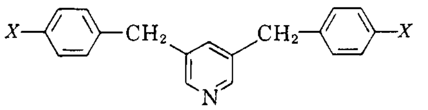
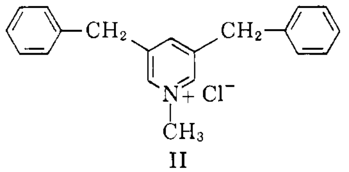
with 2,6-lutidine.[7] The ultraviolet spectrum of Ia (λ_{max} 262, 268, 276 mμ, $\epsilon_{max.}$ 4180, 4650, 3860) is strikingly similar to that of 3,5-lutidine.[8] The infrared spectrum is also consistent with Ia, as is the empirical formula, $C_{19}H_{17}N$.[9]

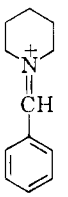




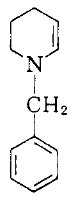
II

Ia. X = H
Ib. X = $N(CH_3)_2$
Ic. X = $N(C_2H_5)_2$

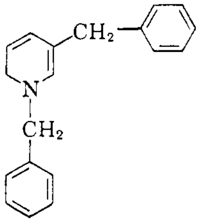
The molecular formulas and ultraviolet spectra reported by Parker and Furst are consistent with structures Ib and Ic.[10] The simplest mechanism for this transformation involves rearrangement of the initially formed Schiff cation III to the enamine IV followed by condensation with benzaldehyde, yielding the dibenzyldihydropyridine V. Condensation with a third molecule of benzaldehyde followed by displacement of the product from the N-benzyl group by piperidine gives 3,5-dibenzylpyridine.



III



IV



V

An analogous condensation was reported in 1891 by Rügheimer,[11] who isolated 3,5-dibenzylpyridine and benzoic acid from the reaction of benzaldehyde with N-benzoylpiperidine in a sealed tube, although his proof of structure was not conclusive. Our results suggest that benzaldehyde reacts with the free base rather than the benzamide, and that water so produced is consumed in hydrolysis of the benzamide. We are investigating other examples of this reaction.

EXPERIMENTAL

3,5-Dibenzylpyridine. A solution of 15 ml. of benzaldehyde, 5 ml. of piperidine, and a few drops of glacial acetic acid in 80 ml. of dry toluene was heated under reflux for 48 hr. under a Dean-Stark trap. The toluene was distilled *in vacuo* leaving 21 g. of dark syrupy residue of which 13.4 g. was dissolved in dry benzene and chromatographed on 550 g. of Merck acid-washed alumina. Non-crystalline material, total weight 5.3 g., was eluted with benzene, benzene-ether mixtures and finally ether. The last ether fractions were combined to give 2.14 g. of crude crystalline 3,5-dibenzylpyridine, m.p. 82–88°. (Thus the product isolated incorporated 25% by weight of the initial piperidine.) This material was recrystallized once from ether, then five times from acetone to give 394 mg., m.p. 90°.

Anal. Calcd. for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found[12]: C, 87.98; H, 6.64; N, 5.43.

Portions of this sample were used for all spectral measurements and for the preparation of the methochloride.

3,5-Dibenzylpyridine methochloride. To a solution of 20 mg. of the free base in 0.2 ml. of carbon tetrachloride was added a slight excess of methyl iodide. The solution turned yellow immediately. After a few minutes the precipitated crystalline methiodide was removed by filtration and stirred with an aqueous slurry of freshly precipitated silver chloride. The suspension was filtered and the clear filtrate was lyophilized to give about 20 mg. of a white, hygroscopic solid. For NMR analysis the methochloride was dissolved in deuterium oxide, filtered, lyophilized to dryness and redissolved in deuterium oxide.

Spectra. NMR spectra were obtained for degassed 10% solutions using the Varian 60 mc. spectrometer. For the free base in carbon tetrachloride solution tetramethylsilane was the internal standard. For the methochloride in deuterium oxide adventitious water was the internal standard. Chemical shifts were measured by the conventional sideband technique. Methochloride samples were not spun.

The ultraviolet spectrum of the free base in 95% ethanol was determined using a Cary recording spectrophotometer.

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(7) Pople, Schneider, and Bernstein, *op. cit.*, p. 128.

(8) R. J. L. Andon, J. D. Cox, and E. F. G. Herington, *Trans. Faraday Soc.*, **50**, 918 (1954).

(9) The analysis given by Skraup and Böhm is only slightly better for $C_{20}H_{19}N$ than for $C_{19}H_{17}N$.

(10) R. H. Poirier *et al.* (paper presented before the St. Louis Meeting of the American Chemical Society, March, 1961, Abstracts 18-O) have also proposed these structures for the compounds of Parker and Furst.

(11) Rügheimer, *Ber.*, **24**, 2186 (1891); **25**, 2421 (1892); *Ann.*, **280**, 36 (1894).

(12) Scandinavian Microanalytical Laboratory, Copenhagen, Denmark.

The Synthesis of 2,2-Diphenyltetrahydro-3-furonitrile

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Received July 5, 1961

In connection with another problem, it became desirable to prepare an authentic sample of the compound named in the title. A synthesis of this material was achieved in the following manner.

Lithium aluminum hydride reduction of ethyl γ,γ-diphenylparaconate[2] (Ia), prepared by a Re-

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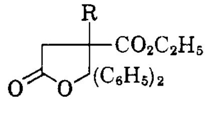
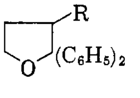
(1) This paper is abstracted from a thesis submitted by Sándor Barcza for the B.A. degree, Princeton University, 1960.

(2) W. Borsche, S. Kettner, M. Gilles, H. Kühn, and R. Manteuffel, *Ann.*, **526**, 1 (1936).

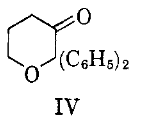
formatsky reaction using benzophenone and ethyl iodosuccinate, gave the expected triol II. The same triol could be prepared somewhat more easily by reduction of the bromolactone Ib,[3] itself formed by the action of bromine on the Stobbe condensation product of benzophenone.



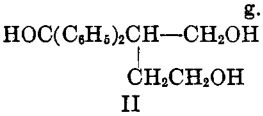
Ia. R = H
b. R = Br



IIIa. R = CH_2OH
b. R = $CH_2OSO_2C_7H_7$
c. R = CO_2H
d. R = $CONH_2$
e. R = CN
f. R = CHO
g. R = CH=NOH



IV



$HOC(C_6H_5)_2CH{-}CH_2OH$, CH_2CH_2OH on CH

II

Acid treatment of triol II could lead to several tetrahydrofurans, but it was expected that IIIa, derived from a tertiary, benzilic carbonium ion, should predominate. The single product formed by warming the triol with *p*-toluenesulfonic acid was assigned this structure on the basis of its ready formation of a *p*-toluenesulfonate (IIIb) and its oxidation to an acid (IIIc) without loss of carbon. Conversion of the acid to the desired nitrile (IIIe) was accomplished in a straightforward manner through dehydration of the amide (IIId) with phosphorus pentachloride.

An alternate route from the alcohol (IIIa) was investigated, employing the recently introduced method of Kornblum,[4] oxidation of primary *p*-toluenesulfonates with dimethyl sulfoxide. After some experimentation, conditions were found which gave the aldehyde (IIIf) in low but reproducible yield. A persistent by-product of this reaction was benzophenone, detected in the reaction mixture by its strong infrared absorption at 6.0 μ, and isolated as its 2,4-dinitrophenylhydrazone. A plausible mechanism for its formation is shown in Fig. 1; the reaction is visualized as a fragmentation[5] reaction.

As tertiary amine oxides have been reported to oxidize alkyl halides to aldehydes,[6] it was not surprising to find that 3-picoline *N*-oxide also converted the tosylate to a mixture of aldehyde IIIf and benzophenone, as evidenced by the infrared spectrum of the reaction mixture.

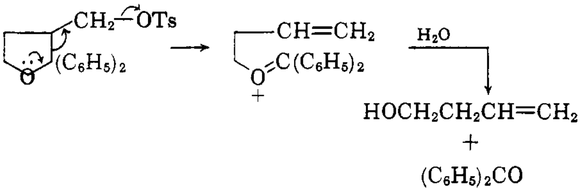


Figure 1

Difficulty in isolating the aldehyde in pure form made it preferable to proceed directly to the oxime IIIg by adding hydroxylamine hydrochloride to the dimethyl sulfoxide reaction mixture. The oxime was dehydrated readily to the nitrile IIIe, identical with the product of the first route.

It has recently been reported that oxidation of cyclohexanone with selenous or selenic acid and hydrogen peroxide gave cyclopentane carboxylic acid.[7] These reagents were used to oxidize 2,2-diphenyltetrahydropyran-3-one (IV), in the hope of effecting ring contraction to the acid, IIIc, but the only product isolated was benzophenone.

EXPERIMENTAL

Melting points were taken in unsealed capillaries, and are uncorrected. Microanalyses were performed by the Schwarzkopf Analytical Laboratory, Woodside, N. Y.

Ethyl-β-bromo-γ,γ-diphenylparaconate (Ib). The following procedure, based on the iodolactonization method of van Tamelen and Shamma,[8] was found preferable to the original method of Stobbe.[3] To a solution of β-carbethoxy-γ,γ-diphenylvinylacetic acid[9] (10 g.) and potassium bromide (36 g.) in 1 l. of 0.9*M* sodium bicarbonate was added dropwise 49.8 g. (17 ml.) of bromine. When the addition was complete, the mixture was stirred for 30 min. and the excess bromine removed by the addition of sodium thiosulfate. The solid bromolactone was filtered, washed well with water, and vacuum dried, affording 12.34 g.(98%) of light yellow crystals, m.p. 92–96°. Recrystallization from acetone-petroleum ether (b.p. 60–70°) gave 9.81 g. of colorless lactone, m.p. 95–96° (lit.[3] m.p. 95.5–96.5°).

1,1-Diphenyl-2-hydroxymethylbutane-1,4-diol (II). A. A suspension of 6.21 g. of ethyl γ,γ-diphenylparaconate[2] (Ia) in 200 ml. of absolute ether was added slowly to a stirred slurry of 3.85 g. of lithium aluminum hydride in 200 ml. of ether. The mixture was stirred overnight, then cooled to 0°, and the excess hydride decomposed by the dropwise addition of 25 ml. of acetic acid. The resulting mixture was shaken with 350 ml. of ice-cold 1:6 sulfuric acid, the layers separated, and the aqueous layer extracted with two 100-ml. portions of ether. The combined ether solutions were washed with dilute bicarbonate, dried, and concentrated, giving 5.1 g. (93%) of the triol, m.p. 122–123°. For analysis, a sample was recrystallized twice from chloroform and once from benzene, and melted at 122–122.5°.

Anal. Calcd. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.79; H, 7.19.

B. A solution of 7.83 g. of ethyl-β-bromo-γ,γ-diphenyl-

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(3) H. Stobbe, *Ann.*, **308**, 89 (1899).

(4) N. Kornblum, W. J. Jones, and G. J. Anderson, *J. Am. Chem. Soc.*, **81**, 4113 (1959).

(5) C. A. Grob, *Experientia* **13**, 126 (1957); *Theoretical Organic Chemistry* (Kekule Symposium), Butterworth, London, 1959, p. 114.

(6) (a) J. Meisenheimer, *Ann.*, **397**, 273 (1913); (b) W. Feely, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, **22**, 1135 (1957), and references cited therein.

(7) G. B. Payne and C. W. Smith, *J. Org. Chem.* **22**, 1680 (1957); H. M. Hellman and A. Rosegay, *Tetrahedron Letters*, No. **13**, 1 (1959).

(8) E. E. van Tamelen and M. Shamma, *J. Am. Chem. Soc.*, **76**, 2315 (1954).

(9) G. H. Daub and W. S. Johnson, *J. Am. Chem. Soc.*, **70**, 418 (1948).

paraconate (Ib) in 100 ml. of ether was reduced with lithium aluminum hydride as described above, and yielded 3.68 g. (68%) of the triol, m.p. 120–122°. Mixed melting point determination and comparison of infrared spectra showed its identity with the product of Part A.

2,2-Diphenyltetrahydro-3-furanmethanol (IIIa). A solution of 1.0 g. of 1,1-diphenyl-2-hydroxymethylbutane-1,4-diol and 0.12 g. of *p*-toluenesulfonic acid in 50 ml. of chloroform was refluxed for 24 hr. After cooling, the solution was dried over sodium sulfate and anhydrous sodium bicarbonate and concentrated at reduced pressure. The residual oil crystallized on the addition of 5 ml. of petroleum ether. The solid was collected and washed with the same solvent, affording 0.77 g. (83%) of colorless microcrystalline needles, m.p. 93.5-94.5°. A sample was recrystallized twice from petroleum ether, b.p. 60–70°, for analysis.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.29; H, 7.40.

The *p*-toluenesulfonate (IIIb) was prepared by keeping a solution of 0.5 g. of the alcohol and 0.4 g. of *p*-toluenesulfonyl chloride in 2.5 ml. of pyridine for 8 hr., then diluting with 50 ml. of ice water. After standing for 1 hr., the solid was filtered, and washed with water, yielding 0.77 g. (96%) of crude tosylate, m.p. 98–99°. Successive recrystallizations from chloroform–hexane, hexane, and hexane–carbon tetrachloride gave colorless crystals, m.p. 102–103°.

Anal. Calcd. for $C_{24}H_{24}O_4S$: C, 70.56; H, 5.92; S, 7.84. Found: C, 70.85; H, 5.99; S, 8.12.

2,2-Diphenyltetrahydro-3-furoic acid (IIIc). To a solution of 5.08 g. of 2,2-diphenyltetrahydro-3-furanmethanol in 15 ml. of acetic acid was slowly added, with stirring, a solution of 2.67 g. of chromic oxide in 35 ml. of acetic acid. Stirring was continued for 1 hr. and the solution kept overnight at room temperature. Dilute sulfuric acid was added and the solution extracted with chloroform; the chloroform solution was in turn extracted with dilute sodium carbonate. Acidification of the carbonate extracts in the cold and filtration of the precipitate gave 1.78 g. (33%) of colorless acid, m.p. 177–179°. Recrystallization from 50% ethanol, then from carbon tetrachloride, and twice more from benzene gave the pure acid, m.p. 188–188.5°.

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.06; H, 6.02.

2,2-Diphenyltetrahydro-3-furamide (IIId). A solution of the above acid (1.78 g.) in 25 ml. of thionyl chloride and 25 ml. of benzene was refluxed for 24 hr. After the solvents were evaporated, ammonia was bubbled into a cold solution of the residue in 50 ml. of benzene. The solid was filtered, washed well with benzene and water, and dried, affording 0.46 g. (26%) of crude amide, m.p. 170–175°. It was purified by recrystallizing twice from ethanol and once from benzene; m.p. 181–181.5°.

Anal. Calcd. for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.43; H, 6.36; N, 5.16.

Reaction of tosylate IIIb with dimethyl sulfoxide. The tosylate (0.1 g.) was added to a suspension of 0.2 g. of sodium bicarbonate in 1.0 ml. of dimethyl sulfoxide, preheated to 150°, and heated for 3 min. at temperatures varying between 145° and 195°. After cooling and filtering, infrared spectra were determined directly on the filtrates. Strong bands were present in the carbonyl region at 5.80 and 6.0 μ; the highest ratio of the 5.80- to the 6.0-μ band intensities was observed from the run at 185°.

The reaction mixtures from three such runs were combined and poured into water, then extracted with chloroform. The oil remaining after concentration of the extracts was treated with Brady's reagent. The crude mixture of 2,4-dinitrophenylhydrazones was boiled with 50% ethanol and filtered hot; from the filtrate crystallized an orange solid, m.p. 165–182°. Recrystallization from chloroform-ethanol gave 0.08 g. of benzophenone 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 238–240°; its infrared spectrum in chloroform was identical with that of an authentic sample. The yellow 2,4-dinitrophenylhydrazone insoluble in 50% ethanol, presumably the derivative of the aldehyde IIIf, was present in insufficient amount for further examination.

When the above oxidation was repeated, substituting 3-picoline *N*-oxide for dimethyl sulfoxide, the infrared spectrum of the crude product mixture was nearly identical with those of previous runs, and contained carbonyl peaks at 5.8 and 6.0 μ.

2,2-Diphenyltetrahydro-3-furaldehyde oxime (IIIg). The tosylate IIIb (1.0 g.) was added to a suspension of 0.82 g. of sodium bicarbonate in 10 ml. of dimethyl sulfoxide, preheated to 150°, and stirred for 3 min. at 185°. After cooling, hydroxylamine hydrochloride (1.36 g.) was added and the mixture kept at 50° for 30 min. with occasional stirring, then poured into water and extracted with chloroform. Concentration of the dried extracts left a light yellow oil, which was allowed to crystallize by slow evaporation of an ether-hexane solution. Unreacted tosylate (0.54 g.) crystallized first, followed by 0.20 g. of crude oxime, m.p. 127–131°. Two recrystallizations from carbon tetrachloride yielded 0.06 g. of colorless needles of the oxime, m.p. 152–153°.

Anal. Calcd. for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.29; H, 6.56; N, 5.51.

2,2-Diphenyltetrahydro-3-furonitrile (IIIe). A. A solution of 0.05 g. of 2,2-diphenyltetrahydro-3-furaldehyde oxime in 15 ml. of benzene was treated with 0.1 g. of phosphorus pentachloride and kept for 2 days at room temperature. The benzene solution was washed with ice water and dilute sodium bicarbonate, dried, and concentrated. The oily residue crystallized when rubbed with a little cold alcohol, giving 0.04 g. of colorless nitrile, m.p. 116–116.5°. Two recrystallizations from chloroform-ethanol at −10° gave large colorless prisms, m.p. 119–119.5°.

Anal. Calcd. for $C_{17}H_{15}ON$: C, 81.90; H, 6.06:, N, 5.62. Found: C, 81.67; H, 6.14; N, 5.62.

B. A suspension of 2,2-diphenyltetrahydro-3-furamide (0.20 g.) in 20 ml. of benzene was treated with 0.3 g. of phosphorus pentachloride, shaken until the solids dissolved and kept overnight. The mixture was worked up as described above, yielding 0.10 g. of crude nitrile, m.p. 107–116°. Several recrystallizations from chloroform-ethanol gave material whose infrared spectrum was identical with that of the nitrile prepared from the oxime.

Reaction of 2,2-diphenyltetrahydropyran-3-one with selenic acid. Selenic acid was prepared by refluxing a solution of 0.090 g. of selenium dioxide in 6.2 ml. of 30% hydrogen peroxide for 2.5 hr.[10] To this solution were added 2.84 g. of 2,2-diphenyltetrahydropyran-3-one,[11] 8 drops of pyridine, 5.5 ml. of 30% hydrogen peroxide, and 15 ml. of *t*-butyl alcohol, and the solution refluxed for 11.5 hr. After cooling, it was diluted with ether, washed with dilute potassium bicarbonate, then with saturated salt solution, dried over magnesium sulfate, and concentrated. The oily residue crystallized when seeded with benzophenone and gave 1.81 g. (88.5%) of benzophenone, m.p. 45–48°. Recrystallization from aqueous alcohol raised the m.p. to 48–49°, undepressed by admixture with an authentic sample.

Isolation of acidic products from the bicarbonate washes gave about 0.2 g. of oil with infrared absorption at 5.61 and 5.80 μ.

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(10) E. R. Huff and C. R. McCrosky, *J. Am. Chem. Soc.*, **51**, 1457 (1929).

(11) K. R. Huffman and D. S. Tarbell, *J. Am. Chem. Soc.*, **80**, 6341 (1958).