NOTES

Δ^1-Nonene-1,9-dicarboxylic Acid

By Felix Bergmann

Recently there appeared some papers[1] on the oxidative splitting of 9,10-dihydroxystearic acid into pelargonic aldehyde and azelaic semialdehyde (I). We have studied this reaction and its products for many years and wish to communicate some results which may be of general interest.

Condensation of I with malonic acid produced the Δ^1-nonene-1,9-dicarboxylic acid (II) in about 24% yield. This acid, although it may be considered as a derivative of acrylic acid, does not combine with 1,4-diphenylbutadiene in boiling xylene. By condensation of I with cyanoacetic acid the Δ^1-nonene-1-cyano-9-carboxylic acid (III) was obtained.

$$\underset{\text{I}}{\text{COOH(CH}_2)_7\text{CHO}} + \text{RCH}_2\text{COOH} \longrightarrow$$

$$\underset{\text{II, R = COOH, III, R = CN}}{\text{COOH(CH}_2)_7\text{CH}{=}\text{CHR} + \text{CO}_2 + \text{H}_2\text{O}}$$

These acids differ from "traumatine" (Δ^1-decene-1,10-dicarboxylic acid)[2] by the lack of one carbon atom only. As there exist big differences in the physiological behavior of aliphatic acids with even or odd number of carbon atoms, respectively, the "traumatinic" action of II and III seems of much interest. So far, only the inhibition of germination was determined. In this respect, the two substances showed no influence at all on wheat germs in the highest doses which were tried.

Experimental

For the condensation reactions we always used the crude aldehydic acid (I), which was obtained by splitting 25 g. of 9,10-dihydroxystearic acid with lead tetraacetate in benzene solution and separating the acid part by bicarbonate extraction.

Δ^1-Nonene-1,9-dicarboxylic Acid (II).—The crude sirup was refluxed with malonic acid (10 g.) pyridine, (10 g.) and piperidine (3 drops), for two hours. The whole mass was then poured into diluted hydrochloric acid, whereby a gray powder was obtained. It was dried on a clay plate and recrystallized from carbon tetrachloride. Clusters of short needles, m. p. 94°; yield 4 g. (24%).

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.7; H, 8.4. Found: C, 61.9; H, 8.8.

The dichloride of II was prepared by means of thionyl chloride in boiling carbon tetrachloride and purified by vacuum distillation; b. p. 184° (2 mm.); colorless liquid; yield, 50%.

Anal. Calcd. for $C_{11}H_{16}O_2Cl_2$: C, 52.6; H, 6.4. Found: C, 52.5; H, 6.35.

The chloride was transformed into the diamide by stirring it with excess concentrated aqueous ammonia. The diamide crystallizes from butyl acetate; m. p. 160–161°.

Anal. Calcd. for $C_{11}H_{20}O_2N_2$: C, 62.25; H, 9.4; N, 13.2. Found: C, 61.8; H, 9.1; N, 13.5.

When the dichloride (2 g.) was mixed with a solution of "septamide" (2.75 g.) in acetone (25 cc.) and pyridine (2 cc.) reaction started immediately. The mixture was left for four hours at room temperature and then poured into dilute acetic acid. The brown mass, so obtained, was recrystallized twice from glacial acetic acid and a little charcoal, m. p. 225°; yield, quantitative.

Anal. Calcd. for $C_{23}H_{30}O_6N_4S_2$: C, 52.9; H, 5.75; N, 10.7. Found: C, 52.3; H, 5.8; N, 10.3.

The acid (II) was recovered unchanged after refluxing it for twelve hours with 1 equiv. of diphenylbutadiene in xylene.

Δ^1-Nonene-1-cyano-9-carboxylic Acid (III).—The crude aldehydic acid (I) was condensed with 10 g. of cyanoacetic acid in boiling pyridine (10 cc.), after adding 5 drops of piperidine. After acidification, the product was extracted with ether and distilled in a high vacuum.

The fraction of b. p. 185–190° (1.0 mm.), a thick, yellow liquid, proved by its analysis to be the desired cyano-acid (III). It has an unpleasant "nitrile"-odor and gives a strong acidic reaction. With concd. sulfuric acid the substance gives first a rose, then a violet, color which, on heating, changed to wine-red, $n^{26.5}D$ 1.4360.

Anal. Calcd. for $C_{11}H_{17}O_2N$: C, 67.7; H, 8.7; N, 7.2. Found: C, 68.2; H, 9.1; N, 7.0.

The pelargonic aldehyde, when condensed in the same way with cyanoacetic acid, yielded the desired 1-cyano-Δ^1-decene, b. p. 105° (4 mm.), $n^{29}D$ 1.4120.

Anal. Calcd. for $C_{11}H_{19}N$: C, 80.0; H, 11.5. Found: C, 80.5; H, 11.3.

The physiological tests were carried out by Dr. Even-Ari of the Botanical Department of the Hebrew University, Jerusalem, to whom the author is very thankful.

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Sulfanilyl Pyrrolidine and Pyrroline

By W. E. Cass

Sulfanilylpyrrolidine and sulfanilylpyrroline whose preparations appear below, and sulfanilyl-

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(1) Nunn and Smedley-MacLean, *Biochem. J.*, **29**, 2742 (1935); Hsing and Chang, This Journal, **61**, 3589 (1939).

(2) English and co-workers, *ibid.*, **61**, 3434 (1939).

piperidine,[1] were tested for anti-pneumococcic activity in mice through the kindness of the Merck Institute for Therapeutic Research, Rahway, New Jersey. Under the experimental conditions these compounds showed little activity in comparison with sulfapyridine.

N^4-Acetylsulfanilylpyrrolidine.—Acetylsulfanilyl chloride (11.7 g., 0.05 mole) was added in several portions to a solution of 8.5 g. (0.12 mole) of pyrrolidine in 40 cc. of dioxane and the resulting solution was allowed to stand overnight. Cold water (200 cc.) was added and the precipitate which formed was filtered and washed with cold water. The crude product (12.5 g.) was treated with decolorizing charcoal and recrystallized from 50% alcohol, yielding 10.3 g. (77%) of tiny colorless plates and needles of m. p. 179° (cor.).

Anal. Calcd. for $C_{12}H_{16}O_3N_2S$: N, 10.44. Found: N, 10.5.

Sulfanilylpyrrolidine.—Five grams of N^4-acetylsulfanilylpyrrolidine was refluxed for one-half hour with 60 cc. of 12% hydrochloric acid. The solution was cooled and 20% sodium hydroxide solution was added with cooling and stirring to slight basicity. The resulting precipitate (4.0 g.) was recrystallized from 50% alcohol as slightly yellowish feathery crystals and from acetone–benzene as small plates of m. p. 167.5–168° (cor.). The yield of pure product was 3.3 g. (79%).

Anal. Calcd. for $C_{10}H_{14}O_2N_2S$: N, 12.38. Found: N, 12.4.

N^4-Acetylsulfanilylpyrroline.—Five grams (0.021 mole) of acetylsulfanilyl chloride was added in portions to a cold solution of 1.5 g. (0.022 mole) of pyrroline and 5 cc. of pyridine in 25 cc. of acetone. The reddish colored solution was heated to boiling and allowed to stand for four hours at room temperature. The product was precipitated by the addition of 300 cc. of cold water and recrystallized from 50% alcohol, using decolorizing charcoal, as fine white needles of m. p. 201–202° (cor.); yield, 3.2 g. (57%).

Anal. Calcd. for $C_{12}H_{14}O_3N_2S$: N, 10.52. Found: N, 10.4.

Sulfanilylpyrroline.—N^4-Acetylsulfanilylpyrroline (2.3 g.) was refluxed one-half hour with 20 cc. of 12% hydrochloric acid. The hydrolyzed product was precipitated by the addition of 20% sodium hydroxide solution with cooling. The crude material was recrystallized from 50% alcohol and from acetone–benzene as small white prisms of m. p. 176–177° (cor.). The yield of pure product was 1.3 g. (67%).

Anal. Calcd. for $C_{10}H_{12}O_2N_2S$: N, 12.49. Found: N, 12.6.

Attempts to prepare N^4-acetylsulfanilylpyrrole, using pyrrole–pyridine mixtures or the potassium derivative of pyrrole and acetylsulfanilyl chloride, were unsuccessful.

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RECEIVED AUGUST 21, 1940

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[1] Goldyrev and Postovskiĭ, *J. Applied Chem.* (U. S. S. R.), **11**, 316 (1938); *C. A.*, **32**, 5800 (1938).

Dehydration of 9-Fluorenylcarbinol: a New Synthesis of Phenanthrene

BY WELDON G. BROWN AND BENNIE BLUESTEIN

It may be anticipated that the hitherto unknown 9-fluorenylcarbinol[1] would undergo a Wagner rearrangment on dehydration by acids to yield phenanthrene. Analogous reactions of β,β-diarylethanols, which yield stilbene derivatives, are known,[2] and the formation of 9,10-diphenylphenanthrene[3] from 9-phenyl-10-benzoylfluorene on reduction with hydriodic acid and phosphorus may be similarly interpreted. However, Courtot,[1b] in his extensive studies of the dehydration of fulvanols, appears not to have encountered this type of rearrangement. Thus it is stated that the methyl and ethyl homologs of 9-fluorenylcarbinol yield methyl- and ethyldibenzofulvene, respectively, rather than methyl- and ethylphenanthrene which would be the rearrangement products.

The synthesis of 9-fluorenylcarbinol has now been accomplished by reduction of 9-formylfluorene with aluminum isopropoxide. On treatment, in boiling xylene solution, with phosphorus pentoxide it loses water to form phenanthrene in practically quantitative yield.

This synthesis offers some promise for the synthesis of phenanthrene derivatives, and of higher angular hydrocarbons, and we are now working in this direction.

Experimental

9-Fluorenylcarbinol.—Ten grams of 9-formylfluorene[4] in 30 cc. of ether was added to a mixture containing 16 g. of aluminum isopropoxide and 32 cc. of isopropyl alcohol. Ether and acetone were removed by slow distillation through a Vigreux column, the bath being maintained at 60–70° for four hours; 63 cc. of 15% sulfuric acid was added to the residue, precipitating a light yellow solid which was collected and extracted with hot alcohol. After precipitation from the alcohol extract by the addition of water it was recrystallized several times from high boiling ligroin as long needles, colorless, m. p. 99.5–100.0°; yield 5 g.

Anal. Calcd. for $C_{14}H_{12}O$: C, 85.68; H, 6.17. Found: C, 85.54; H, 6.36.

9-Fluorenylcarbinol-3,5-dinitrobenzoate.—M. p. 212°.

Anal. Calcd. for $C_{21}H_{16}N_2O_6$: N, 7.18. Found: N, 7.46.

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[1] For previous attempts at the synthesis of this alcohol, see (a) Sieglitz and Jassay, *Ber.*, **55**, 2032 (1922); (b) Courtot, *Ann. chim.*, (9) **4**, 157 (1915).

[2] Ramart and Amagat, *ibid.*, (10) **8**, 263 (1927).

[3] Werner and Grob, *Ber.*, **37**, 2887 (1904).

[4] Prepared by the condensation of fluorene and methyl formate according to Wislicenus and Waldmüller, *ibid.*, **42**, 785 (1909).

Dehydration of 9-Fluorenylcarbinol.—One gram of 9-fluorenylcarbinol in 10 cc. of xylene, refluxed with phosphorus pentoxide for thirty minutes, yielded, after evaporation of the xylene at room temperature, nearly 1 g. of yellow solid. On recrystallizing twice from alcohol it was obtained in colorless plates, m. p. 97°. No change in m. p. resulted when the substance was sublimed in vacuum.

Anal. Calcd. for $C_{14}H_{10}$: C, 94.34; H, 5.66. Found: C, 94.27; H, 5.90.

This product formed a picrate, m. p. 144° (lit., phenanthrene picrate, m. p. 145°).

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RECEIVED SEPTEMBER 21, 1940

Oxidation of the Hydroxybiphenyls

BY J. C. COLBERT AND CURTIS LEE HENSLEY

Substitution in *o*- and *m*-hydroxybiphenyl leads to isomers whose orientation must be established. While in one such study[1] in this Laboratory structure was established by a second synthesis of the new compound, this common method is not always available. It has been long known[2] that upon oxidation certain halogenated biphenyls yield benzoic or substituted benzoic acids, thus indicating the position of substituents. Although a systematic study[3] of polyhalogenated biphenyls has been reported, oxidation of the hydroxybiphenyls has been neglected. The formation of benzoic acid by the oxidation of a substituted hydroxybiphenyl would indicate the ring entered by the substituent, while formation of a substituted hydroxybenzoic acid would orient groups entering the ring containing the phenolic group. The present investigation represents a preliminary study of the conditions necessary for the formation of benzoic and hydroxybenzoic acids from the hydroxybiphenyls.

The method of oxidation followed is a modification of the use of chromic anhydride in acetic acid solution.[4] After standardizing the procedure by a study of the oxidation of biphenyl a study was made of the oxidation products from *o*-, *m*- and *p*-hydroxybiphenyl, 3-bromo-4-hydroxybiphenyl, 3,5-dibromo-4-hydroxybiphenyl and 3,5-dinitro-2-hydroxybiphenyl. In all of these cases benzoic acid and a small amount of unchanged starting material were the only substances isolated. Yields were low and differences insufficient to establish influences due to groups and their positions in the ring.

The phenolic ring in the hydroxybiphenyls may be protected against complete oxidation in two ways, namely, by the steric effect of nitro groups in the diortho positions, and by the protective influence of a heavy ester group. 3,5-Dinitro-4-hydroxybiphenyl yields 3,5-dinitro-4-hydroxybenzoic acid, while in the case of 3-nitro-4-hydroxybiphenyl no benzoic acid and only a trace of the corresponding hydroxybenzoic acid could be isolated. When 2-hydroxybiphenyl was converted into the benzenesulfonate[5] and submitted to oxidation the only product isolated was benzenesulfonylsalicylic acid. This ester was readily transformed into salicylic acid.

Procedure

Benzoic Acid from Biphenyl.—Thirty-five grams of chromic anhydride in 32 cc. of 37.5% acetic acid was added drop by drop with vigorous mechanical stirring and occasional warming over a period of thirty minutes to a hot solution of 5 g. of biphenyl in 50 cc. of glacial acetic acid. The reaction mixture was refluxed gently with stirring for two hours. The flame was removed, 6 cc. of acetaldehyde in 15 cc. of glacial acetic acid added, and gentle refluxing continued for an additional fifteen minutes; 50 cc. of water and 50 cc. of saturated salt solution was then added. The reaction mixture was extracted three times with ether, the ether distilled off and the residue made basic with concd. ammonium hydroxide. Solution in alcohol followed by dilution with water led to the recovery of 0.43 g. of unchanged biphenyl. The filtrate from the addition of ammonium hydroxide was acidified with concd. hydrochloric acid, boiled with Norit, filtered and cooled. The product gave 0.26 g. of benzoic acid upon recrystallization from water. An additional 0.20 g. was obtained by ether extraction of the filtrates. A second ether extract of the reaction mixture gave 0.32 g. of benzoic acid. Steam distillation of the reaction mixture (400 cc. of distillate) gave a small amount of impure acid. A second steam distillation, which was concentrated after making it alkaline, gave 0.55 g. of the acid. A final ether extraction of the reaction mixture yielded 0.21 g. more of the acid. The total weight of benzoic acid obtained from 5 g. of biphenyl was 1.54 g. or 38.88%. The addition of concd. hydrochloric acid to the reaction mixture gave a low yield, 5.7% of *m*-chlorobenzoic acid. When the oxidation was repeated with very slight modifications the yields of benzoic acid were as follows: from *o*-, *m*-, and *p*-hydroxybiphenyl 17.2%, 10% and 11.2%, respectively. 3-Bromo-4-hydroxybiphenyl, 3,5-dibromo-4-hydroxybiphenyl and 3,5-dinitro-2-hydroxybiphenyl gave 14.3%, 16.67% and 16.4% of benzoic acid. 3,5-Dinitro-4-hydroxybiphenyl gave a 5.0% yield of 3,5-dinitro-4-hydroxybenzoic acid and upon oxidation the benzene sulfonate of 2-hydroxybiphenyl gave 16.35% yield of benzenesulfonylsalicylic acid. The hydrolytic trans-

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[1] Colbert, Meigs and Jenkins, THIS JOURNAL, **59**, 1122 (1937).

[2] Schultz, *Ann.*, **174**, 206 (1874).

[3] Case, THIS JOURNAL, **61**, 3487 (1939).

[4] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Inc., Boston, Mass., 1935. p. 230.

[5] Hazlet, THIS JOURNAL, **59**, 287 (1937).

formation of this substance into salicylic acid was 70% efficient.

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RECEIVED JUNE 15, 1940

Preparation of Tetramethylene Bromide

BY SHERMAN FRIED AND RICHARD D. KLEENE

Tetramethylene bromide has previously been available by the reaction between N-benzoylpyrrolidine and phosphorus pentabromide.[1] We have now found that the cleavage of tetrahydrofuran by hydrogen bromide, which is analogous to the reaction previously applied by Starr and Hixon,[2] for the preparation of the corresponding chlorohydrin, is much simpler and gives a comparable yield from more readily available starting materials.

Furan was prepared by the decarboxylation of furoic acid in the presence of copper oxide and quinoline,[3] using, however, a Dewar jacketed trap cooled with dry-ice to prevent entrainment of the furan by escaping carbon dioxide. The furan was readily hydrogenated in 95% yield to tetrahydrofuran using palladium–palladium oxide as a catalyst.[4]

Dry hydrogen bromide was passed into the tetrahydrofuran in a flask fitted with a side-tube, reflux condenser and thermometer, until the temperature reached 150°, when the theoretical quantity of hydrogen bromide had been added. The resulting black tarry product was washed thoroughly with water and then with sodium bicarbonate solution until it was free of hydrobromic acid. It was then taken up with ether and dried over anhydrous copper sulfate. The product was fractionated under diminished pressure and 134 g. (yield, 70%) of tetramethylene bromide (b. p. 198° at normal pressure) was collected.

The authors gratefully acknowledge the assistance of Professor W. G. Brown, who designed the apparatus used in the preparation of the furan.

(1) Von Braun and Muller, *Ber.*, **39**, 4124 (1906).

(2) Starr and Hixon, THIS JOURNAL, **56**, 1595 (1934).

(3) Wagner and Simmons, *J. Chem. Ed.*, **13**, 270 (1936).

(4) Shriner and Adams, THIS JOURNAL, **46**, 1683 (1924).

DEPARTMENT OF CHEMISTRY
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RECEIVED AUGUST 23, 1940

The Isolation of Eriodictyol and Homoeriodictyol. An Improved Procedure

BY T. A. GEISSMAN

The question of the existence of a substance having vitamin-like properties in its effect upon capillary permeability, and called "Vitamin P" by Szent-Györgyi[1] remains unanswered. So far practically all the studies that have been made upon the putative vitamin have been made upon "citrin," a crude flavanone fraction isolated from lemon peel. Reports of experiments in which this material has been used in clinical studies and in animal (guinea pig) tests are conflicting[2] and allow no definite conclusion to be drawn as to the physiological action of "citrin," although the balance of the evidence seems to support the belief that it does contain some substance which exerts a vitamin-like action, when acting in conjunction with vitamin C, in certain types of hemorrhagic diathesis.

Szent-Györgyi has attributed the vitamin activity of "citrin" to the presence of an eriodictyol glycoside[3] although definite experimental proof of its presence in "citrin" is lacking. It is probable, however, that "citrin" does contain eriodictyol (as a glycoside?) since certain color tests (ferric chloride, hot aqueous alkali) shown by "citrin" are also given by pure eriodictyol. It is clear that even if it can be shown that "citrin" contains eriodictyol this will not constitute proof that eriodictyol is "vitamin P." Indeed, Scarborough's results[2c] indicate that hesperidin (also a constituent of "citrin") has "citrin" activity in certain types of purpura.

In an approach to the problem through studies on pure flavanones which are known to be or suspected of being present in "citrin" the preparation of pure eriodictyol has been undertaken.

Eriodictyol (5,7,3′,4′-tetrahydroxyflavanone) has been isolated from *Eriodictyon californicum* by Power and Tutin[4] and from *Lespedeza cyrtobotrya* by Ohira.[5] It has been isolated, along with homoeriodictyol, for the present study from *Eriodictyon californicum* by a procedure which combines the best features of the method of Power and Tutin with those of the method used by Mossler[6] in isolating homoeriodictyol from the same plant. The yields of both eriodictyol and homoeriodictyol were about double those obtained by Power and Tutin but this improvement may not be inherent in the present method since studies now in progress in this Laboratory have indicated that considerable variation can occur

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(1) Szent-Györgyi, *et al.*, *Nature*, **138**, 27, 798 (1936); *Z. physiol. Chem.*, **255**, 216 (1938).

(2) (a) Szent-Györgyi, *et al.*, *Nature*, **139**, 326 (1937); **140**, 426 (1938); (b) Zilva, *Biochem. J.*, **31**, 915, 1488 (1937); (c) Scarborough, *ibid.*, **33**, 1400 (1939).

(3) Bruckner and Szent-Györgyi, *Nature*, **138**, 1057 (1936).

(4) Power and Tutin, *Pharm. Rev.*, **24**, 301 (1907); *Pharm. J.*, **77**, 381 (1906); Tutin and Clewer, *J. Chem. Soc.*, **95**, 81 (1909).

(5) T. Ohira, *J. Agr. Chem. Soc. Japan*, **9**, 448 (1933).

(6) Mossler, *Ann.*, **351**, 223 (1907).

in the flavanone content of samples of *Eriodictyon* collected in various parts of this state. The material used in the procedure described was a commercially available product collected near Colusa, California, and marketed as "yerba santa."

The flavanones are being tested for "vitamin P" activity.

Experimental

Eriodictyol.—A total of 700 g. of powdered *Eriodictyon californicum* was extracted in about 70-g. portions with 500 ml. of ether in a Soxhlet extractor. The deep brown-green ether solution was filtered and shaken with successive portions of ammonium carbonate solution to remove acidic tarry material and then with 400 ml. of cold 10% sodium carbonate solution. A thick yellow precipitate of the sodium salt of homoeriodictyol formed and was collected by filtration on a large Büchner funnel, the filtrate being allowed to drop directly into dilute hydrochloric acid. The tarry precipitate from the filtrate was taken up in ether and again shaken with cold 10% sodium carbonate solution and the precipitate of sodium homoeriodictate collected by filtration. The filtrate, again dropping directly into dilute acid, deposited a tarry mass which was removed, transferred to a 2-liter round-bottomed flask and boiled with several 1.5-liter portions of water. The aqueous extracts were decanted from the tar and, after cooling, extracted with ether. The combined ether extracts were shaken with 300 ml. of ice-cold 10% sodium carbonate and the aqueous layer kept in an ice-bath for thirty minutes and then filtered from a rather small amount of precipitated sodium homoeriodictate. The filtrate was acidified with dilute hydrochloric acid, yielding a yellowish-brown tar. The tar was separated from the aqueous layer, transferred to a small beaker and rubbed with ether until the crystalline powder (A) which formed was no longer sticky. The product (about 8 g., moist) was collected and the filtrate allowed to evaporate slowly. A further amount (1 g.) of solid separated (B).

The first crop of material (A) was recrystallized from dilute alcohol, yielding 2.85 g. of colorless needles, m. p. 262–265°, dec. Dilution of the mother liquor yielded an additional 0.84 g. of product, m. p. 261–264° dec. Recrystallization of crop (B) yielded 0.78 g., m. p. 260–263° dec. The total yield was thus 4.47 g. of crude eriodictyol (0.64%). Recrystallized from dilute alcohol the substance formed tiny colorless needles, m. p. 265–266° dec. Descriptions of eriodictyol in the literature fail to record the fact that the m. p. of the compound depends upon the heating rate. Taken in the usual way, the m. p. may vary between 262 and 266°, with decomposition to a red liquid. If a sample is plunged into a preheated bath it melts at 267° (the usually recorded m. p.) to a pale yellow liquid.

Since the most probable impurity in the eriodictyol was homoeriodictyol a methoxyl determination was carried out but no methoxyl was found. The acetate, prepared with acetic anhydride–sodium acetate, formed colorless needles, m. p. 136–137° (literature[7] 137°).

The purified material dissolves in cold 10% sodium hydroxide solution to give a colorless solution which upon standing rapidly darkens. A solution of eriodictyol in 10% sodium hydroxide develops an intense blood-red color upon heating. Ferric chloride in methanol causes a transient green color which is immediately succeeded by brown-red.

Homoeriodictyol.—The various fractions of sodium salt collected as described above were combined and recrystallized from water. The moist salt (nearly colorless needles) was dissolved in about 400 ml. of boiling glacial acetic acid. Upon cooling there was obtained 40.5 g. of pale buff homoeriodictyol, m. p. 220°. Recrystallization raises the m. p. to the reported[7] value, 224°.

The acetate, prepared with sodium acetate-acetic anhydride, melted at 161–162° (reported[7] 163°).

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RECEIVED SEPTEMBER 23, 1940

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[7] Shinoda and Sato, *J. Pharm. Soc. Japan*, **49**, 71 (1929).

Isotopic Composition of Cuprite Oxygen

BY W. HEINLEN HALL AND CLARENCE HOCHANADEL

The isotopic composition of oxygen in carbonate rocks and iron oxide ores recently has been determined by Dole and Slobod.[1] We wish to report similar data for cuprite (Dana 224), one of the naturally occurring oxides of copper. The sample used by us was obtained from Ward's Natural Science Establishment and came from Bisbee, Arizona.

The technique which we used consisted in the reduction[2] of the oxide with commercial electrolytic hydrogen followed by a comparison of the density of the resulting water with that of water formed with the same hydrogen and atmospheric oxygen. The procedure used in purifying the water and determining the densities was the same as that used in earlier work.[3]

Densities were determined to within 1 p. p. m. by the buoyancy balance method in which temperature (measured with two Bureau of Standards calibrated Beckmann thermometers) was the observed variable. A completely submerged Pyrex float was used.[4]

After repeated purification of both samples, we observed that the floating temperature for water prepared from cuprite oxygen and commercial hydrogen was 0.021° lower than the floating temperature for water prepared by burning the same hydrogen in atmospheric oxygen under con-

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(1) Malcolm Dole and R. L. Slobod, THIS JOURNAL, **62**, 471–479 (1940).

(2) Reduction was carried out in such a way that the sample of hydrogen reacted completely, thus avoiding any fractionation.

(3) Hall and Johnston, THIS JOURNAL, **57**, 1515–1517 (1935).

(4) In this and other work extending over a period of five years, we have found variations in the floating temperature for any given float using ordinary water. We have attributed this to the dissolving of the float and/or to changes in the thermometers. It would appear from the observation made by Dole and Slobod that the thermometers may be responsible for the change since they found no appreciable effect when using a platinum resistance thermometer.

ditions previously shown to produce no fractionation.[5]

This indicates that the contribution of the cuprite oxygen to the density of the water formed from it is 5.5 p. p. m. less than that of atmospheric oxygen.

This is only 1 p. p. m. less than the difference between the density contributions of atmospheric and ordinary water oxygen[5] and indicates therefore that the isotopic composition of the cuprite oxygen is practically the same as that of ordinary water.

This probably indicates that the original copper sulfide deposit was altered by reaction with water and not with atmospheric oxygen.

(5) Hall and Johnston, THIS JOURNAL, **58**, 1920–1922 (1936).

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RECEIVED SEPTEMBER 6, 1940

The Freezing Points and Low Temperature Viscosities of Diacetone Alcohol–Acetone Mixtures[1a]

BY V. LANTZ

In determining the viscosities of diacetone alcohol and its mixtures with acetone at temperatures near the freezing points of the solutions, it was observed that the commercially pure diacetone alcohol used[1b] (d^{20}_4 0.9377, n^{20}_D 1.4235) had a freezing point considerably higher than the only published values that could be found. The published values are −55°[2] and −57 to −54°,[3] whereas the value found was −45°. A second sample of commercial "pure diacetone" from the same source (d^{20}_4 0.9375, n^{20}_D 1.4235) had a freezing point of −45.9°. A portion of the second sample was distilled at 50 mm. pressure using a 20 to 1 reflux ratio in a two-meter vacuum-jacketed column packed with glass helices. The 80% heart cut (d^{20}_4 0.9382, n^{20}_D 1.4232) had a freezing point of −44.0°. Similar results (−44.9°) have recently been obtained by W. C. B. Smithuysen of the Bataafsche Petroleum Maatschappij, Amsterdam.[4]

The freezing points of acetone–diacetone alcohol solutions, shown in Table I, indicate that from 15 to 20% of acetone, the most likely impurity in diacetone alcohol, would need to be present to lower the freezing point of diacetone alcohol to the previously published values. The especially purified acetone used to obtain the data in Table I had the following constants: d^{20}_4 0.7914, n^{20}_D 1.3587.

TABLE I

FREEZING POINT OF ACETONE–DIACETONE ALCOHOL SOLUTIONS

Acetone, by wt.	0	4.3	8.6	13.0	20.0
F. p., °C.	−44.0	−46.9	−50.4	−52.5	−55.5

Freezing points were determined by noting the break in a temperature–time curve obtained by slowly warming a mush of crystals and liquid in an air jacketed test-tube held at a nearly constant temperature above the freezing point of the solution. This method was found to be more satisfactory for determining initial freezing points than the use of cooling curves because the high viscosities of the solutions at their freezing points led to excessive under-cooling. Temperatures were measured with an iron–constantin thermocouple, calibrated against a platinum resistance thermometer.

Kinematic viscosities of diacetone alcohol and of a solution containing 12.8% by weight of acetone were measured at temperatures near their freezing points, using a Ubbelohde type viscometer.[5] Viscosities are shown in Table II.

TABLE II

LOW TEMPERATURE VISCOSITIES OF DIACETONE ALCOHOL AND OF A SOLUTION OF ACETONE IN DIACETONE

Diacetone alcohol		12.8% acetone 87.2% diacetone alcohol	
Temp., °C.	Viscosity centistokes	Temp., °C.	Viscosity centistokes
− 1.8	7.8	−33	15.0
− 2.7	8.1	−44	30.6
−15.0	15.3	−55.1	78.0[a]
−30.9	43.6		
−42.7	128		
−49.5	298[a]		

[a] Supercooled liquids

(1a) Original manuscript received July 19, 1939.

(1b) Supplied by Shell Chemical Company, San Francisco, California.

(2) T. H. Durrans, "Solvents," 4th ed., D. Van Nostrand Co., New York, N. Y., 1938, p. 112.

(3) "Handbook of Chemistry and Physics," 23rd ed., Chemical Rubber Publishing Company, Cleveland, Ohio, 1939, p. 750.

(4) Private communication.

(5) Ubbelohde, *Ind. Eng. Chem., Anal. Ed.*, **9**, 85 (1937).

SHELL DEVELOPMENT CO.
EMERYVILLE, CALIFORNIA
RECEIVED SEPTEMBER 9, 1940

The Stable Form of Sucrose Octaacetate

BY R. P. LINSTEAD, A. RUTENBERG, W. G. DAUBEN AND W. L. EVANS[1]

In a recent preparation of sucrose octaacetate, a quantity of sucrose was heated in the usual way with sodium acetate and acetic anhydride. The only abnormal feature of the reaction was that the time of reacting was prolonged to twenty

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(1) After the authors became aware that work was being done simultaneously in the chemical laboratories of Harvard University and The Ohio State University on the stable form of sucrose octaacetate, they agreed to publish a joint paper on their results concerning this very important compound.

hours. A crystalline solid product was obtained in good yield, which, after one recrystallization from ether, formed bold prismatic needles, melting at 89°. The ordinary form of sucrose octaacetate known for more than fifty years has a melting point of about 69–70°.[2] It seemed probable that the new compound was a dimorphous modification of the octaacetate, or possible that some isomeric change or acetolysis had occurred.

The literature contains three descriptions of high melting forms of sucrose octaacetate. Pictet[3] observed the change of the usual form on standing into a "form II" of m. p. 75°. Frèrejacque[4] described the preparation of a "form III," m. p. 87°, by diluting an alcoholic solution of the usual form with water. Sandera[5] obtained a form of m. p. 83°. We believe that the product of the experiments which we now describe is a slightly purer version of Frèrejacque's "form III." We are led to publish this account of our work because our results supplement those of Frèrejacque, which we had overlooked when the work was carried out. We have not encountered Pictet's "form II."

It was first established that the compound of m. p. 89° was the octaacetate of a disaccharide, $C_{28}H_{38}O_{19}$, by elementary analysis and by the determination of acetyl values. The rotatory power of the new octaacetate was almost identical with that reported in the literature for the form of m. p. 69°. Hydrolysis of the material of m. p. 89° by Zemplén's method yielded sucrose with the correct melting point and rotatory power.

We have made a considerable number of preparations of sucrose octaacetate using a variety of experimental conditions, and have been quite unable to prepare the well-known form of m. p. about 69°. All our products have been more or less pure preparations of the 89° form. The usual precautions have been taken—different operators have performed the preparation and different rooms have been used—but without avail. We conclude that these laboratories are now seeded with the stable 89° form.

A sample of the 69° form was kindly supplied by Dr. Clifford Purves. When this was crystallized once from ether, either with or without conscious seeding with the 89° form, material melting at about 85° was obtained. Two commercial samples of sucrose octaacetate were also examined. One of these (Eastman Kodak Company) melted at 72–74° and after two crystallizations from ether was converted almost quantitatively into the 89° form. The second (Niacet Chemical Company) melted at 79–84° in the crude state and at 86° after one crystallization from ether.

These results leave no doubt that sucrose octaacetate is polymorphous and that the form of m. p. 89° is the most stable modification.

Experimental

Experiment 1.—The sucrose used had m. p. 183–184°, $[\alpha]^{22}D$ +66.6°, in water. A mixture of 150 g. of sucrose, 100 g. of anhydrous sodium acetate and 850 cc. of acetic anhydride was heated on the steam-bath for twenty hours. The product was poured onto 3 liters of ice water and left at 5° overnight. The hard solid so obtained was collected by filtration, washed with ice water and roughly dried in air. After one crystallization from 500 cc. of 95% alcohol (charcoal), 224 g. of **sucrose octaacetate** was obtained, m. p. 88–89°. The compound forms fine sheaves of glistening prismatic needles from dry ether or from alcohol, m. p. 89°. It is very soluble in benzene, insoluble in water and petroleum ether. It does not reduce Fehling solution even after prolonged boiling. For analysis the sample was dried to constant weight over alkali at 15 mm.

Anal. Calcd. for $C_{28}H_{38}O_{19}$: C, 49.56; H, 5.60. Found: C, 49.82, 49.82, 49.58, 49.33, 49.70, 49.74; H, 5.47, 5.83, 5.76, 5.59, 6.14, 5.60.

Acetyl Values. By hydrolysis with 0.1 *N* alcoholic potash for thirty minutes. Calcd. for $8(CH_3CO)$: CH_3CO, 50.72. Found: CH_3CO, 50.42, 50.55, 50.51.

Rotation. α, +2.99°; c, 2.566 in absolute alcohol; 2-dm. tube $[\alpha]^{25.4}D$ +58.5°. For the octaacetate of m. p. 69°, Georg found $[\alpha]^{28}D$ +57.8° in alcohol, c 2.733.[6]

Experiment 2.—Sucrose octaacetate was also obtained under the following experimental conditions which involve certain changes in concentration, temperature, time and technique from that given above. A mixture of 10 g. of sucrose, $[\alpha]^{22}D$ 66.7° (H_2O), m. p. 185–186°, 5 g. of anhydrous sodium acetate and 45 cc. of acetic anhydride was heated on a steam-bath for three hours and then let stand for thirty-six hours at room temperature. The mixture was again heated on a steam-bath and the hot solution poured slowly into 10 liters of *mechanically stirred* ice water. The reaction product separated as a white crystalline solid. The crude product was separated by filtration, washed well with cold water and dried in the open air (yield, 19 g. crude). It was then dissolved in hot 95% ethanol, decolorized with Carboraffin and allowed to crystallize (yield 17.3 g., 87.3%, m. p. 89°). Recrystallization from dry ether yielded the same white needles.

This experiment was repeated five times and the same results were obtained in each case. The use of potassium acetate for sodium acetate gave the same results.

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(2) Herzfeld, *Ber.*, **13**, 267 (1880); Koenigs and Knorr, *ibid.*, **34**, 4347 (1901); Hudson and Johnson, THIS JOURNAL, **37**, 2748 (1915); Brigl and Scheyer, *Z. physiol. Chem.*, **160**, 214 (1926); Pictet and Vogel, *Helv. Chim. Acta*, **11**, 436 (1928).

(3) Pictet, *ibid.*, **13**, 698 (1930).

(4) Frèrejacque, *Compt. rend.*, **203**, 731 (1936).

(5) Sandera, *Chem. Listy*, **33**, 139 (1939).

(6) Georg, *Helv. Chim. Acta*, **16**, 141 (1933).

Rotation. α, +0.95°; *c*, 0.795 in absolute chloroform; *l*, 2 dm.; $[\alpha]^{23}\text{D}$ +59.7°. This value is in close agreement with that reported by Hudson and Johnson,[3] $[+59.6]^{20}\text{D}$ ($CHCl_3$).

Anal. Calcd. for $C_{12}H_{14}O_{11}$: $(COCH_3)_8$ = acetyl,[7] 11.78 cc. of 0.1 *N* NaOH per 100 mg. of sample. Found: acetyl, 11.82, 11.81, 11.74 cc.

Crystallographic Analysis.—Lath-like crystals which show parallel extinction, but the character of the interference figures indicates monoclinic system of crystallization: optically negative, medium large optic angle, n_γ = 1.500 (±0.002), n_β = 1.488 (±0.002), n_α = 1.470 (±0.002).

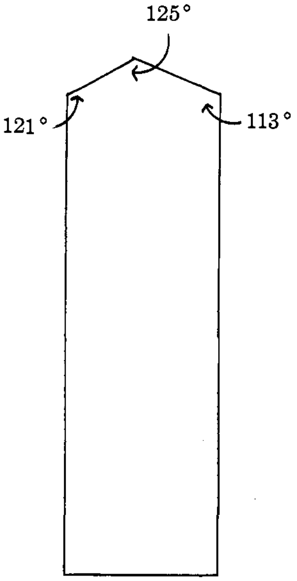

Fig. 1.—Characteristic crystal structure.

Experiment 3.—(Compare Koenigs and Knorr, ref. 2.) A mixture of 20 g. of sucrose, 40 g. of anhydrous sodium acetate and 120 cc. of acetic anhydride was heated to 110°, when reaction set in and heat was evolved. The mixture was kept at 125–135° for thirty minutes, allowed to cool to about 85°, and then diluted with 100 cc. of water. After the vigorous decomposition of the excess of the reagents, the product was poured onto ice. The sticky solid so formed was washed with fresh ice water from time to time until it was hard (4.5 hours). It was filtered and dried on a clay plate; yield, 30.5 g., m. p. (crude) 83–85°; 88–89° after one crystallization from ether.

Hydrolysis.—The octaacetate of m. p. 89° was hydrolyzed by sodium methoxide at room temperature following the method of Pictet and Vogel.[8] The white powder produced was dissolved in a little water and precipitated by the addition of a mixture of 5 parts of alcohol and 1 part of ether. The sucrose so obtained, after crystallization from 80% alcohol, had m. p. 183–184°, $[\alpha]^{23}\text{D}$ +66.5° in water.

Experiment 4.—In order to determine whether the sucrose octaacetate could be prepared by the method of acetylation which involves the use of pyridine and acetic anhydride, the following experiments were also carried out. A mixture of anhydrous sucrose (10 g.) and anhydrous pyridine (180 cc.) was shaken in a thermostat at 50° until solution of the sucrose was complete (sixteen hours). Acetic anhydride was added in 3-cc. portions (total, 45 cc.) and the temperature was not allowed to go above 52°. After remaining at 50° for about forty-eight hours the reaction mixture was poured into 10 liters of ice water and stirred vigorously for thirty minutes. The crude product was separated by filtration and the mother liquor allowed to stand at room temperature for twenty-four hours. From this clear water, upon standing, a second product was obtained in some quantity (7 g. air-dried). The acetate yielded beautiful needle-like crystals (m. p. 86°). Both products were crystallized from hot and cold ethanol and in all four cases the same sucrose octaacetate was obtained (combined yield 8.5 g., 43.7%, m. p. 89°). On repetition of this experiment at 0°, 3.5 g. of the pure sucrose octaacetate was obtained.

Experiment 5.—In this experiment the product was worked up as far as possible in the absence of free acetic acid. A mixture of 6 g. of sucrose, 4.5 g. of sodium acetate and 30 cc. of acetic anhydride was heated on the steam-bath under reflux for thirty minutes. The product was poured into a large bulk of ice and water and extracted twice with ether (total, 150 cc.). The combined ether extract was in turn extracted with successive quantities of aqueous sodium bicarbonate solution until free from acid. It was then washed with water and dried over sodium sulfate. Removal of the ether left an oil which soon solidified. The solid melted at 86° alone and at 87–89° on admixture with the 89° form.

Experiment 6.—(In this the product was worked up at high acidity.) Sucrose octaacetate (4 g., m. p. 89°) was dissolved in a mixture of 3 parts of acetic anhydride and 1 part of acetic acid. The mixture was heated to boiling and poured into 100 cc. of water. After standing overnight, the hard cake was filtered off. It melted at 86–87° in the crude state.

The lowest melting samples of octaacetate which could be obtained were made by ether extraction as under (5) above, followed by evaporation and rubbing of the resulting oil with alcohol. Products melting initially at about 79–80° were so obtained. On crystallization these gave the form of m. p. 89°.

Attempted Conversion of the 89° Form.—(i) The form of m. p. 89° was melted under high vacuum. On cooling the product set to a clear glass. Crystallization of this from hot water, ether and alcohol gave products melting severally at 82–83°, 81–83° and 89°. (ii) On crystallization of the 89° form from dilute or glacial acetic acids, products were obtained melting at about 86°. Recrystallization of these from alcohol or ether raised the m. p. to 89°. (iii) A solution of the 89° form in ether was seeded with the 69° form. The resulting crystals melted at 85°. These experiments indicate a slight tendency for the high melting form to revert to a lower melting modification.

Conversion of the 69° into the 89° Form.—(i) A sample of the octaacetate kindly provided by Dr. C. B. Purves melted at 69°. After two crystallizations from pure ether the m. p. was raised to 88°; mixed m. p. with the 89° form, 88–89°. A similar result was obtained when the ethereal

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(7) A. Kunz and C. S. Hudson, This Journal, **48**, 1978 (1926).

(8) Pictet and Vogel, *Helv. Chim. Acta*, **11**, 441 (1928).

solution was seeded with the 89° form. (ii) A sample of commercial sucrose octaacetate had m. p. 72–74°. One crystallization from ether gave material of m. p. 86–87°. Crystallization from alcohol, acetic acid, water and chloroform gave in all cases products melting between 80° and 88°, and after further crystallization at 89°. (iii) In quantitative conversions, 7.4 g. of the octaacetate, m. p. 72–74°, yielded 7.1 g. of m. p. 88° after two crystallizations from ether. In another experiment 5.6 g. of the low melting octaacetate was dissolved in ether. The solution was filtered, seeded with the 89° octaacetate and the solvent removed; 5.6 g. of product was obtained, m. p. 87–88°. (iv) On one occasion a product melting at 72° was obtained by the use of the procedure employed in experiment 2. At the end of two days, the specimen had changed to the high melting compound (89°). Many attempts were made to repeat this experiment but the high melting compound was always obtained.

Acknowledgment.—The authors are gratefully indebted to Professor Arthur M. Brandt, Department of Mineralogy, The Ohio State University, for the crystallographic data.

COLUMBUS, OHIO
CAMBRIDGE, MASS.

RECEIVED JUNE 19, 1940

Hydrogen Bonds Involving the C–H←F Link. XII[1]

BY C. S. MARVEL, M. J. COPLEY[2] AND E. GINSBERG

Although strong F–H←F bonds are present in the solid, liquid, and vapor phases of hydrogen fluoride, almost no evidence has been presented heretofore to indicate that a fluorine atom attached to a carbon atom is capable of acting as a donor atom for hydrogen bond formation. Zellhoefer, Copley, and Marvel[3] noted that the substitution of fluorine for chlorine in chloroform and in methylene chloride decreases the ratio of their observed to "ideal" (calculated from Raoult's law) solubilities at 3° in donor solvents. This effect is illustrated by the data[3] given in Table I when dimethyl ether of tetraethylene glycol is used as the solvent. The solubilities of the halogenated hydrocarbons were determined at partial pressures corresponding to their vapor pressure at 3°.

TABLE I

SOLUBILITY OF HALOGENATED HYDROCARBON IN TETRAETHYLENEGLYCOL DIMETHYL ETHER AT 3°

	Mole fraction Obsd.	Mole fraction Ideal	Ratio Obsd./Ideal
$CHCl_3$	0.625	0.283	2.20
$CHCl_2F$	.706	.381	1.85
$CHClF_2$	.740	.449	1.65
CH_2Cl_2	.600	.311	1.93
CH_2ClF	.647	.398	1.62

The decrease in the ratio may be explained by assuming that the smaller negative deviations observed with the fluorine derivatives are caused by weak C–H←F bonds between fluorinated hydrocarbon molecules. Unfortunately, fluoroform, for which the effect might be expected to be a maximum, is difficult to obtain and was not available.

It occurred to the authors that further evidence might be discovered by making a comparison of the heats of mixing with donor liquids of the vinylogs[4] $C_6H_5CF_3$ and $C_6H_5CCl_3$, respectively, of CHF_3 and $CHCl_3$. One would predict that the para hydrogens of the vinylogs are sufficiently activated to form hydrogen bonds with donor nitrogen or oxygen atoms. If the fluorine atoms have donor properties, some association through C–H←F bonds should be present in $C_6H_5CF_3$. The breaking of these bonds to form more stable C–H←N or O bonds on mixing with a donor liquid would lead to a smaller heat of mixing for $C_6H_5CF_3$ than for $C_6H_5CCl_3$. (This prediction contains the assumption that a chlorine atom does not bond or that at most it has a smaller donor capacity than a fluorine atom.)

The method followed in making these measurements has been described in a previous publication.[5] The data are tabulated in Table II.

TABLE II

HEATS OF MIXING IN CALORIES PER MOLE OF SOLUTION AT 3° FOR EQUIMOLAR MIXTURES

	Benzotrifluoride	Benzotrichloride
N,N-Dimethylacetamide	125	305
Dimethylcyclohexylamine	120	410
Ethyl phosphate	135	160
Ethyl ether	140	123
Acetone	40	40

The maxima in the heat of mixing curves occurred at approximately equimolar mixtures. A pronounced effect in the expected direction was observed with each of the nitrogen compounds but the results with the oxygen compounds are not conclusive. Apparently the para hydrogens of the ring are not sufficiently activated to form C–H←O bonds of any greater strength than the C–H←F bonds already present in the

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(1) For the eleventh communication in this series see Marvel, Copley and Ginsberg, THIS JOURNAL, **62**, 3109 (1940).

(2) Present address: Eastern Regional Research Laboratory, U. S. Department of Agriculture, Chestnut Hill Station, Philadelphia, Pennsylvania.

(3) Zellhoefer, Copley and Marvel, THIS JOURNAL, **60**, 1337 (1938).

(4) Fuson, *Chem. Rev.*, **16**, 1 (1935).

(5) Zellhoefer and Copley, THIS JOURNAL, **60**, 1343 (1938).

benzotrifluoride. Previous results[6] have shown that a nitrogen atom is a considerably stronger donor than an oxygen atom. Further evidence of the existence of C–H←F bonds in benzotrifluoride or other fluorinated hydrocarbons should be obtainable from infrared absorption studies.

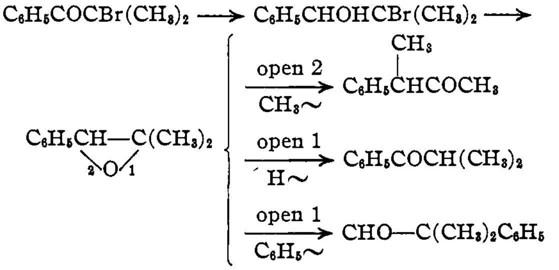
(6) Copley, Zellhoefer and Marvel, THIS JOURNAL, **60**, 2666 (1938).

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS RECEIVED SEPTEMBER 10, 1940

The Reduction of α-Bromo Ketones by Aluminum Isopropylate. II

BY PHILIP G. STEVENS[1] AND OWEN C. W. ALLENBY[2]

In our recent paper[3] we proposed a mechanism involving an intermediate oxide to explain the formation of methylbenzylcarbinol from α-bromopropiophenone and aluminum isopropylate. The carbinol mixture, which we obtained from α-bromoisobutyrophenone in a similar way, we have now identified, and the results lend further support to our proposed mechanism. Since no solid derivatives could be obtained, we oxidized with chromic acid, and then identified the resulting ketones or acids. In this way we obtained mainly isobutyrophenone, and a little dimethylphenylacetic acid. The other expected ketone, methylphenylacetone, was shown to be present solely by oxidation with sodium hypoiodide, whereby small amounts of iodoform were obtained. The formation of these substances can be attributed to isomerization of the intermediate oxide in three different ways, depending on the way the oxide opens, and on which group shifts.[4] The carbonyl compounds so formed are then reduced to carbinols



In addition we isolated a somewhat higher boiling bromine-free substance, very likely a glycol ether, and large amounts of the low-boiling compound previously mentioned.[1] This was carefully purified by fractional distillation, and analysis again confirmed the composition as $C_{13}H_{20}O$. As cleavage with hydriodic acid yielded isopropyl iodide, this substance is undoubtedly an isopropyl ether of one or more of the above three carbinols.

Experimental Part

Reduction of α-Bromoisobutyrophenone.—318 grams of the bromo ketone was reduced with 4.2 moles of 1 molar aluminum isopropylate by boiling for twenty-one hours, the acetone, etc., being separated continuously by an effective column. An analysis of the distillate showed that 22% of the bromine appeared as isopropyl bromide. The product was then worked up as usual, and separated by repeated fractional distillation into three fractions. The ether fraction, b. p. (9 mm.) 84.8–85.0°, 33.5 g., $n^{25}D$ 1.4741, d^{25}_4 0.8881, was bromine-free, and did not reduce potassium permanganate: *MR* calcd., 60.28; found, 60.77. *Anal.* Calcd. for $C_{13}H_{20}O$: C, 81.2; H, 10.4. Found: C, 81.0; H, 10.5.

The alcohol fraction, b. p. 100.5–103° (9 mm.), weighed 65 g., $n^{25}D$ 1.5205. The third and smallest fraction, b. p. 113° (9 mm.), $n^{25}D$ 1.5175, was not further investigated. There was a considerable tarry residue.

Cleavage of the Low-boiling Ether.—Seven and one-half grams of the ether was heated to gentle boiling with 30 g. of constant-boiling hydriodic acid. A volatile halide was evolved, which was separated by distillation, and identified as isopropyl iodide by conversion with anhydrous trimethylamine to the quaternary iodide. This was recrystallized from alcohol, m. p. 290°, and showed no depression in melting point with an authentic sample.

Oxidation of the Carbinol Mixture. A.—Fifty grams of the carbinol fraction was dissolved in 325 ml. of acetic acid, and then treated with 100 g. of chromic acid likewise in 325 ml. of acetic acid. The temperature was kept below 23°, the addition with stirring taking five hours. Three liters of water was added, and the mixture extracted well with chloroform. This extract was neutralized with sodium carbonate solution, then made just faintly acid, washed well with water, and dried over anhydrous sodium sulfate. The solvent was partially evaporated, the residual liquor extracted with sodium carbonate solution, re-acidified and washed with water, dried over anhydrous potassium carbonate, and the remaining solvent evaporated *in vacuo*. The ketone mixture was investigated directly with 2,4-dinitrophenylhydrazine. Two such hydrazones were isolated after repeated recrystallizations from mixtures of alcohol and chloroform or dioxane. The main one, which constituted about 65% of the total, m. p. 159.5–160.5°, was quite soluble in hot alcohol, and was identified as a derivative of isobutyrophenone. The second was red, insoluble in hot alcohol, and melted at 241–242°.

The alkaline extract above was acidified with acetic acid and extracted with ether. The ether extract was

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[2] Graduate student, McGill University, holding a Canadian National Research Council Bursary, for which grateful acknowledgment is hereby made.

[3] Stevens, Allenby and DuBois, THIS JOURNAL, **62**, 1424 (1940).

[4] Lévy and Tabart, *Bull. soc. chim.*, [4] **49**, 1776 (1940).

dried over anhydrous sodium sulfate and evaporated. After some manipulation, 0.3 g. of a solid acid was obtained, which crystallized from aqueous alcohol, m. p. 77–78°.[5] The amide, prepared in the usual way, melted at 158–158.5°,[3] and so the acid was judged to be dimethylphenylacetic acid.

B.—Ten grams of the carbinol mixture was treated with sodium hypoiodide solution (prepared using 30 g. iodine, 60 g. potassium iodide, 240 ml. water and excess 10% sodium hydroxide solution). Only a few tenths of a gram of iodoform was obtained. The reaction was continued using 90 g. of bromine and excess sodium hydroxide solution. Some benzoic acid and a little oily acid with the odor of methylphenylacetic acid were obtained. The amount of the latter however was too small for further identification.

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(5) Wallach, *Chem. Zentr.*, **70**, II, 1047 (1899).

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Received August 16, 1940

The Heat of Dilution of Aqueous Hydrochloric Acid at 25°

By Julian M. Sturtevant

Subsequent to the publication of data on the heats of dilution of hydrochloric acid solutions by the author,[1] Gucker and Pickard[2] pointed out the necessity for correcting such data for the heat effects resulting from differences in the vapor pressures of the concentrated and diluent solutions. The required corrections have now been made.

Table I

Integral Heats of Dilution of Hydrochloric Acid Solutions at 25°

Square root of concentration (moles per 1000 g. $H_2O)^{1/2}$ Initial	Final	Diluent	Heat of dilution from initial to final concentration $-\Delta H$, joules (int.) per mole
1.2513	0.3541	0	1617
1.4840	.4229	0	2069
1.7214	.4757	0	2666
1.7783	.4528	0	2891
1.8267	.0678	0	3798
1.8267	.0943	0	3706
1.8267	.1132	0	3621
1.8267	.1339	0	3574
1.8267	.1919	0	3466
1.8267	.2230	0	3412
1.8267	.2332	0	3381
1.8267	.2676	0	3325
1.8267	.3349	0	3233
1.8267	.3367	0	3217
1.8267	.3454	0	3198
1.8267	.3836	0	3143
1.8267	.4463	0	3041
1.8267	.4748	0	2999
1.8267	.5377	0.3050	2903
1.8267	.5434	0	2883
1.8267	.6128	0.4214	2782
1.8267	.7604	.6264	2532
1.8267	.8623	.7651	2361
1.8267	.9628	.8345	2176
1.8267	.9695	.8917	2164
1.8267	1.0647	.9800	1979
1.8267	1.2179	1.1470	1651

Table II

Apparent and Partial Relative Molal Heat Content of Solute and Partial Relative Molal Heat Content of Solvent in Hydrochloric Acid Solutions at 25°

Square root of molality of hydrochloric acid	Heat content, joules (int.) per mole $\Phi_H - \Phi_H^0$	$\bar{L}_2$	$\bar{L}_1$
0.0000	0	0	0
.0500	100		
.1000	199	297	− 0.0177
.1500	295		
.2000	388	570	− .131
.2500	475		
.3000	560	810	− .405
.3500	642		
.4000	722	1039	− .914
.4500	801		
.5000	880	1271	− 1.76
.5500	959		
.6000	1039	1519	− 3.11
.6500	1120		
.7000	1202	1784	− 5.14
.7500	1285		
.8000	1369	2060	− 7.97
.8500	1455		
.9000	1544	2360	− 11.9
.9500	1636		
1.0000	1731	2699	− 17.4
1.0500	1830		
1.1000	1932	3064	− 24.7
1.1500	2038		
1.2000	2147	3467	− 34.2
1.2500	2259		
1.3000	2374	3891	− 46.2
1.3500	2492		
1.4000	2613	4348	− 61.3
1.4500	2739		
1.5000	2870	4857	− 80.5
1.5500	3005		
1.6000	3146	5436	−106
1.6500	3293		
1.7000	3443	6027	−135
1.7500	3596		
1.8000	3752	(6628)	(−168)
1.8267	3838		

The vapor pressure and density data have been taken from the "International Critical Tables." The vapor pressure of hydrogen chloride over the solutions used is small enough so that no correction for vaporization or condensation of hydrogen chloride need be applied. Both the correction for distillation of water into the air space over the more concentrated solution, and that for the con-

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(1) Sturtevant, This Journal, **62**, 584 (1940).

(2) Gucker and Pickard, *ibid.*, **62**, 1464 (1940).

densation of water from the air space over the diluent have been applied. The corrected dilution heats are listed in Table I, and the derived values of the apparent and partial molal heat content of the solute and the partial molal heat content of the solvent are given in Table II. The average deviation of the experimental points from a smooth curve drawn through them is ±3 joules per mole, if the two runs at the lowest concentrations are omitted. One run recorded in the original paper has been discarded.

The chief effect of the application of these corrections is on the extrapolation to infinite dilution, which is an arbitrary procedure at best. Thus the relatively large changes in the values of $\Phi_H - \Phi_H^0$ correspond to considerably smaller changes in the actual heats of dilution.

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RECEIVED SEPTEMBER 7, 1940

Preparation of β-Alanine Methyl Ester[1]

BY HARRY H. WEINSTOCK, JR.,[2] AND EVERETTE L. MAY[2]

The use of β-alanine ester in the synthesis and "partial synthesis" of pantothenic acid[3] has made desirable a rapid and convenient method for the preparation of that substance. Because of the instability of the free ester,[4] quantities of the material cannot be kept on hand, and must be made up immediately before use. We have found the preparation of the ester from the ester hydrochloride to be inconvenient and the yields poor.

Kuhn and Brydowna[5] have prepared a number of α-amino acid esters by esterification with diazomethane. This method has been applied to the preparation of the methyl ester of β-alanine, the product being finally obtained in high purity and good yield. The comparative instability of the final product has necessitated working out certain conditions which must be followed closely for good results.

Experimental

To 4 g. of β-alanine was added one-half of an ether solution of diazomethane freshly prepared from 20 g. of nitrosomethylurea.[6,7] After 1 cc. of water had been added, the reaction mixture was stirred mechanically until the ether solution had become colorless (fifteen to thirty minutes). The remainder of the ether solution of diazomethane was added and stirring continued another two hours. At this time gas evolution was scarcely noticeable, and only a small amount of semi-solid material remained undissolved. Omission of mechanical stirring was found to reduce the yield considerably. The ether solution was decanted and dried over anhydrous sodium sulfate in the refrigerator for one hour. The ether solution was filtered and distilled from a 10 cc. "spitzkolben" under water pump pressure at a water-bath temperature not exceeding 35°. The flask containing the crude amino acid ester was removed from the bath, the bath was warmed quickly to 75–80°, the distillation flask was again immersed and the ester distilled under vacuum utilizing a good condensing system and well-cooled (0°) receivers. A fore-run boiling 40–49° (12 mm.) (0.55 g.) was collected. The main fraction of ester (2.9 g.) came over at 50–52° (12 mm.), 54–55° (13 mm.). Conversion of the ester in the fore run to the hydrochloride indicated an additional 0.2 g. of ester, making the total yield of β-alanine methyl ester 67%.

Identification was effected by heating a small portion of the ester for one hour with water, evaporation almost to dryness and addition of 95% ethanol. The product which crystallized out melted at 194–195°. A mixed melting point with an authentic specimen of β-alanine showed no depression. The ester was further characterized through its chloroplatinate which melted, without recrystallization, at 192°. After one recrystallization from 90% ethanol–ether the m. p. was 193°. The melting point of the crude chloroplatinate is indicative of the purity of the ester.

We are grateful for the suggestions of Dr. Roger J. Williams and Dr. Donald Price who, at different times, directed this research, and to Robert Eakin and Herschel K. Mitchell for preliminary work at Oregon State College.

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[1] This research is a continuation of preliminary work carried out at Oregon State College, under a grant of the Rockefeller Foundation.

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[3] Woolley, Waisman and Elvehjem, THIS JOURNAL, **61**, 977 (1939); Williams, *Science*, **89**, 486 (1939): Williams, Mitchell, Weinstock and Snell, THIS JOURNAL, **62**, 1784 (1940); Stiller, Harris, Finkelstein, Keresztesy and Folkers, *ibid.*, **62**, 1785 (1940).

[4] Abderhalden, *Z. physiol. Chem.*, **85**, 118 (1913).

[5] Kuhn and Brydowna, *Ber.*, **70**, 1333 (1937).

(6) Gatterman and Wieland, "Laboratory Methods of Organic Chemistry," Macmillan Co., New York, N. Y., p. 272.

(7) The ethereal solution was allowed to stand over a few potassium hydroxide pellets for fifteen minutes.

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RECEIVED OCTOBER 1, 1940

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p-Nitrobenzoyl-*d*(−)- and *p*-Aminobenzoyl-*d*(−)-glutamic Acid

BY HARRY C. WINTER

Some contradictions exist in the literature as to the properties of the *p*-nitrobenzoyl derivatives of the optical isomers of glutamic acid. J. Van der Scheer and K. Landsteiner[1] reported the preparation of *p*-nitrobenzoyl-1(+)-glutamic acid and

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[1] Van der Scheer and Landsteiner, *J. Immunol.*, **29**, 371 (1935).

described it as crystallizing from water in the form of platelets, melting point 112–113°. Later, G. Ivánovics and V. Bruckner[2] described this compound and also *p*-nitrobenzoyl-*d*(−)-glutamic acid as having melting points of 170°; since no analyses were given, the purity of these products may be open to question. In each instance, the compounds were prepared by the reaction of *p*-nitrobenzoyl chloride with l(+)- or *d*(−)-glutamic acid, a reaction known to produce racemization. Corresponding amino derivatives were obtained by reduction. No optical properties of these compounds have been reported.

p-Nitrobenzoyl-*d*(−)-glutamic acid has been prepared in this Laboratory by resolution of *p*-nitrobenzoyl-*dl*-glutamic acid through repeated recrystallization of the strychnine salt from water. The slightly soluble salt of the *d*(−)-enantiomorph was obtained in good yield. After removal of strychnine, the free acid derivative crystallized from aqueous solution in fine white needles which softened at 77° and melted at 115–116° (*Anal.* Calcd. for $C_{12}H_{12}N_2O_7$: N, 9.46. Found: N, 9.39). This is in good agreement with the melting point of the l(+)-derivative reported by Van der Scheer and Landsteiner.[1] The specific rotation of the aqueous solution containing 2 moles of alkali was −16.02°.

p-Aminobenzoyl-*d*(−)-glutamic acid has been prepared in this Laboratory by the reduction of the nitro compound using the method of Van der Scheer and Landsteiner[1] for the preparation of *p*-aminobenzoyl-l(+)-glutamic acid. The compound crystallized from water in clusters of microscopic needles (*Anal.* Calcd. for $C_{12}H_{14}N_2O_5$: N, 10.53. Found: N, 10.50) melting at 166–167°, somewhat lower than that (175°) reported by Ivánovics and Bruckner.[2] Its specific rotation in aqueous solution containing 2 moles of alkali was −27.4°; in 9% hydrochloric acid +15.5°. It is possible that some racemization occurred under the conditions of the reduction.

(2) Ivánovics and Bruckner, *Z. Immunitäts.*, **93**, 119 (1938).

BIOCHEMICAL RESEARCH FOUNDATION
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RECEIVED AUGUST 1, 1940

The Preparation of Tetraphenylgermanium

BY DAVID E. WORRALL

Two classical methods for the preparation of organometallic derivatives are those of Grignard and Fittig. Surprising it is, therefore, that both are said to give poor results in the synthesis of tetraarylgermanes.[1] Perhaps that is why most investigators have not reported yields. Morgan and Drew[2] found it necessary to employ 36 molar equivalents of phenylmagnesium bromide, obtaining a 40% yield of tetraphenylgermanium. Kraus and Foster[3] modified the usual procedure by converting the intermediate magnesium compound into diphenylzinc in an atmosphere of nitrogen, subsequently replacing the ether with toluene. Excellent yields are obtainable but the procedure is elaborate and time consuming and a rather large excess of reagent is used.

It has been found in this Laboratory that the presence of zinc compounds or a large excess of the organomagnesium derivative is unnecessary. A good yield of tetraphenylgermanium may be obtained by the usual technique provided only that toluene is substituted for ether. A similar replacement in the Fittig synthesis of the same compound gives fair results.

Experimental

A solution of phenylmagnesium bromide prepared from 29 g. of monobromobenzene was filtered by decantation mixed with 100 cc. of dry toluene and heated on a water-bath to remove ether. While still warm and connected to a reflux condenser, 10 g. of germanium tetrachloride mixed with 10 cc. of toluene was run in with occasional shaking at such a rate that vigorous boiling took place. The mixture was then heated for two hours on an oil-bath. Following hydrolysis using hydrochloric acid, several hundred cc. of warm toluene was added and the filtered toluene layer concentrated to a small bulk. White needle-like crystals separated from the yellow solution. It was filtered by suction, washed first with a few cc. of cold toluene, then with several volumes of alcohol; yield 14.1 g., m. p. 225–226° (uncor.).

In another experiment a mixture containing 10 g. of germanium tetrachloride, 100 cc. of toluene, 9 g. of granulated sodium and 30 g. of monobromobenzene was heated cautiously under a reflux condenser until the reaction started. Once started the reaction became violent so that outside cooling from time to time was necessary. The mixture was heated for an hour after the spontaneous reaction ceased and worked up while still hot. Although the solution was deeper colored than that obtained by the magnesium method, the product was perfectly white; yield 9.6 g. Longer heating or the replacement of toluene with xylene did not noticeably increase the yield.

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RECEIVED SEPTEMBER 19, 1940

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(1) Simons, Wagner and Müller, THIS JOURNAL, **55**, 3705 (1933).

(2) Morgan and Drew, *J. Chem. Soc.*, **127**, 1760 (1925).

(3) Kraus and Foster, THIS JOURNAL, **49**, 457 (1927).