **183**, 748, 1110 (1926).

[3] P. N. Craig, THIS JOURNAL, **74**, 129 (1952).

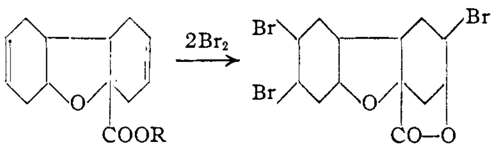
[4] E. M. Schultz, C. M. Robb and J. M. Sprague, *ibid.*, **69**, 2454 (1947).

[5] N. R. Easton, J. H. Gardner and J. R. Stevens, *ibid.*, **69**, 2941 (1947).

[6] Microanalyses by Mr. S. Alpert.

imino-ether formation involving the resulting hydroxy nitrile ester has not been demonstrated. We observed, however, that the saturated compound, 2,2-diethylvaleronitrile (obtained by hydrogenation of 2,2-diethyl-4-pentenenitrile over Pd:CaCO$_3$, b.p. 84–86° (20 mm.)), when subjected to the same experimental conditions was recovered largely unchanged; only a small amount of the amide[7] (crystallized from petroleum ether, m.p. 68–69.5°) was formed.

Craig[3] demonstrated that similar cyclizations of α-disubstituted allylacetic acids or esters could be carried out by the use of bromine. We became aware of this possibility during a study of the reactions of 2,3,4,5-bis-(Δ^2-butenylene)-tetrahydrofuroic acid (IV)[8] (octahydrodibenzofuran-4a-carboxylic acid). When either the acid or its methyl ester was treated with an excess of bromine in chloroform at 0°, there was obtained a neutral, colorless crystalline product (needles from acetic acid, m.p. and mixed m.p. 228–230° dec.) which contained but three atoms of bromine. *Anal.* Calcd. for $C_{13}H_{15}O_3Br_3$: Br, 52.2. Found: Br, 51.8, 52.2. This we believed to be the tribromolactone (V).



IV V

R = H, CH$_3$–

More detailed study of the mechanism of the transformations involving allylic systems of this type may be expected to contribute to the knowledge of the structure of the compounds related to IV and V. It has been pointed out that such a study has been undertaken in another laboratory.[9]

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[7] C. L. Carter and S. N. Slater, *J. Chem. Soc.*, 130 (1946).

[8] This structure was proposed by J. C. Hillyer, *et al.*, *Ind. Eng. Chem.*, **40**, 2216 (1948). An extensive series of compounds may be derived from the aldehyde formed by condensation of furfural with butadiene. We do not regard this structure as unequivocally established.

[9] See Craig, ref. 3, footnote 6.

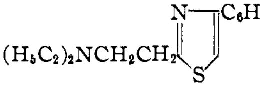
RESEARCH LABORATORIES
THE NATIONAL DRUG COMPANY
PHILADELPHIA 44, PA.

β,β'-Di-(2-thiazolyl)-diethyl Sulfides

BY EDGAR A. STECK AND LYNN T. FLETCHER

RECEIVED APRIL 29, 1952

A recent publication of Dahlbom[1] prompts us to record observations of similar nature in attempts to prepare 2-(β-diethylaminoethyl)-4-phenylthiazole (I). It was found that the action of hydrogen sulfide on β-diethylaminopropionitrile had not produced the expected thioamide (II), but, rather, another substance, since (I) did not result from the reaction of the intermediate with phenacyl bromide. The intermediate, which we did not obtain in crystalline form, was indicated to be β,β'-thiodi-(propionthioamide) (III) through analyses of the compounds (IV) and (V) formed by reaction with phenacyl bromide and chloroacetone. Only the β,β'-di-(4-substituted-2-thiazolyl)-diethyl sulfide type could be isolated, and no further study was done. Dahlbom[1] has given the problem more detailed consideration.



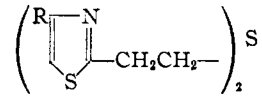
I

$(H_5C_2)_2NCH_2CH_2CSNH_2$

II

$S(CH_2CH_2CSNH_2)_2$

III



IV, R = C_6H_5
V, R = CH_3

Experimental

β,β'-Thiodi-(propionthioamide) (III).—A mixture of 139.0 g. (4.1 moles) of hydrogen sulfide, 180.9 g. (1.43 moles) of β-diethylaminopropionitrile and 700 cc. of absolute ethanol was shaken at 60° for 10 hours. The viscous, brownish residue which remained after removal of the low-boiling material weighed 150.0 g. (50.5% yield). Attempts to induce the thioamide to crystallize were unsuccessful.

β,β'-Di-(4-phenyl-2-thiazolyl)-diethyl Sulfide (IV).—A solution of 17.5 g. (0.08 mole) of crude (III) in 175 cc. of absolute ethanol was treated with 20.0 g. (0.1 mole) of phenacyl bromide and refluxed three hours. The cooled mixture gave a greenish-white solid (21.3 g., m.p. 192–193°) when a large volume of ether was added. The crude dihydrobromide was converted to the base (IV) with aqueous ammonia. After three crystallizations from hexane, 8.7 g. (43%) of pure (IV) resulted; m.p. 68.2–69.2° cor. (lit.[1] m.p. 68–69°).

Anal. Calcd. for $C_{22}H_{20}N_2S_3$: N, 6.86; S, 23.54; mol. wt., 408.6. Found:[2] N, 6.98; S, 23.48, 23.62; mol. wt., 420.

β,β'-Di-(4-methyl-2-thiazolyl)-diethyl Sulfide (V).—The reaction of 0.08 mole of crude (III) with 0.1 mole of chloroacetone in ethanol was run as indicated above. A crude yield of 11.0 g. of dihydrochloride of (V), m.p. 195–197°, resulted; two crystallizations from ethanol–hexane gave 7.4 g. (42%) of fine white needles, m.p. 215–216°. The base (V) was an oil.

Anal. Calcd. for $C_{12}H_{16}N_2S_3 \cdot 2HCl$: N, 7.84; S, 26.91; Cl$^-$, 19.84. Found:[2] N, 8.05; S, 26.97; Cl$^-$, 19.91.

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[1] R. Dahlbom, *Acta Chem. Scand.*, **5**, 690 (1951).

[2] Analyses by Mr. M. E. Auerbach and staff of the Analytical Laboratories of this Institute.

STERLING–WINTHROP RESEARCH INSTITUTE
RENSSELAER, NEW YORK

Polarographic Behavior of 12-Ketosapogenins

BY CONSTANTINE RICCIUTI, C. O. WILLITS, M. E. WALL AND M. M. KRIDER

RECEIVED DECEMBER 19, 1951

Steroidal compounds containing α,β-unsaturated keto groups are polarographically reducible. Eisenbrand and Picher[1] and Sartori and Bianchi[2] found that steroids such as testosterone, progesterone, pregnenol-17-one-3 and desoxycorticosterone, are reducible at the dropping electrode in aqueous ethanol solutions and give waves which are proportional to concentration. The polarographic method was applicable only to the Δ^4-unsaturated-3-ketosteroids, for their saturated analogs did not give polarographic waves. Wolfe, Hershberg and Fieser[3,4] investigated Δ^1-cholestenone and found that it was reducible. All of these reducible compounds contain an α,β-unsaturated keto group. They also extended the polarographic method to include 17-ketosteroids and 20-ketosteroids by reaction of these steroids with Girard Reagent T to form polarographically reducible Girard derivatives.

There have been no previous reports on the polarographic behavior of 12-ketosapogenins which

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[1] J. Eisenbrand and H. Picher, *Z. physiol. Chem.*, **260**, 83 (1939).

[2] G. Sartori and E. Bianchi, *Gazz. chim. ital.*, **74**, 8 (1944).

[3] J. K. Wolfe, E. B. Hershberg and L. F. Fieser, *J. Biol. Chem.*, **136**, 653 (1940).

[4] J. K. Wolfe, E. B. Hershberg and L. F. Fieser, *ibid.*, **140**, 215 (1941).

TABLE 1

IDENTIFICATION CHARACTERISTICS OF SAPOGENINS USED IN THIS STUDY

Sapogenin	Melting point, °C.[a] Genin	Melting point, °C.[a] Acetate	Specific rotation[b] Genin	Specific rotation[b] Acetate	Infrared absorption
Tigogenin	207–209	205–206	−70	−74	Carbonyl absent
Hecogenin	260–261	245–246	+ 7	− 5	Carbonyl max. at 1706 cm.$^{-1}$
Kammogenin	241–243	253–254	−54	−80	Carbonyl max. at 1714 cm.$^{-1}$
Manogenin	244–246	248–250	− 2	−42	Carbonyl max. at 1709 cm.$^{-1}$
9,11-Dehydromanogenin[c]	232–233	258–260	− 7.8	..	Carbonyl max. at 1676 cm.$^{-1}$ C=C max. at 1602 cm.$^{-1}$

[a] All melting point determinations made with the Kofler block. [b] Rotations determined at 25°, sodium lamp, concentrations between 8–10 mg./ml. [c] 95% pure, as estimated from ultraviolet and infrared absorption, with approximately 5% of a non-conjugated carbonyl sapogenin.

are important as precursors in steroid syntheses. The present method for the determination of polarographic behavior of these compounds allows the use of a non-aqueous medium consisting of a lithium chloride methanol–benzene electrolytic solution in which the 12-ketosapogenins are soluble.

Experimental

A Sargent Model XXI Polarograph was used to obtain the current–voltage curves. The capillary had t and m values of 1.35 seconds and 3.587 mg. per sec., respectively, which gave a capillary constant of 2.46 mg.$^{2/3}$sec.$^{-1/2}$. The m and t values were obtained in an open circuit, with the polarographic cell maintained at 25.0°, and with the capillary dipping into the non-aqueous electrolytic solution. The capillary constant at −1.80 volts under the above conditions was 2.38. This value has been used to calculate the diffusion current constant of the 9,11-dehydromanogenin.

The electrolytic cell was a modified Lingane H-cell[5] with a saturated calomel reference electrode. This cell had an open circuit resistance of 1175 ohms, and all half-wave potentials were corrected for IR drop. Half-wave potential readings were made against the saturated calomel electrode, and the polarograms were obtained at 25 ± 0.1°. The sapogenins were isolated and characterized by methods developed at this Laboratory.[6] Descriptive data for these compounds are presented in Table I. Thirty milliliters of the electrolytic solution, consisting of 0.3 M lithium chloride in a 50–50 (by volume) mixture of absolute methanol–benzene, was measured into the sample arm of the H-cell. The solution was degassed with high-purity nitrogen, and a polarogram was recorded. The sample was then added (10–40 mg.), and the solution was again degassed with nitrogen. A polarogram was recorded, and from the increase in wave height, the diffusion current of the reducible sapogenin was calculated.

TABLE II

POLAROGRAPHIC CHARACTERISTICS OF 9,11-DEHYDROMANOGENIN

Wt. sample per 40 ml.	Mole per liter	i_d, µa.	i_d/C	$i_d/Cm^{2/3}t^{1/6}$
0.0121	0.000885	4.76	5516	2.32
.0258	.001887	10.10	5489	2.31
.0390	.003019	15.70	5643	2.37

Results and Discussion

Tigogenin, which has no keto group, shows no polarographic reduction. Hecogenin and manogenin, both having a 12-keto group but no unsaturated linkage, show no reduction. Kammogenin, which has a 12-keto group and a Δ^5-unsaturated linkage, also does not reduce. However, 9,11-dehydromanogenin, which has both a 12-keto group and a conjugated unsaturated linkage, reduces at the dropping electrode with a half-wave potential of −1.72 volts $vs.$ S.C.E. and has a diffusion current constant of 2.33. This diffusion current constant is similar to that found for other conjugated ketones in the non-aqueous electrolyte. Mesityl oxide, for example, has a diffusion current constant of 2.07. The reducibility of the 12-keto group of 9,11-dehydromanogenin in the non-aqueous electrolyte was expected because of the conjugated carbonyl group in this compound. Table II shows that the wave height of the 9,11-dehydromanogenin is directly proportional to concentration in the range studied (10 to 40 mg./30 ml.). The use of the lithium chloride non-aqueous electrolyte made possible the direct polarographic analysis of these water-insoluble steroidal compounds.

Acknowledgment.—The authors acknowledge the assistance of C. R. Eddy in obtaining the infrared data for the sapogenins.

EASTERN REGIONAL RESEARCH LABORATORY[7]
PHILADELPHIA 18, PENNSYLVANIA

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(5) C. O. Willits, C. Ricciuti, H. B. Knight and D. Swern, *Anal. Chem.*, in press.

(6) M. E. Wall, *et al.*, *J. Biol. Chem.*, in press.

(7) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

The Heat of Neutralization of Hydrogen–Bentonite

BY W. H. SLABAUGH

RECEIVED APRIL 5, 1952

Many clays undergo stoichiometric reactions with various types of reagents. Reactions which involve the base-exchange character of clays have been widely investigated and are adequately reviewed elsewhere.[1] In previous work[2] there was good indication that the exchangeable hydrogen which was present in electrodialyzed bentonite systems was of two principal types, namely, hydrogen ions in the adsorbed layer of the colloidal micelles and hydrogen ions at the base-exchange sites. Further, these ions showed primary and secondary characteristics comparable to a typical diprotic acid. The present work which consists of a thermodynamic study of the neutralization of these hydrogen ions gives good indication that there is a fundamental difference between these types of hydrogen ions and that, during storage, there is a definite tendency for the absorbed ions to become more intimately associated with the clay micelles.

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(1) E. A. Hauser, *Chem. Revs.*, **37**, 307 (1945); C. E. Marshall, "The Colloid Chemistry of the Silicate Minerals," Academic Press, Inc., New York, N. Y., 1949.

(2) W. H. Slabaugh and J. L. Culbertson, *J. Phys. Colloid Chem.*, **55**, 744 (1951).

Experimental Methods

A 2% suspension of a typical Wyoming bentonite obtained from the Baroid Division of the National Lead Company was permitted to stand for three months. After this time, the supernatant suspension was decanted and electrodialyzed in a Mattson cell from which the so-called hydrogen–bentonite was obtained. Another procedure for the preparation of the acid clay made use of a 30-inch column of Amberlite 120 ion-exchange resin which had previously been converted to its acid form by leaching the column with 10% H_2SO_4.[3] After the column was washed with distilled water until the effluent was neutral, the supernatant clay suspension was passed through the column.

The base-exchange values of this bentonite as determined by titration of these two differently prepared hydrogen-bentonites were 75 milliequivalents per 100 g. of bentonite for the electrodialyzed clay and 106 milliequivalents per 100 g. of bentonite for the columned clay. By the Graham and Sullivan method[4] of $NH_4C_2H_3O_2$ adsorption on the original clay, the base-exchange capacity was 86 milliequivalents per 100 g. of bentonite.

The calorimeter (Fig. 1) which was constructed for this study was contained in a 1-liter dewar flask. A 57-junction copper–constantan thermocouple constructed after the suggestions of White,[5] showed a sensitivity of 2.20 millivolts per degree at 23.5°. In actual operation, the potential produced by the thermocouple was measured by observing the deflection of the galvanometer of the potentiometer. The galvanometer, a Leeds and Northrup Type R, showed a deflection at 1 meter of 4100 mm. for each degree. Over the length of the scale (500 mm.) the relationship between temperature and galvanometer deflection was observed to be exactly linear. Both the potentiometer and heater coil of the calorimeter were operated from heavy duty storage batteries, the potentials of which were essentially constant, during a particular determination. The heater which served to calibrate the calorimeter during each run was a coil of 30 gage constantan wire and had a resistance of 31.65 ohms at 23.5°. The outside end of the thermocouple was immersed in water which was contained in a second dewar flask. The whole assembly was immersed in a 30-liter water-bath which was insulated with 10 cm. of glass wool. The water-bath was controlled to ±0.001° and the whole apparatus was located in a room whose temperature was controlled at 24.5 ± 0.1°.

The over-all reliability and accuracy of the calibrations of this instrument are shown by the results of a study wherein 0.00165 mole of hydrochloric acid in 220 ml. of water reacted with an equivalent amount of sodium hydroxide (10.00 ml. of 0.165 N NaOH). The alkali was added in 1.00-ml. portions and the amount of heat evolved was observed for each of these portions. The actual quantity of heat released in each of these steps was approximately 2.45 calories. The quantity was converted to the corresponding molar heat of neutralization. The mean value for the heat of neutralization of HCl by NaOH based upon these ten determinations was 13,550 ± 195 calories. The probable error was determined by the expression $p = 0.6745\sqrt{\frac{\Sigma\delta^2}{n(n-1)}}$ where p is the probable error of the mean, δ is the deviation of each observation from the mean, and n is the number of observations. In view of the small amount of acid and base involved in these measurements, and the classical values of Richards and Rowe[6] at comparable concentrations (13,640 calories per mole), the accuracy of this method appears adequate.

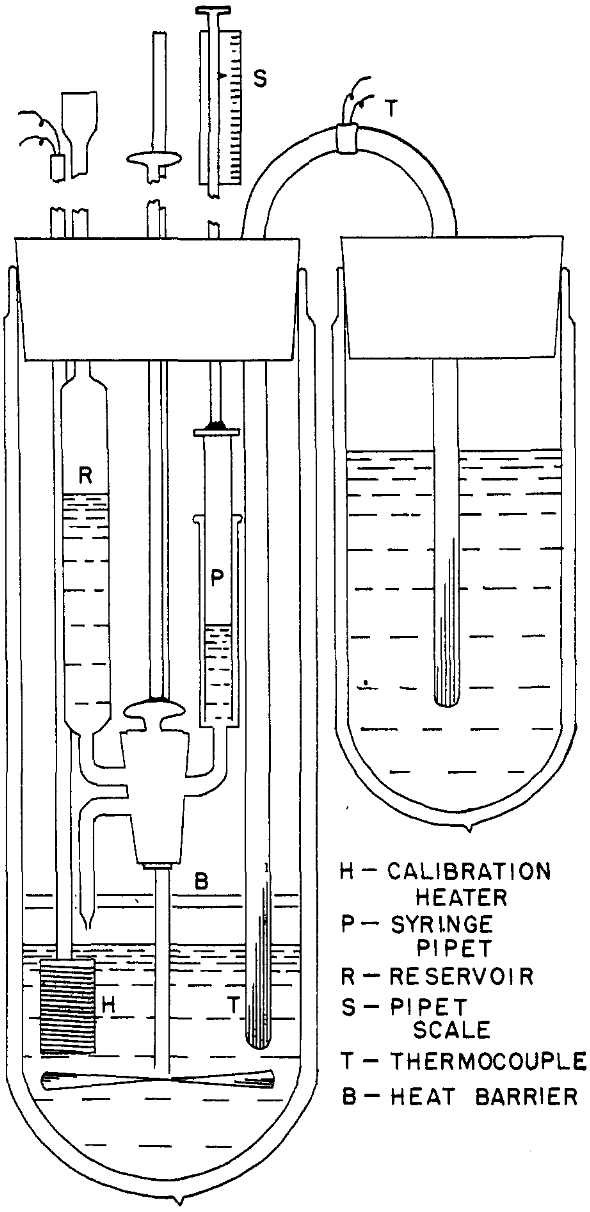

Fig. 1.—The calorimeter for the determination of the stepwise neutralization of hydrogen–bentonite.

In making a determination, 220 ml. of a clay suspension was placed in the calorimeter dewar flask and its temperature was adjusted to 23.50 ±0.01°. The reservoir was filled with 0.165 N NaOH at the same temperature, and the calorimeter was assembled and immersed in the water-bath. Both the clay suspension and the bath were adequately agitated with paddle type stirrers. In order to make certain that thermal equilibrium had been attained the calorimeter remained thus for 8 hours before the actual observations were started. Temperature readings as shown by the galvanometer were observed at half-minute intervals in order to establish the slope of the time–temperature curve. One ml. of NaOH was then added by means of the syringe pipet and temperatures were noted until the slope of the time–temperature curve became constant; this usually required about 5 minutes. One-ml. portions of NaOH were repeatedly added until a 50% excess of alkali had been added. Then, three separate calibrations of the heat capacity of the calorimeter were made by passing 0.19 ampere through the heater coil for 10.0 seconds. On occasion, calibrations of the heat capacity were made prior to or during the observations of the neutralization reactions and, in any one run, the calibrations were essentially identical to those obtained at the end of the run. The method used for the calculation of the heat of neutralization from these data is similar to that of Harkins and Dahlstrom.[7] Operation of the syringe and stopcock in the calorimeter produced no detectable quantity of heat.

All data presented in this paper are the results of duplicate or triplicate runs. The results of the measurements of the heats of neutralization of hydrogen–bentonite are summar-

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[3] Loren C. Hurd and Wm. L. Van Horne, U. S. Patent, 2,431,481.

[4] Robert P. Graham and J. D. Sullivan, *J. Am. Ceram. Soc.*, **21**, 176 (1939).

[5] W. P. White, THIS JOURNAL, **36**, 1856, 2292 and 2313 (1914).

[6] T. W. Richards and A. W. Rowe, *ibid.*, **44**, 684 (1922).

[7] W. D. Harkins and R. Dahlstrom, *Ind. Eng. Chem.*, **22**, 897 (1930).

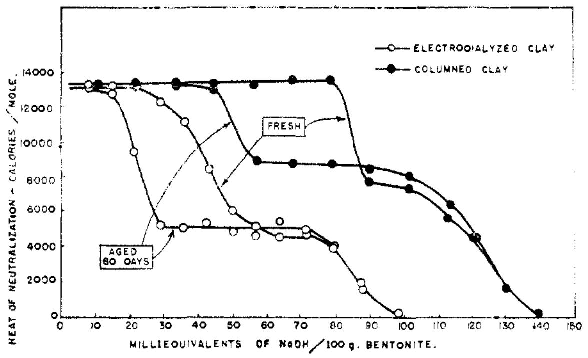


Fig. 2.—Heat of neutralization of electrodialyzed bentonite and bentonite exchanged with hydrogen in an Amberlite IR 120 column.

ized in Fig. 2. The ΔH values were calculated on the basis of molar quantities of alkali added in each step of the neutralization process. For example, when 1 ml. of 0.165 N NaOH (0.0165 millimole) is added to an acid system a certain quantity of heat is evolved. This amount of heat multiplied by $(0.0000165)^{-1}$ gives the amount of heat which would be evolved by the reaction of a mole of NaOH with a given portion of the hydrogen ions in the clay system. The ΔH values do not represent the total heat of neutralization but, rather, the quantity of heat evolved in each successive step in the neutralization process. In plotting these data, the quantity of alkali is expressed in terms of the number of milliequivalents of NaOH per 100 g. of oven-dried bentonite. By determining the total area under the ΔH curves it is possible to express the mean heat of neutralization. The electrodialyzed clay gave values of 8,000 calories per mole for the freshly prepared samples, and 6,700 calories per mole for the aged samples. The columned clay gave values of 10,400 calories and 9,400 calories per mole for the fresh and aged samples, respectively.

In Fig. 3 are the potentiometric titration data for the same system. A glass electrode and a sleeve type calomel cell were used in these titrations.

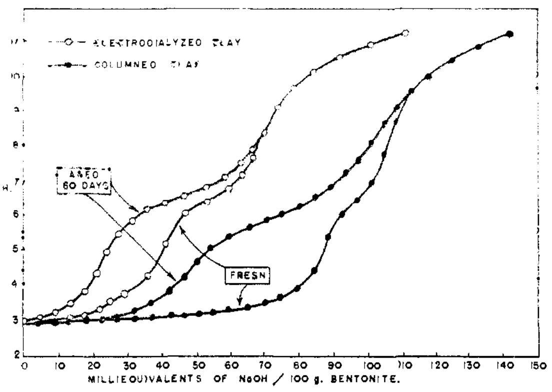


Fig. 3.—Potentiometric titration of electrodialyzed bentonite and bentonite exchanged with hydrogen in an Amberlite IR 120 column.

Discussion

The experimental data obtained in this work show further indication of the existence of two types of available hydrogen in the hydrogen–bentonite system. In the acid-clay from the electrodialysis and column procedures, the early portions of alkali react with hydrogen ions which are completely ionized. During the latter part of the neutralization process, the hydrogen ions show a much different character. The lower heat of reaction shows that these secondary hydrogen ions are less highly ionized, possible less available geometrically, and that considerable energy is required for the hydration of these ions. These two types of hydrogen ions correspond to the plateaus in the ΔH curves.

Considerable heat is evolved by the addition of NaOH beyond the stoichiometric end-point which follows the second plateau in the ΔH curves. This is attributed to the greater degree of covalency of the hydrogen ions which are neutralized only at an alkalinity above pH 9.0. It is doubtful if this heat is associated with the physical adsorption of NaOH which is described by Kayser and co-workers.[8] Apparently, up to 75 milliequivalents of NaOH beyond the stoichiometric end-point can be physically adsorbed. Since this is probably a van der Waals adsorption, the heat of adsorption would likely be too small to detect by the present method.

A significant contrast between the electrodialyzed and columned bentonite is shown by the end-point in the titration curves. For the electrodialyzed clay, the primary end-points require one-half and one-third as much of base as is required for total neutralization of fresh and aged samples, respectively. In the case of the columned clay, the primary end-points require 80 and 50% as much base as is required for the total neutralization of fresh and aged samples, respectively.

Although the total amount of titratable hydrogen ion remains essentially the same, aging produces pronounced effects upon the ratio of primary to secondary hydrogen ions in the clay systems. The curves in Figs. 2 and 3 represent the maximum change in this respect which the hydrogen–clay underwent in 60 days. These data suggest that in the aging process the highly reactive hydrogen ions, which are probably concentrated to a considerable extent in the adsorbed ion layer of the colloidal micelles, migrate into the micelle and occupy positions which are geometrically closer to the negatively charged points on the clay lamina, the base-exchange sites. These ionic migrations provide experimental evidence for Pauling's electrostatic valence principle which was applied to clays by Hendricks.[9] The principle states that ionic systems are statistically neutral on the smallest possible scale. In freshly prepared hydrogen–bentonite, the hydrogen ions have not reached their most stable positions. Due to the small ionic radius of the hydrated proton it is conceivable that if enough base-exchange sites are available, most of the hydrogen ions in the hydrogen–clay system would eventually migrate into the laminar structure of these layer silicates, whereupon they would attain their maximum covalency.

(8) F. Kayser, J. M. Bloch and G. Gommery, *Bull. soc. chim. France*, 462 (1951).

(9) S. B. Hendricks, *Ind. Eng. Chem.*, **37**, 625 (1945).

DEPARTMENT OF CHEMISTRY
KANSAS STATE COLLEGE
MANHATTAN, KANSAS

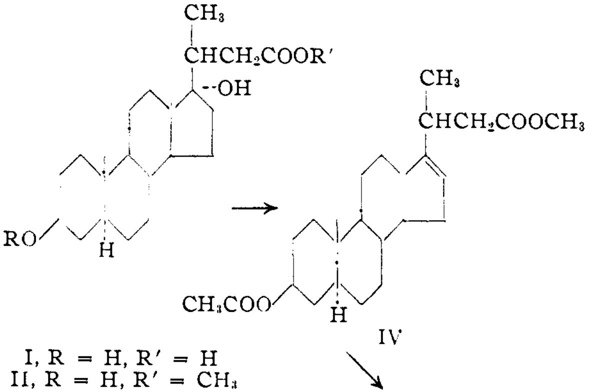
3β,17α-Dihydroxynorcholanic Acid Lactone

BY AUGUST I. RYER AND WILLIAM H. GEBERT

RECEIVED MARCH 17, 1952

Recently we reported the isolation of a new by-product of the oxidation of sitosterol acetate dibromide, 3β-acetoxy-17α-hydroxynor-5-cholenic acid lactone.[1] We now describe the reduction of the 3-hydroxy derivative to give a mixture of the corresponding norcholanic and allonorcholanic lactones and the conversion of the latter to the known 3β-hydroxyallonorcholanic acid.[2] As in our previous work,[1] the allonorcholanic lactone was opened with alkali to give the hydroxy acid (I). The 3-acetate methyl ester (III) was dehydrated with thionyl chloride to the Δ^{16}-norcholenate (IV) and reduction of the latter gave the allonorcholanate (V).

The Δ^{16}-norcholenate (IV) had an absorption band at 12.20 microns in the infrared (Nujol mull)[3] which is typical of the structure $R_2C{=}CHR$. Neither III nor V had absorption in this region.



I, R = H, R′ = H
II, R = H, R′ = CH_3
III, R = CH_3CO, R′ = CH

V. Methyl-3β-acetoxy-allonorcholanate

Experimental[4]

3β,17α-Dihydroxyallonorcholanic Acid Lactone.—A suspension of 12 g. of 3β,17α-dihydroxynor-5-cholenic acid lactone [m.p. 282–283°; $[\alpha]^{22}D$ −94.4° (2% in $CHCl_3$)][1] was hydrogenated at atmospheric pressure and room temperature using 1.2 g. of platinum oxide catalyst. The reduction was stopped when 1055 ml. of hydrogen had been consumed (35 minutes). Since the product was completely in solution at the end of the hydrogenation, the catalyst was removed by filtration and the volume of the filtrate reduced to 100 ml. The solution was poured into water and the resulting precipitate filtered, washed neutral with water and dried to give 12.0 g. of a mixture of the isomeric saturated lactones, m.p. 220–263°. The crude product from several hydrogenations (44.0 g.) was recrystallized twice from acetone to give 23.0 g. of 3β,17α-dihydroxyallonorcholanic acid lactone (needles) melting at 284.0–285.4°; $[\alpha]^{20}D$ −16.4° (2% in $CHCl_3$). (Surprisingly, a mixture with a sample of the unhydrogenated hydroxy lactone showed no depression in the melting point.) The acetone filtrates were held for the isolation of the other saturated lactone below.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.20; H, 10.25.

3β-Acetoxy-17α-hydroxyallonorcholanic Acid Lactone.—The allolactone (above) (4.0 g.) was acetylated by refluxing two hours with 40 ml. of acetic anhydride. The crude product (4.38 g.) melting at 239.0–241.5° was recrystallized from methanol and acetone to give 3.08 g. of 3β-acetoxy-17α-hydroxyallonorcholanic acid lactone (long needles), m.p. 240.6–242.6; $[\alpha]^{22}D$ −21.1° (2% in $CHCl_3$).

Anal. Calcd. for $C_{25}H_{38}O_4$: C, 74.59; H, 9.52. Found: C, 75.00; H, 9.80.

3β,17α-Dihydroxynorcholanic Acid Lactone.—The acetone mother liquor from the crystallization of the crude hydrogenation mixture, after removal of the bulk of the hydroxy allolactone, was concentrated to dryness. An 8.0-g. portion of this material was dissolved in hot benzene, concentrated to a low volume and while hot, an equal volume of naphtha (b.p. 90–120°) was added. After cooling to 25°, the crystals were filtered and washed with a mixture of equal parts of benzene and naphtha to give 5.5 g.; m.p. 211–220°. This material was dissolved in hot acetone, concentrated to a heavy slurry of crystals, cooled and filtered to give an additional yield of 1.4 g. hydroxyallolactone, m.p. 279–282°. The mother liquor upon concentrating to dryness (3.7 g.) melted at 213.5–224.0°. A solution of this residue in 200 ml. of benzene was chromatographed using 20 g. of 60–100 mesh Florisil.[5] The column was eluted with benzene and the eluate collected in 300-ml. fractions which were each concentrated to dryness. The first two fractions contained only a slight trace of oil, and the next seventeen fractions contained only a new lactone, melting sharply at 234.5–235.5°. Further elution of the column gave a mixture of the two isomers. The sharp melting fractions were combined (1.53 g.), dissolved in hot acetone and concentrated to a low volume. The acetone was completely replaced with ethyl ether by distillation, concentrated to a heavy slurry of crystals, cooled to 5° and filtered to give 1.2 g. of 3β,17α-dihydroxynorcholanic acid lactone (needles), m.p. 234.6–236.4°; $[\alpha]^{20}D$ −15.2° (2% in $CHCl_3$).

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.69; H, 10.30.

3β,17α-Dihydroxyallonorcholanic Acid (I).—A solution of 18.2 g. of 3β,17α-dihydroxyallonorcholanic acid lactone in 1300 ml. of 5% ethanolic potassium hydroxide was refluxed for two hours and the mixture poured into 5 l. of water. Dilute hydrochloric acid was added to the solution of the potassium salt until it was just faintly acid to litmus and the precipitated free acid filtered, washed neutral and air-dried. The crude acid (19.0 g.) was dissolved in hot methanol, treated with activated carbon, and concentrated to a low volume. The methanol was replaced with ethyl ether by distillation and the ether solution concentrated to a heavy slurry of crystals. After cooling to 5°, the crystals were filtered to give 13.8 g. of I, $[\alpha]^{22}D$ −1.58 (2% in methanol). When the melting point capillary was inserted at 260°, the acid immediately melted and bubbled up the tube, solidified and finally remelted at the melting point of the hydroxy allolactone (282.0–284.0°).

Anal. Calcd. for $C_{23}H_{38}O_4$: C, 72.97; H, 10.12. Found: C, 72.80; H, 10.50.

Methyl 3β,17α-Dihydroxyallonorcholanate (II).—The silver salt of the hydroxy acid (I) was prepared by a modification of the method of Allen and Wilson.[6] To a solution of 15.0 g. of the acid (I) and 2.81 g. of 87% potassium hydroxide in 200 ml. of methanol and 200 ml. of water was added a solution of 7.4 g. of silver nitrate in 50 ml. of water with agitation and the suspension of silver salt stirred for 10 minutes. Methyl iodide (57 g.) was added, and after stirring for 15 minutes the mixture was filtered. The filter cake was extracted with hot methanol and the extracts added to the original filtrate. The combined liquids were concentrated to a small volume, poured into water and filtered to give 14.5 g. of crude ester (II). The crude ester (3.0 g.) was recrystallized from methanol to give 2.0 g. of fine needles, $[\alpha]^{22}D$ −0.4° (2% in methanol). When the sample was inserted in the melting point bath at 125°, it melted at 150–153° with bubbling, resolidified at approximately 170° and finally remelted at 282–284°. When heated, the methyl ester apparently lost the elements of methanol to regenerate the lactone.

Anal. Calcd. for $C_{24}H_{40}O_4$: C, 73.43; H, 10.33. Found: C, 73.40; H, 10.70.

Methyl 3β-Acetoxy-17α-hydroxyallonorcholanate (III).—A solution of 13.5 g. of the methyl ester (II) in 67 ml. of dry pyridine and 13.5 ml. of acetic anhydride was warmed at 60° for one hour, allowed to stand overnight and then poured into water. The precipitate was filtered, washed thoroughly with water and dried. The crude product was recrystallized from methanol to give 10.7 g. of (III), m.p. 196.0–198.4°; $[\alpha]^{21}D$ −10.25° (2% in $CHCl_3$). When the

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(1) A. I. Ryer and W. H. Gebert, THIS JOURNAL, **74**, 41 (1952).

(2) P. A. Plattner and J. Pataki, *Helv. Chim. Acta*, **26**, 1241 (1943).

(3) R. B. Barnes, R. C. Gore, R. W. Stafford and V. Z. Williams, *Anal. Chem.*, **20**, 402 (1948).

(4) All melting points are corrected. Microanalysis and microrotations by Edwin Conner and staff of these laboratories.

(5) Obtained from the Floridin Company, Warren, Pennsylvania.

(6) C. F. H. Allen and C. V. Wilson, *Org. Syntheses*, **26**, 52 (1946).

melting point sample, after melting, was heated to 250° and cooled, the resolidified material remelted at 236–238° [lactone acetate].

Anal. Calcd. for $C_{26}H_{42}O_5$: C, 71.85; H, 9.74. Found: C, 72.08; H, 9.95.

Methyl 3β-Acetoxyallonor-16-cholenate (IV).—A solution of 11.3 g. of the acetoxy ester (III) in 114 ml. of dry pyridine was cooled in an ice–salt-bath and 11.4 ml. of redistilled thionyl chloride added. The mixture was allowed to stand for two hours in an ice–salt-bath and for one hour at room temperature, then poured into ice-water and stirred for one hour. The crystals were filtered and washed neutral with water to give 10.9 g., m.p. 94–170°. The crude product was dissolved in hot methanol, the solution concentrated to 55 ml., cooled and filtered to give 8.0 g., m.p. 103–180°. These crystals were dissolved in 300 ml. of ethyl ether, the volume reduced to 100 ml., cooled and the crystals filtered to give 1.6 g. of needles, m.p. 236–238°. A second crop of needles (0.25 g.) with the same melting point was obtained from the mother liquor at a volume of 35 ml. A mixture of these needles with a sample of the acetoxy lactone showed no depression in the melting point. It is apparent that relactonization occurs during the dehydration reaction. The mother liquor after removal of the lactone acetate was concentrated to dryness and the residue recrystallized several times from methanol and ethanol to give 3.1 g. of IV (fine needles) melting at 120.6–123.4°; $[\alpha]^{21}D$ +2.0° (2% in $CHCl_3$).

Anal. Calcd. for $C_{26}H_{40}O_4$: C, 74.96; H, 9.68. Found: C, 74.70; H, 9.83.

Methyl 3β-Acetoxyallonorcholanate (V).—A solution of 2.0 g. of the unsaturated acetoxy ester (IV) dissolved in 300 ml. of absolute alcohol was hydrogenated at 760 mm. and 25° using 0.6 g. of 10% palladium-on-charcoal. The reduction was stopped when 109 ml. of hydrogen had been consumed (22 minutes). Fine needle-like crystals were formed during the reduction. The mixture of catalyst and crystals was removed by filtration and the filter cake washed thoroughly with chloroform to remove the sterol. The filtrate was concentrated to a small volume, the chloroform replaced completely with ethanol by distillation and the volume reduced to 40 ml. After cooling to 5°, the crystals were filtered to give 1.70 g. of V (needles), m.p. 157.5–159.0°. After recrystallization from acetone and methanol the analytical sample melted at 159.4–160.8°; $[\alpha]^{25}D$ +11.0° (2% in $CHCl_3$). This product corresponds in its properties to the methyl 3β-acetoxyallonorcholanate described by Wieland and Miescher[7] and by Plattner and Pataki.[2]

Anal. Calcd. for $C_{26}H_{42}O_4$: C, 74.60; H, 10.11. Found: C, 74.50; H, 9.95.

3β-Hydroxyallonorcholanic Acid.—The acetoxy ester (V) was saponified by refluxing with 2% methanolic potassium hydroxide. After recrystallization from ethyl acetate and acetone, the product melted at 226.0–226.8°; $[\alpha]^{24}D$ +22.8° (1% in ethanol). These constants agree with those reported by Plattner and Pataki.[2]

Acknowledgment.—We wish to thank Dr. W. B. Tarpley and Miss C. Vitiello of our Chemical Research Division for the infrared data herein reported.

[7] P. Wieland and K. Miescher, *Helv. Chim. Acta*, **30**, 1876 (1947).

CHEMICAL DEVELOPMENT DEPARTMENT
SCHERING CORPORATION
BLOOMFIELD, NEW JERSEY

β-Glycerol Ethers Isomeric with Mephenesin

BY W. A. WEST AND B. J. LUDWIG

RECEIVED APRIL 14, 1952

In a search for drugs that exhibit muscle-paralyzing activity more intense and with a longer duration of action than mephenesin (3-*o*-toloxy-1,2-propanediol), numerous compounds have been synthesized wherein variations were made in the nature and distribution of substituents in the aromatic nucleus, and modifications were made in the hydroxylated side chain.[1] Among the previously reported compounds are three isomers of mephenesin, 3-*m*-toloxy-1,2-propanediol, 3-*p*-toloxy-1,2-propanediol and 3-benzyloxy-1,2-propanediol, all of which have the formula $C_7H_7OCH_2CHOHCH_2OH$, but no reference has been made to the preparation of the corresponding β-glycerol ethers. This paper describes the preparation and physical constants of the four isomeric β-glycerol ethers having the formula $C_7H_7OCH(CH_2OH)_2$. These compounds are of interest not only because of their structural relationship to mephenesin but also because of their similarity to the anticonvulsant drug 2,2-diethyl-1,3-propanediol (DEP). The results of pharmacological studies carried out with these compounds will be reported elsewhere.

Synthesis of the 2-toloxy-1,3-propanediols was accomplished through the lithium aluminum hydride reduction of the corresponding toloxymalonic esters following the procedure described by Chaikin for the reduction of ethyl phenoxymalonate.[2] Since ethyl benzyloxymalonate could not be readily prepared by direct condensation of ethyl chloromalonate and sodium benzylate, 2-benzyloxy-1,3-propanediol was synthesized by the condensation of benzyl chloride and the sodium salt of 5-hydroxy-2-phenyl-*m*-dioxane followed by hydrolysis of the cyclic acetal.

The melting point of each of the 2-toloxy-1,3-propanediols is lower than that of the corresponding 3-toloxy-1,2-propanediol. However, the 2-benzyloxy derivative was isolated as a solid whereas the 3-benzyloxy compound has been reported to be a liquid.[3] The β-glycerol ethers reported here have water solubilities comparable to those of the corresponding α-glycerol ethers, with the exception of 2-*m*-toloxy-1,3-propanediol, which possesses an abnormally high water solubility.

Experimental[4]

Ethyl Toloxymalonates.—The three isomeric ethyl toloxymalonates were prepared by condensation of ethyl chloromalonate with the appropriate sodium cresolate in absolute ethanol following the procedure described for ethyl *m*-toloxymalonate by Niederl and Roth.[5]

2-Toloxy-1,3-propanediols.—The diols were obtained by reduction of the corresponding toloxymalonic esters with lithium aluminum hydride[2] followed by acid hydrolysis of the aluminate. The *o*-toloxy compound was purified by fractionation under diminished pressure, the meta- and para-isomers by crystallization from benzene–ligroin solution.

5-Benzyloxy-2-phenyl-*m*-dioxane (VII).—To a well-stirred suspension of 4.3 g. (0.11 mole) of sodium amide in 200 ml. of anhydrous toluene, there was added portionwise 18.0 g. (0.1 mole) of 1,3-benzylidene glycerol[6] and the mixture was refluxed until the evolution of ammonia had ceased. A solution of 16.0 g. (0.12 mole) of benzyl chloride in 50 ml. of anhydrous toluene was added over a period of 15 minutes and refluxing continued for six hours. The mixture was cooled, washed with two 50-ml. portions of water, dried over sodium sulfate and concentrated *in vacuo*.

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[1] For a listing of the pertinent references in this field, see: B. J. Ludwig, W. A. West and W. E. Currie, THIS JOURNAL, **74**, 1935 (1952).

[2] S. W. Chaikin, *ibid.*, **70**, 3522 (1948).

[3] J. C. Sowden and H. O. Fischer, *ibid.*, **63**, 3244 (1941).

[4] All temperatures reported are uncorrected. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Middle Village, Long Island, New York.

[5] J. B. Niederl and R. T. Roth, THIS JOURNAL, **62**, 1154 (1940).

[6] H. Hibbert and N. M. Carter, *ibid.*, **51**, 1608 (1929).

TABLE I

Compd. no.	Compounds	Yield, %[a]	B.p., °C.	B.p., Mm.	n^{25}D	M.p., °C.[b]	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
I	2-*o*-Toloxy-1,3-propanediol	60	150–153	2.0	1.5391	....	$C_{10}H_{14}O_3$	65.95	66.16	7.69	7.81
II	2-*m*-Toloxy-1,3-propanediol	92	.....	..	....	66–67	$C_{10}H_{14}O_3$	65.95	66.22	7.69	7.81
III	2-*p*-Toloxy-1,3-propanediol	68	.....	..	....	68–69	$C_{10}H_{14}O_3$	65.95	65.98	7.69	7.59
IV	2-Benzyloxy-1,3-propanediol	87	185–187	10.0	....	38.5–40	$C_{10}H_{14}O_3$	65.95	65.88	7.69	7.59
V	Ethyl *o*-toloxymalonate	69	140–142	2.0	....	49.5–50	$C_{14}H_{18}O_5$	63.15	62.75	6.77	6.77
VI	Ethyl *p*-toloxymalonate	65	110–114	0.1	1.4908	....	$C_{14}H_{18}O_5$	63.15	63.32	6.77	6.81
VII	5-Benzyloxy-2-phenyl-*m*-dioxane	60	.....	..	....	75.5–76.5	$C_{17}H_{18}O_3$	75.55	75.85	6.71	7.01

[a] Yields are based on material of reasonable purity and do not taken into account the recovery of starting materials. [b] M.p. data are for analytically pure samples.

The residual oil, which solidified on standing, was purified by crystallization from benzene–ligroin solution.

2-Benzyloxy-1,3-propanediol (IV).—A solution of 32.5 g. (0.12 mole) of 5-benzyloxy-2-phenyl-*m*-dioxane (VII), 170 ml. of ethanol, 60 ml. of water and 2.0 ml. of concentrated sulfuric acid was refluxed for two hours. Most of the ethanol was removed by distillation, the residue cooled and neutralized with sodium bicarbonate and the benzaldehyde steam distilled from the mixture. The aqueous solution of the diol was saturated with potassium carbonate and extracted with three 50-ml. portions of ether. After drying over magnesium sulfate, the ethereal solution was concentrated and the residual oil distilled under reduced pressure. The distillate solidified on cooling and was further purified by crystallization from benzene.

Table I summarizes the physical constants and analytical data for these compounds.

RESEARCH DIVISION
WALLACE LABORATORIES, INC.
NEW BRUNSWICK, N. J.

The Reduction of 1,2-Isopropylidene-D-glucuronolactone with Lithium Aluminum Hydride[1]

BY SAUL ROSEMAN

RECEIVED JULY 28, 1952

In the synthesis of 6-C^{14}-glucose described recently by Sowden,[2] the final step is the reduction of 6-C^{14}-1,2-isopropylidene-D-glucuronolactone with sodium borohydride followed by acid hydrolysis of the resultant mixture to yield glucose. With the particular lot of ion exchange resin (Duolite A-4) available for our first experiments, some difficulty was experienced in complete removal of the borate ion. A modification of the reduction step was therefore developed, utilizing lithium aluminum hydride. Although this reagent has a disadvantage in that it requires anhydrous conditions for its action, it possesses two advantages: (1) an increased yield of glucose, (2) it is possible to isolate the intermediate 6-C^{14}-1,2-isopropylidene-D-glucose in good yield.

Experimental

1,2-Isopropylidene-D-glucose.—The reaction vessel is a three-necked Grignard reaction flask into which are inserted a condenser and a dropping funnel, both protected with drying tubes. Stirring is performed with a magnetic stirrer, 8 ml. of a 1.6 *M* solution of lithium aluminum hydride (clear[3]) is added through the third opening in the flask followed by 10 ml. of anhydrous ether (stored over sodium) and the flask is stoppered; 1.08 g. of 1,2-isopropylidene-D-glucuronolactone is dissolved in 150 ml. of boiling anhydrous ether, the solution is allowed to cool, and is then added dropwise over a period of 30 minutes to the stirred lithium aluminum hydride solution. About 50 ml. more of ether is used to rinse in the last trace of lactone. The flask is placed in a water-bath at 50–60°, the solution is stirred and refluxed for 25 minutes, and is then cooled. Absolute alcohol is cautiously added at this point until the excess reagent is destroyed and then more rapidly with vigorous stirring until 25 ml. have been added. A clear, colorless solution should result. A solution of concentrated hydrochloric acid in alcohol is then added (4 parts concentrated hydrochloric acid to 10 parts absolute ethanol). The acid is added dropwise with stirring until a sample tested with phenolphthalein in alcohol shows that the mixture is barely acid (requires about 4 ml. of concentrated hydrochloric acid). The mixture should be essentially clear at this point. The solution is quickly cooled and is then poured into an iced mixture of 150 ml. of petroleum ether and 100 ml. of 0.01 *M* hydrochloric acid. The aqueous layer is separated and the ether layer is extracted once more with 100 ml. of 0.01 *M* hydrochloric acid. To deionize the solution, the combined aqueous extracts are passed through alternating layers of IR-120, H and IR-4B. In the isotope experiments where it is not desired to recover the resin, the two resins are mixed intimately before use—this being the most efficient procedure for maintenance of a neutral *p*H. The final resin layer is always the IR-120, H and the total volumes used are about 100 ml. of each resin (somewhat more in the case of the alternating layers). The neutral, colorless solution is concentrated at 50–55° *in vacuo* and yields 1.05 g. of slightly yellowish crystals, m.p. 153–157°. Recrystallization from ethyl acetate yields 0.70 g. of white crystals, melting at 161–162° and $[\alpha]^{24}$D −12.0° (*c* 5.4, water). There was no depression of the melting point when the sample was mixed with an authentic specimen. A second crop was obtained upon the cautious addition of petroleum ether to the ethyl acetate mother liquors, 0.20 g., m.p. 158–160°, $[\alpha]^{24}$D −12.2° (*c* 5.1, water).

D-Glucose.—The procedure described above for the reduction is followed up to, and including, the addition of alcohol to the reaction flask. The clear solution is then poured into a separatory funnel containing 200 ml. of water, 2 ml. of concentrated sulfuric acid, and 150 ml. of petroleum ether. The aqueous extract is removed and the ether layer washed once more with 50 ml. of 0.1 *M* sulfuric acid. The combined aqueous extracts are then heated for 1.5 hours on the steam-bath, and the colorless solution is cooled and treated with an excess of barium carbonate with shaking until the mixture is alkaline. The mixture is centrifuged and the precipitate is washed three times with water and finally with boiling water. Complete deionization is obtained by passing the solution through a 20-ml. layer of IR-120,H then 20 ml. of IR-4B and finally 10 ml. of IR-120,H. The combined eluate and washings are colorless, negative toward the naphthoresorcinol uronic acid test, and contain 0.85 g. of glucose according to a quantitative anthrone and reducing sugar analysis. The solution is concentrated, yielding a colorless sirup which is then treated with 4 ml. of 95% ethanol and seeded. After standing for one week, crystallization is complete, yielding 0.72 g. of anhydrous dextrose, m.p. 146°, $[\alpha]^{24}$D 52.3°, equilibrium in

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[1] This investigation was supported by grants from the National Heart Institute of the National Institutes of Health, U. S. Public Health Service, and the Helen Hay Whitney Foundation.

[2] J. C. Sowden, THIS JOURNAL, **74**, 4377 (1952); preliminary report, 119th Meeting, ACS, Milwaukee, April, 1952. I would like to express my gratitude to Dr. Sowden for his many valuable suggestions.

[3] W. G. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 484.

water. No depression of the melting point was observed on mixing the sample with an authentic specimen.

DEPARTMENTS OF PEDIATRICS AND BIOCHEMISTRY
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

The Molecular Structure of Perfluorobutyne-2. Critical Marks for the Description of Electron Diffraction Curves

BY W. F. SHEEHAN, JR.,[1] AND VERNER SCHOMAKER

RECEIVED MARCH 31, 1952

A complete structure determination, rather highly precise because it is based mainly on microwave spectroscopic data and only partly on electron diffraction, has been achieved for trifluoromethylacetylene.[2] The present electron diffraction study has led to almost identical bond angle and bond distance values for perfluorobutyne-2: see Table I. The sample[3] was generously supplied by Professor Henne and the detailed techniques were those currently used in these laboratories.[4]

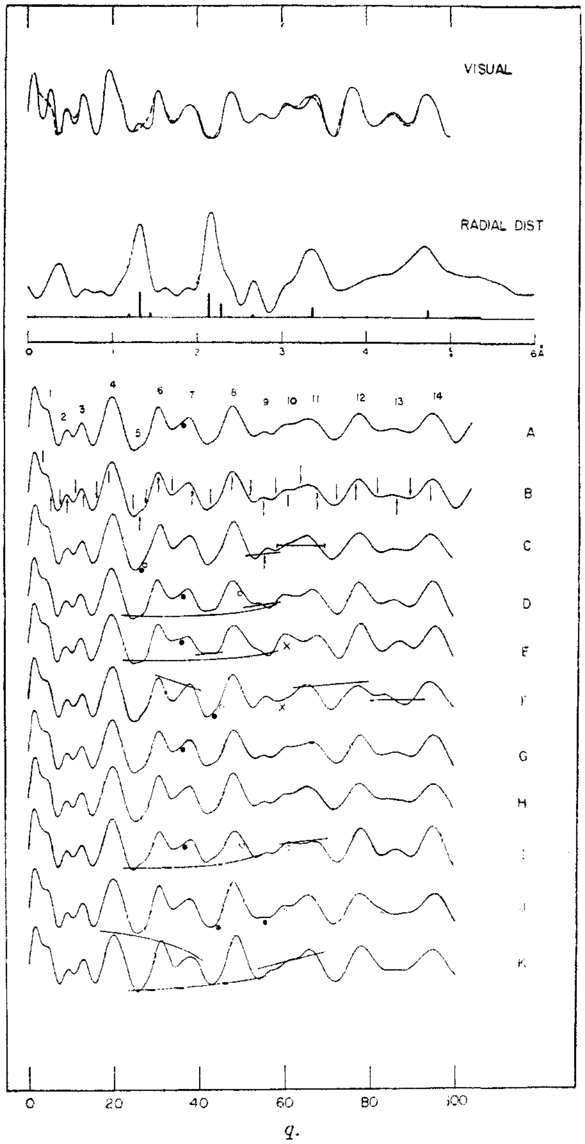

Fig. 1.—Electron diffraction curves for $F_3C—C'\equiv C''—C'''F_3$. Visual: Solid, W.S.; as modified by dashed additions, V.S. Both drawn with the help of differential comparisons with the best theoretical curve and photographs of trifluoromethylacetylene.[1] Radial distribution: Based on *solid* visual curve. Theoretical: Final curves including all interactions, for the following models, illustrating the indicated total range of models studied.

Curve	F—F	C—C′	C′≡C″	$q_{\text{calcd.}}/q_{\text{obsd.}}$[e]
A[a]	2.15	1.46	1.21	1.007
B[a,b]	2.15	1.46	1.21	1.006
C[c]	2.15	1.43	1.20	1.009
D[d]	2.15	1.49	1.20	1.008
E[d]	2.13	1.47	1.20	1.013
F[d]	2.17	1.47	1.20	1.000
G[a]	2.15	1.47	1.20	1.008
H[a]	2.15	1.45	1.23	1.004
I[c]	2.15	1.49	1.14	1.011
J[c]	2.15	1.43	1.29	1.008
K[d]	2.13	1.37	1.26	1.013
Range	2.11-2.17	1.35-1.51	1.14-1.29	(C—F = 1.33)

[a] Satisfactory curve. [b] Account taken of the effective slight shortening of C···C‴ and C···F′ expected to result from C—C≡C bendings. [c] Curve near the limit of acceptability, either within or without. [d] Completely unacceptable curve. [e] For 8 best (reasonably symmetrical and well-located) features; average deviation, Model B, 0.006 (for 22 best features, 0.019). Measurements by W. S.

TABLE I

	$F_3C—C\equiv C—H$[1]		$F_3C—C\equiv C—CF_3$	
	Value	Limit of error	Value	Limit of error
C—F, Å.	1.335	0.01	1.340	0.020[a]
C—C, Å.	1.464	.02	1.465	.055[a,b]
C≡C, Å.	1.201	.002	1.22	.09[a]
C—H, Å.	1.056	.005	.....	.....
∠F—C—F	107.5°	1.0°	107.5°	1.0°

[a] Including 1.0% estimated limit of scale error. [b] If C≡C were assumed to be precisely 1.22 Å., the limit of error for C-C would be reduced to 0.040 Å. but the other limits would be essentially unchanged.

About one hundred seventy-five theoretical intensity curves were calculated in order to cover the rigid-model shape-parameter problem completely and the temperature factor problem, with its considerable and uncertain dependence on possible instrumental effects as well as the low frequencies[2] and large amplitudes of C—C≡C bendings (estimated root-mean-square δ∠C—C≡C, 9.5°), in some detail. All the models were given D_3 symmetry, and when the long F···F terms were finally included for some of the curves, free internal rotation was assumed. The significant points regarding the theoretical curves illustrated in Fig. 1 are indicated by marks in the figure itself rather than by the usual tedious verbal description.

Such *critical marks* can be generally self-explanatory (Table II seems almost unnecessary, except by way of introduction), and they are convenient, terse, highly legible (aiding, not distracting, the eye), and reasonably precise (more so than ordinary verbal description, especially since they aren't affected by limitations of space); their use should

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[1] U. S. Rubber Co. Predoctoral Fellow, 1950-1951. Present address: Shell Development Company, Emeryville, California.

(2) J. N. Shoolery, R. G. Shulman, W. F. Sheehan, Jr., Verner Schomaker and Don M. Yost, *J. Chem. Phys.*, **19**, 1364 (1951).

(3) A. L. Henne and W. G. Finnegan, THIS JOURNAL, **71**, 298 (1949).

(4) See K. Hedberg and A. J. Stosick, *ibid.*, **74**, 954 (1952).

significantly simplify and shorten electron diffraction articles, while improving readability. These marks are also very helpful, we have found, in the course of the work itself.

TABLE II

EXPLANATION OF CRITICAL MARKS OF FIG. 1

Curve	Mark	Meaning
A	Dot	Creation operator: inner slope should be more convex upwards
B	Arrows	Positions (q_{obsd}) of rings as measured on photographs, adjusted by multiplication by $q_{\text{calcd}}/q_{\text{obsd}}$. Best curve
C	Dot circle	Circle is destruction operator: 5 max. too far up to the right
C	Line	Indicates desired levels: 9 min. too deep; 10 min. too shallow
C	Arrow	Duplicated from best curve: 9 max. significantly misplaced relative to adjacent features
C	Terminated line	Indicates desired width: feature too narrow
D	Curved line	Indicates desired levels: 8 min. too shallow *re* 5 min. and 9 min.
E	Line (short)	Feature, bottom of 8 min., too symmetrical; should tip, and lie closer to 8 max. than to 7 max.
E	Cross	Completely unacceptable feature; *cf.* standards (best curve and visual)
F	Lines	7 max. too high *re* 6 max.; 11 max. too high *re* 12 max.; 13 max. should lie between minima of almost equal depth
K	Curved lines	6 max. too high *re* 4 max. and 7 max.; depth of 8 min. about right *re* **5** min. and 9 min.
K	Line	Region should slope upwards more gently

A more complete presentation of the structure determination is available.[5]

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(5) W. F. Sheehan, Jr., Thesis, California Institute of Technology (1952).

CONTRIBUTION No. 1672
GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA

X-Ray Diffraction Patterns of Cuprous Acetate and Cupric Oxyacetate

BY H. SHIMIZU AND S. WELLER

RECEIVED MARCH 27, 1952

In the course of some experiments on catalytic hydrogenation, it became desirable to prepare and to obtain the X-ray diffraction patterns of cuprous acetate, $CuOOCCH_3$, and anhydrous cupric oxyacetate, $Cu_2O(OOCCH_3)_2$. Cuprous acetate was prepared by Calvin's procedure[1]; the method involves solution of cuprous oxide in acetic acid–acetic anhydride, filtration of the hot solution, cooling, and filtration of the separated cuprous acetate, all in the absence of air or moisture. The cuprous acetate was pure white; it contained 50.9% Cu (theor. for $CuOOCCH_3$, 51.8% Cu).

THE *d/n* VALUES AND INTENSITIES OBTAINED FROM DEBYE–SCHERRER X-RAY PHOTOGRAPHS OF THIS MATERIAL

d/n	*I*	*d/n*	*I*	*d/n*	*I*
11.0	vw	2.48	s	1.67	w
10.0	vvs	2.42	s	1.63	vw
5.4	vvw	2.31	s	1.57	w
5.0	vw	2.25	vw	1.55	w
4.05	w	2.15	w	1.50	vw
3.69	vw	2.00	w	1.465	vw
3.50	vw	1.95	w	1.405	vw
3.15	vvs	1.89	vw	1.32	vvw
3.01	vs	1.81	w		
2.62	s	1.72	w		

The unit cell parameters obtained by Hull[2] for a compound listed as "cuprous acetate monohydrate" apply to cupric acetate monohydrate; calculated interplanar spacings, d_{hkl}, from Hull's data agreed within experimental error with the *d/n* values obtained from the diffraction pattern of the cupric salt.

Attempts to prepare cupric oxyacetate by oxidation of a quinoline solution of cuprous acetate failed because of a catalyzed oxidation of the quinoline. It was found possible, however, to prepare the anhydrous oxyacetate by oxidation of dry cuprous acetate; at 100°, the oxygen absorption is stoichiometric. On prolonged heating at higher temperatures (150–200°), the oxyacetate decomposes, with the production of metallic copper. Cupric oxyacetate is dark bluish-green in color. Microscopic examination of the samples prepared showed the crystals to be acicular or prismatic and possibly of equidimensional cross-section. The crystals were too small for interference observations, but the presence of birefringence indicates that the material is not cubic. Bjorstrum charts for tetragonal and hexagonal crystals were prepared for comparison with the observed X-ray diffraction lines obtained from the oxyacetate. As the following table indicates, a possible fit was found in the tetragonal system with $c/a = 1.35$, $c = 16.26$ Å., $a = 12.04$ Å.

I, obsd.	*d/n*, obsd.	*d*, calcd.	*hkl*
vvs	12.0	12.04	100
s	8.0	8.13	002
s	7.4	7.55	111
ms	6.0	6.02	200
vvw	5.4	5.42	003
vvw	5.0	5.10	211
s	3.75	3.78	222
vvvw	3.35	3.37	204
vvvw	3.00	3.01	400
vvw	2.71	2.71	006
m	2.46	2.47	206
w	2.14	2.14	335
w	2.09	2.10	424
vvw	1.89	1.89	444
vvw	1.85	1.85	622
vvw	1.80	1.80	604
vvvw	1.505	1.505	800
vvvw	1.280		

RESEARCH AND DEVELOPMENT LABORATORIES
HOUDRY PROCESS CORPORATION
LINWOOD, PENNA.

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(1) M. Calvin, THIS JOURNAL, **61**, 2230 (1939).

(2) R. B. Hull, University of Pittsburgh Bulletin, **35**, 142 (1938).