NOTES

Ribitol Pentaacetate

By W. W. Binkley[1] and M. L. Wolfrom

The acetates of the sugars and sugar alcohols are significant reference compounds especially in certain types of chromatographic techniques.[2] All of the acetates of the pentitols have been described in crystalline form save that of ribitol (synonym, adonitol). We wish to report herein the crystallization of such a derivative of this naturally occurring pentitol.

Experimental

A mixture of 2.00 g. of ribitol, 0.3 to 0.4 g. of freshly fused zinc chloride, and 20 ml. of acetic anhydride was surrounded with an ice- and water-bath and was stirred for sixteen hours. The temperature of the bath was allowed to rise gradually to 25° during this period. The reaction mixture was poured on 30 g. of finely crushed ice, was stirred for thirty minutes, and was adjusted to a *p*H of 6 with sodium bicarbonate. This solution was extracted with four 25-ml. portions of chloroform. Solvent removal from the dried extract yielded crystalline material; yield 4.78 g. Pure material was obtained on recrystallization from diethyl ether; yield 3.87 g., m. p. 51°. A further crop of less pure material (0.33 g.) was obtainable from the mother liquor on the addition of petroleum ether (b. p. 60–65°). The substance crystallized in elongated prisms that were soluble in benzene, chloroform, ethanol and diethyl ether.

Anal. Calcd. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12; CH_3CO, 13.80 ml. of 0.1 *N* NaOH per 100 mg. Found: C, 49.62; H, 6.07; CH_3CO, 13.82 ml.

(1) Sugar Research Foundation Fellow of The Ohio State University Research Foundation (Project 190).

(2) W. H. McNeely, W. W. Binkley and M. L. Wolfrom, This Journal, **67**, 527 (1945).

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Dihydro-*exo*-dicyclopentadiene

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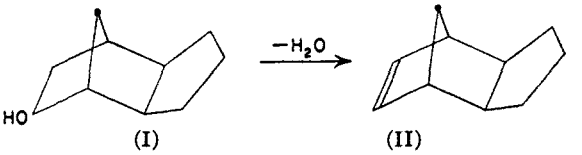
Recently Bartlett and Goldstein[2] showed that the hitherto rare *exo* isomer of dicyclopentadiene can be readily obtained by dehydrohalogenation of iodo-dihydro-*exo*-dicyclopentadiene[3] which may conveniently be prepared by warming ordinary *endo*-dicyclopentadiene with hydriodic acid.[3]

By dehydrating hydroxy-tetrahydro-*exo*-dicyclopentadiene[4] (I) with phosphoric acid we have obtained the corresponding dihydro-*exo*-dicyclopentadiene (II) in which the residual double bond is in the bridge endomethylene ring.



(I) (II)

This completes the series of isomeric dihydrodicyclopentadienes.

Experimental

Dihydro-*exo*-dicyclopentadiene.—A mixture of 15 g. of sirupy 85% phosphoric acid and 198 g. of hydroxytetrahydro-*exo*-dicyclopentadiene[4] which had twice been recrystallized from nitroethane to m. p. 53°, was stirred and heated in an oil-bath under a reflux condenser to which was attached a water separator device. After heating for about one hour at 150–230°, 40 cc. of oily liquid and 20 cc. of water had collected in the separator. The residual oil in the still flask was washed with water and distilled under reduced pressure to yield 40 g. of oil boiling at 80–95° (40 mm.). This was combined with the 40 cc. of oil distillate and the mixture redistilled. A fraction (68 g.) boiling at 89–93° (40 mm.) was thus secured. This was refractionated through an efficient packed column to yield 61 g. of colorless oil b. p. 89–91° (39 mm.) having $n^{25}D$ 1.4993; d^{25}_4 0.9571. It boiled at 182° (768 mm.).

Anal. Calcd. for $C_{10}H_{14}$: C, 89.55; H, 10.44. Found: C, 89.45; H, 10.43.

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(1) Present address: Industrial Rayon Corporation, Cleveland, Ohio.

(2) Bartlett and Goldstein, This Journal, **69**, 2553 (1947).

(3) Previously referred to as iodo-dihydro-*nor*-dicyclopentadiene, Bruson and Riener, *ibid.*, **67**, 1179 (1945).

(4) Previously referred to as hydroxy-tetrahydro-*nor*-dicyclopentadiene, Bruson and Riener, *ibid.*, **67**, 727 (1945).

Addition of Organolithium Compounds to the Azomethine Linkage of γ-Picoline and 6-Methoxyquinoline

By Henry Gilman and H. Smith Broadbent[1]

In connection with some studies on compounds having possible physiological activity, occasion arose to prepare some "anil addition" compounds of γ-picoline and 6-methoxyquinoline.

At −80° *n*-butyllithium was found to be without observable action on γ-picoline in ether solution. Upon carbonation of the reaction mixture, γ-picoline and valeric acid were the only isolable products. At −10°, however, addition to the anil linkage is the predominant reaction yielding first the lithium salt of 2-*n*-butyl-4-methyl-1,2-dihydropyridine (not isolated) which upon acidification and air oxidation gave 2-*n*-butyl-4-methylpyridine.

Addition of α-thienyllithium to 6-methoxyquinoline at the reflux temperature of ether similarly yielded 2-(α-thienyl)-6-methoxyquinoline.

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Experimental

2-*n*-Butyl-4-methylpyridine.—Twenty-three grams (0.25 mole) of γ-picoline in 75 ml. of anhydrous ether was added dropwise with stirring to an equivalent amount of 0.94 molar butyllithium in ether, which was maintained at −10° in an ice–salt-bath. A yellow precipitate formed. After one and one-half hours stirring the mixture was carbonated by pouring jet-wise into a slurry of Dry Ice and ether. After the Dry Ice had evaporated, the mixture was extracted with 20% sodium hydroxide solution. On acidifying the alkaline extract only a very small amount of red gum was obtained from which a very small amount (*ca.* 10–20 mg.) of unidentified crystalline material, m. p. 148–150°, separated on cooling. The alkali-insoluble portion was a yellow oil, which was aerated to oxidize the dihydropyridine to the pyridine, dried over barium oxide and distilled. Five grams of the anil addition product was obtained boiling at 200–202° (740 mm.). A Siwoloboff boiling point determination gave reproducible values at 201–202°: $n^{20}D$ 1.4778; sp. gr.$^{27}_{27}$ 0.885.

Anal. Calcd. for $C_{10}H_{15}N$: N, 9.39. Found: N, 9.50.

The picrate was prepared in boiling ethanol giving bright yellow crystals, melting at 88.5–90.5° after two recrystallizations from ethanol.

Anal. Calcd. for $C_{16}H_{18}O_7N_4$: N, 14.8. Found: N, 14.9.

2-(α-Thienyl)-6-methoxyquinoline.—Thiophene, 30.3 g. (0.36 mole) in 100 ml. of anhydrous ether, was metalated with 0.3 mole of butyllithium in the conventional apparatus under a nitrogen atmosphere. Then 34 g. (0.214 mole) of 6-methoxyquinoline in 60 ml. of ether was added dropwise to the stirred α-thienyllithium at such a rate as to maintain reflux. A greenish-white precipitate formed. After stirring the mixture for one hour, it was hydrolyzed carefully with 200 ml. of water.

The ether phase was separated, mixed with 25 ml. of nitrobenzene to oxidize the dihydroquinoline, and distilled. A fraction (nitrobenzene, aniline, thiophene) was collected at 90–105° (18 mm.). Then 26 g. (a 75% recovery) of 6-methoxyquinoline was obtained boiling at 105–114° (18 mm.). (Its identity was checked by preparing its picrate and comparing the picrate prepared from an authentic sample of 6-methoxyquinoline. Both melted at 217–218°, with no depression on mixing.) A final fraction of 3.5 g. (6.8%) boiling 200–210° (18 mm.), was collected and crystallized from a benzene and ligroin mixture; melting point, 137–138.5°.

Anal. Calcd. for $C_{14}H_{11}ONS$: N, 5.81. Found: N, 5.69.

A picrate of the product was prepared and recrystallized from ethanol. The melting point was 190.5–192°.

Anal. Calcd. for $C_{20}H_{14}O_8N_4S$: N, 11.9. Found: N, 11.75.

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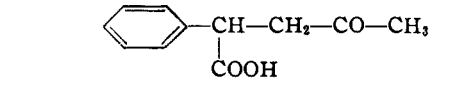
α-Phenyl-levulinic Acid, a Product of the Alkaline Degradation of Penicillin G

BY M. W. GOLDBERG, WILLIAM R. SULLIVAN AND W. E. SCOTT

In the course of studies on the chemistry of penicillin G carried out in 1945, we encountered significant amounts of a degradation product which was readily identified as α-phenyl-levulinic acid (I). It was obtained from penicillin G, along with larger quantities of phenylacetic acid, by treatment with aqueous sodium hydroxide.



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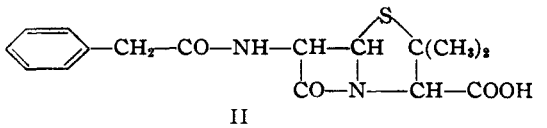

II

At that time no information was available to us concerning results of degradative studies carried out in other laboratories. Meanwhile, there have appeared several publications on the chemistry of penicillin[1] which discuss in survey form the experimental evidence that led to the general acceptance of formula II for penicillin G. These publications, while mentioning a great number of degradation products obtained from the various penicillins, do not contain any reference to α-phenyl-levulinic acid.

The accepted β-lactam formula for penicillin G (II) does not contain the carbon skeleton of α-phenyl-levulinic acid, and it is not readily apparent to us by what series of reactions this C-11 acid could be formed from it. The β-lactam structure is based upon such a wide variety of evidence that it seems necessary to conclude that our product is an artifact formed somehow by a reductive condensation of certain of the penicillin G degradation products. The mechanism, however, is obscure.

There is no question that the α-phenyl-levulinic acid isolated by us is actually formed from penicillin G. The preparation has been repeated several times during the past two and a half years, using sodium penicillin G of high purity, obtained by different methods from different lots of penicillin. The α-phenyl-levulinic acid has been isolated as such and in the form of its methyl ester and as the *p*-nitrophenylhydrazone, all of which have proved to be identical with authentic synthetic specimens.

Experimental

Isolation of α-Phenyl-levulinic acid.—Crystalline penicillin G sodium salt (2.694 g.), a composite of several pure samples obtained by a chromatographic process, was dissolved in 140 ml. of *N* sodium hydroxide which had been freed of dissolved oxygen by boiling in a stream of nitrogen. The solution was boiled under reflux for one hundred minutes, while nitrogen was passed into the mixture through a capillary. Ammonia was evolved. After cooling, the solution was acidified with sulfuric acid, saturated with sodium chloride, and extracted with ether. Removal of the solvent from the extract left 1.106 g. of a deep purple oil which was sublimed *in vacuo*. The fraction subliming between 75° and 129° (201 mg.) was recrystallized twice from ligroin and gave 54 mg. of an acid melting at 121–124°. This was combined with corresponding fractions from other experiments and recrystallized from *n*-hexane, which raised the melting point to 124–125.5°. The melting point of a mixture with a

(1) Committee on Medical Research, O. S. R. D., *Science*, **102**, 627 (1945); du Vigneaud and co-workers, *ibid.*, **104**, 431 (1946); Editorial Board of Monograph on the Chemistry of Penicillin, *ibid.*, **105**, 653 (1947); **106**, 503 (1947).