With 3.2 g. of phenylacetyl chloride in ether and aqueous sodium bicarbonate, 3.2 g. of the decahydro compound gave 4.4 g. of *4a-phenyl-1-phenylacetyldecahydroquinoline*, plates from ligroin, m.p. 106–107°.

Anal. Calcd. for $C_{23}H_{27}NO$: C, 82.8; H, 8.16; N, 4.2. Found: C, 83.0; H, 8.05; N, 4.4.

Reduction of the phenylacetyl derivative (3.3 g.) was effected with 1.75 g. of lithium aluminum hydride in 30 ml. of ether by boiling 20 hr. *4a-Phenyl-1-phenethyldecahydroquinoline* was isolated by decomposition with 10% sodium hydroxide. The *hydrobromide* formed colorless crystals (3.6 g.) from ethyl acetate–alcohol, m.p. 243–244°.

Anal. Calcd. for $C_{23}H_{29}N$ + HBr: C, 69.0; H, 7.55; N, 3.50. Found: C, 69.3; H, 7.50; N, 3.48.

The *hydrochloride* had m.p. 228–230°.

Anal. Calcd. for $C_{23}H_{29}N$ + HCl: C, 77.6; H, 8.5; N, 3.94. Found: C, 77.9; H, 8.78, N, 3.97.

1-Methyl-4a-phenyl-Δ^8-octahydro-2,7-quinolinedione (10 g.) reduced with 8.7 g. of lithium aluminum hydride (8.7 g.) gave 7.93 g. of crude product. This was purified through its *picrate*, yellow needles (12.3 g.) from alcohol, m.p. 182–184°.

Anal. Calcd. for $C_{16}H_{21}N$ + $C_6H_3NO_7$: C, 57.9; H, 5.3; N, 12.3. Found: C, 58.8; H, 5.43; N, 12.3.

Regenerated from its picrate, *1-methyl-4a-phenyl-Δ^7-octahydroquinoline* (VI, 87% yield) had b.p. 172–173° at 13 mm., n_D^{25} 1.5653 (supercooled); m.p. 57–59°; weak absorption at 1642 cm.$^{-1}$ ($CHCl_3$).

Anal. Calcd. for $C_{16}H_{21}N$: C, 84.5; H, 9.31. Found: C, 84.4; H, 8.91.

The *hydroiodide* formed crystals from water, m.p. 256–258° dec.; weak absorption at 1645 cm.$^{-1}$ (Nujol).

Anal. Calcd. for $C_{16}H_{21}N$ + HI: C, 54.1; H, 6.24; N, 3.94. Found: C, 54.4; H, 6.19; N, 4.02.

The *perchlorate* formed crystals from alcohol, m.p. 253–255° dec.; weak absorption at 1645 cm.$^{-1}$ (Nujol).

Anal. Calcd. for $C_{16}H_{21}N$ + $HClO_4$: C, 58.6; H, 6.77; N, 4.27. Found: C, 58.8; H, 6.73; N, 4.22.

When VI (5.5 g.) was shaken with Raney nickel in alcohol under hydrogen at 30 lbs., one equivalent of the gas was absorbed and 5.14 g. of 1-methyl-4a-phenyldecahydroquinoline was obtained, b.p. 160–161° at 8 mm., $n_D^{25.5}$ 1.5541; reported[11] 126–128° at 3 mm. Its hydrochloride had m.p. 224–226°, reported,[11] 225–226°. Its perchlorate formed crystals from alcohol m.p. 210–211°.

Anal. Calcd. for $C_{16}H_{23}N$ + $HClO_4$: C, 58.3; H, 7.33; N, 4.25. Found: C, 58.5; H, 7.38; N, 4.11.

Oxidation of 3.1 g. of 1-methyl-4a-phenyldecahydroquinoline was effected by heating it with 16.7 g. of mercuric acetate in 135 ml. of 5% acetic acid for 1 hr. at 95°. Mercurous acetate (99–100% yield) was then removed by filtration, and the remainder of the mercury was precipitated with hydrogen sulfide. The resulting crude enamine (VII), a pale yellow oil, showed strong absorption at 1638 cm.$^{-1}$. Treatment with perchloric acid in alcohol gave 2.3 g. of *1-methyl-4a-phenyl-Δ^8-octahydroquinoline perchlorate*, prisms m.p. 134–136°; strong absorption at 1671 cm.$^{-1}$

Anal. Calcd. for $C_{16}H_{21}N$ + $HClO_4$: C, 58.6; H, 6.77; N, 4.27. Found: C, 58.9; H, 6.75; N, 4.21.

The same perchlorate was obtained in 70% yield from the base obtained from 3 g. of 1-methyl-4a-phenyl-Δ^8-octahydro-2-quinolone by treatment with 1.4 g. of lithium aluminum hydride in 100 ml. of ether for 10 hr.

Regenerated from its perchlorate, *1-methyl-4a-phenyl-Δ^8-octahydroquinoline* (VII) formed an oil that darkened on exposure to air; b.p. 125–127° at 3 mm.; n_D^{25} 1.5718.

Anal. Calcd. for $C_{16}H_{21}N$: C, 84.5; H, 9.31. Found: C, 84.7; H, 9.25.

Acknowledgment. The authors thank Mrs. O. Hamerston and Mr. W. C. Kuryla for analytical results.

MINNEAPOLIS, MINN.

(11) N. Sugimoto, H. Kugita, and T. Fujita, *J. Pharm. Soc. Japan*, **75**, 177 (1955); *Chem. Abstr.* **50**, 1814 (1956).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF PHARMACY, UNIVERSITY OF ILLINOIS]

The Synthesis of *trans*-2,4-Dioxo-3-hydroxydecahydroquinazoline[1]

LUDWIG BAUER AND C. N. V. NAMBURY

Received August 1, 1960

The synthesis of *trans*-hexahydrophthalo(benzoylhydroxamic) and 5-norbornene-*endo-trans*-2,3-dicarbo(benzoylhydroxamic) acids, III and IV, is described. Various rearrangements of these hydroxamic acids are discussed.

The synthesis of 3-hydroxy-[2] and 3-benzenesulfonyloxy-5,6-dihydrouracil[3] was extended to a synthesis of 2,4-dioxo-3-hydroxydecahydroquinazoline, V, and to several of its derivatives. Our original intention was to prepare both the *cis* and *trans* isomers of V by unequivocal syntheses from the corresponding *cis* and *trans* methyl hexahydrophthalates.

To avoid isomerization during the synthesis of methyl *cis*-hexahydrophthalate, *cis*-hexahydrophthalic anhydride was refluxed with methanol to afford methyl hydrogen *cis*-hexahydrophthalate[4] which in turn was treated with diazomethane. The *cis* ester so obtained was identical with that made more conveniently by the esterification of the anhydride with methanol in the presence of sulfuric acid.[5] Isomerization of the *cis* ester by sodium ethoxide in methanol at 100° according to the method of Hückel[6] yielded the *trans* ester.

(1) The authors would like to express their appreciation for the support of this work through Grant CY-4661 from the National Cancer Institute of the National Institute of Health, United States Public Health Service.

(2) C. D. Hurd, C. M. Buess, and L. Bauer, *J. Org. Chem.*, 19, 1140 (1954).

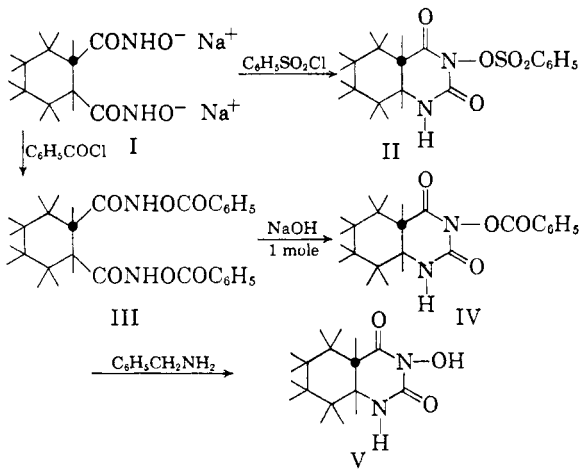
(3) C. D. Hurd and L. Bauer, *J. Am. Chem. Soc.*, 76, 2791 (1954).

(4) C. G. Overberger and P. Kabasakalian, *J. Org. Chem.*, 21, 1124 (1956).

(5) H. A. Smith and T. Fort, *J. Am. Chem. Soc.*, 78, 4000 (1956).

(6) W. Hückel and E. Groth, *Ber.*, 58, 449 (1925).

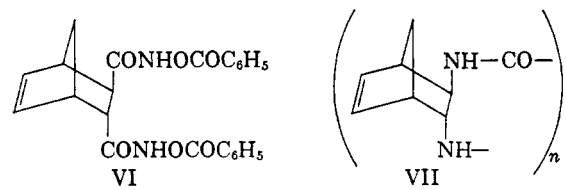
The reactions of hydroxylamine and sodium methoxide with either the *cis* or the *trans* ester gave a sodium hydroxamate, I, which on benzoylation afforded only *one* benzoylhydroxamic acid, III, m.p. 188°. However, the notable difference was the yield of III: 6% from the *cis* and 45% from the *trans* ester. Furthermore, acidification of the sodium hydroxamate from the *cis* ester yielded no crystalline product, while that from the *trans* ester gave *trans*-hexahydrophthalohydroxamic acid, m.p. 191–192°. We feel that this hydroxamic acid is identical to one previously described[7] as "cis"-hexahydrophthalohydroxamic acid, m.p. 191–193°, which was prepared by heating methyl *cis*-hexahydrophthalate with hydroxylamine and sodium methoxide at 100° for half an hour, followed by acidification. During that preparation, the *cis* ester isomerized to the *trans* ester (*vide et supra*) and the product subsequently isolated was *trans*-hexahydrophthalohydroxamic acid.



Rearrangement of III with *one* mole of sodium hydroxide afforded IV, presumably *via* an intermediate isocyanatobenzoylhydroxamic acid, which cyclized spontaneously. Excess sodium hydroxide on III yielded a mixture from which a small amount of V could be isolated. Ammonolysis with benzylamine smoothly removed the benzoyl group in IV to give V. Attempted hydrolysis of the benzoyl group of IV with sodium hydroxide led to a mixture thus indicating that more deep-seated changes had occurred.

The action of benzenesulfonyl chloride on I according to the method previously described[8] afforded the sulfonate ester II. Nucleophilic attack[8] on II by hydroxide ion followed by hydrolysis yielded the expected *trans*-1,2-cyclohexanediamine while attack by sodium ethoxide gave *trans*-1,2-di(carboethoxyamino)cyclohexane.

This series of reactions was applied to 5-norbornene-*endo*-2,3-dicarboxylic anhydride. Treatment of this anhydride with methanol and *p*-toluenesulfonic acid afforded the *cis* ester which was isomerized with sodium methoxide to the *trans* ester. The latter was converted by hydroxylamine and sodium ethoxide to sodium 5-norbornene-*endo*-*trans*-2,3-dicarbohydroxamate, from which we could not obtain a cyrstalline hydroxamic acid, nor would the reaction with benzenesulfonyl chloride yield a crystalline analog of II. However, benzoylation of this sodium salt afforded the benzoylhydroxamic acid, VI. However, the attempt to rearrange one hydroxamic acid grouping in VI followed by ring closure to an analog of IV failed. The only product of the reaction with one or preferably two moles of sodium hydroxide was the polymeric urea (VII). The structure of VII was established by the



following criteria: (a) Its elemental analysis indicated an empirical formula $C_8H_{10}N_2O$. (b) Its infrared spectrum exhibited two broad absorption peaks between 1520 and 1660 cm.$^{-1}$ [in potassium bromide] which resembled those shown between 1520 and 1680 cm.$^{-1}$ [in potassium bromide] by the polymeric urea, $[—NH(CH_2)_4NHCO—]_n$. The latter was prepared by the rearrangement of adipo(benzoylhydroxamic) acid.[9] When cyclization of the intermediate *β*-isocyanatobenzoylhydroxamic acid is impossible, rearrangements of the second benzoylhydroxamic group occurs to yield polyureas.[9]

In a recent paper,[10] a benzoylhydroxamic acid, m.p. 178–179°, is described, whose gross structure resembles VI, but neither its exact preparation nor its stereochemistry were reported.

EXPERIMENTAL[11]

Methyl cis- and trans-hexahydrophthalates. The *cis* ester b.p. 82° (0.5 mm.), n_D^{23} 1.4580 was prepared[5] in 85% yield from the *cis*-hexahydrophthalic anhydride[12] and converted in 82% yield to *trans* ester,[6] b.p. 72–75° (0.5–0.75 mm.) n_D^{24} 1.4539. The infrared spectra (Beckman IR-4; 10% chloroform solution) of the two esters showed the following bands:

cis Ester (in cm.$^{-1}$): 3050 (m); 2960 (s); 2880 (m); 1725 (vs); 1445 (s); 1430 (m); 1370 (inflection); 1335 (w); 1300 (m); broad absorption 1250–1170 (s); 1128 (s); 1098 (w); 1070 (w); 1038 (s); 1000 (m); 915 (vvw); 895 (w); 880 (w).

(7) M. A. Stolberg, W. A. Mosher, and T. Wagner-Jauregg, *J. Am. Chem. Soc.*, 79, 2617 (1957).

(8) For the mode of action see C. M. Buess and L. Bauer, *J. Org. Chem.*, 20, 34 (1955).

(9) C. D. Hurd and D. G. Botteron, *J. Org. Chem.*, 11, 207 (1946).

(10) F. Winternitz and C. Wlotzka, *Bull. soc. chim., France*, 511 (1960).

(11) All melting points are uncorrected. Microanalyses were carried out by Dr. Kurt Eder, Geneva, Switzerland, and Micro-Tech Laboratories, Skokie, Ill.

(12) Kindly supplied by the National Aniline Division of the Allied Chemical and Dye Corp.

trans Ester (in cm.$^{-1}$): 3050 (m); 2960 (s); 2880 (m); 1725 (vs); 1445 (s); 1432 (s); 1370 (w); 1350 (w); 1320 (s); 1300 (inflection); 1252 (s); 1215 (s); 1170 (s); 1112 (m); 1067 (w); 1042 (s); 1010 (w); 975 (w); 910 (w); 903 (w).

Sodium trans-hexahydrophthalohydroamate. Methyl *trans*-hexahydrophthalate (20.0 g.; 0.1 mole) was added to an ethanolic solution of hydroxylamine (prepared from 15.4 g. hydroxylamine hydrochloride and an equivalent amount of sodium ethoxide). This solution was stirred at 25° with a solution of sodium ethoxide (from 5.0 g. of sodium in 150 ml. ethanol). After 0.5 hr. the salt was collected and dried *in vacuo*. It weighed 24 g. and was used without further purification for the reactions described below.

trans-Hexahydrophthalohydroxamic acid. An aqueous solution of the sodium *trans*-hexahydrophthalohydroxamate (6.0 g. in 8 ml. of water) was cooled to 10° and 5% hydrochloric acid added dropwise until the solution was neutral. The hydroxamic acid (1.5 g.; 30%) crystallized and melted at 191–192°. Recrystallization from dioxane-water yielded colorless tufts, m.p. 192°.

Anal. Calcd. for $C_8H_{14}N_2O_4$ (202.2): C, 47.52; H, 6.93; N, 13.86. Found: C, 47.65; H, 6.89; N, 13.80.

trans-Hexahydrophthalo(benzoylhydroxamic) acid. Sodium *trans*-hexahydrophthalohydroxamate (7.4 g.; 0.03 mole) was dissolved in an aqueous solution of sodium acetate trihydrate (8.1 g. in 60 ml.water) and a trace of saponin was added. This solution was stirred and cooled to about 0°. Benzoyl chloride (9 ml.) was then added dropwise, the temperature of the mixture being kept between 0 and 5°. After 0.25 hr., more benzoyl chloride (3 ml.) was added and the mixture stirred for another 0.75 hr. Acidification with concentrated hydrochloric acid (7.5 ml.) yielded a solid which was filtered and was washed with 1:1 mixture of benzene-ligroin (b.p. 60–90°). The crude solid was recrystallized from dioxane and was obtained as shining plates, m.p. 188°.

Anal. Calcd. for $C_{22}H_{22}N_2O_6$ (410.4): C, 64.39; H, 5.37; N, 6.83. Found: C, 64.44; H, 5.44; N, 6.92.

The yield was 5.5 g. or 45%, based on methyl *trans*-hexahydrophthalate.

trans-2,4-Dioxo-3-benzoyloxydecahydroquinazoline. trans-Hexahydrophthalo(benzoylhydroxamic) acid (6.15 g.; 0.015 mole) was suspended in a sodium hydroxide solution (0.6 g.; 0.015 mole in 50 ml. water) and the mixture was stirred and heated on the steam bath for 1 hr. A light voluminous solid (3.5 g.; 81%) was formed which crystallized from ethanol in shining needles, m.p. 210–211°.

Anal. Calcd. for $C_{15}H_{16}N_2O_4$ (288.2): C, 62.55; H, 5.55; N, 9.75. Found: C, 62.63; H, 5.67; N, 9.69.

trans-2,4-Dioxo-3-hydroxydecahydroquinazoline. A solution of *trans*-2,4-dioxo-3-benzoyloxydecahydroquinazoline (2.88 g.; 0.01 mole) in benzylamine (1.08 g.; 0.01 mole) was heated at 150° for 40 min. The solution was cooled and triturated with 5*N* acetic acid (25 ml.). A solid (2.0 g.; m.p. 100–107°) which separated, was filtered and crystallized from benzene–petroleum ether (b.p. 60–90°) and was identified as *N*-benzylbenzamide, m.p. 105–107°, lit.,[13] m.p. 105–106°.

The aqueous filtrate was evaporated to dryness and the residue boiled with benzene (125 ml.) and this residue (1.15 g.; 62.5%), m.p. 201–203°, was recrystallized from chloroform-cyclohexane to form colorless rhombs, m.p. 204–205°.

Anal. Calcd. for $C_8H_{12}N_2O_3$ (184.1): C, 52.17; H, 6.52; N, 15.21. Found: C, 52.39; H, 6.47, N, 15.44.

An aqueous solution of this compound gave an intense red color with feric chloride.

trans-2,4-Dioxo-3-benzenesulfonyloxydecahydroquinazoline. A suspension of sodium *trans*-hexahydrophthalohydroxamate (24.0 g.; 0.1 mole) in tetrahydrofuran was stirred vigorously at 20° while a solution of benzenesulfonyl chloride (28 ml.; 0.22 mole) in tetrahydrofuran (65 ml.) was added dropwise (20 min.) so that the temperature of the reaction mixture remained at 25°. After 30 min., sodium acetate trihydrate (10.4 g.) was added to the mixture and stirring continued for another 45 min. The reaction mixture was filtered and the filtrate concentrated to one third of its volume and allowed to crystallize. The product (8.1 g.; 25%) crystallized, m.p. 203–205°. One recrystallization from tetrahydrofuran raised the m.p. to 208–209.°

Anal. Calcd. for $C_{14}H_{16}N_2O_5S$ (324.1): C, 51.86; H, 4.95; N, 8.67; S, 9.91. Found: C, 52.21; H, 4.96; N, 9.00; S, 10.22.

Rearrangement of trans-2,4-dioxo-3-benzenesulfonyloxydecahydroquinazoline (a) *With sodium ethoxide.* To a suspension of *trans*-2,4-dioxo-3-benzenesulfonyloxydecahydroquinazoline (2.4 g; 0.0075 mole) in boiling ethanol (115 ml.) was added dropwise sodium ethoxide solution (0.2 g.; sodium in 8. ml. ethanol) over a period of 10 min. The solution was then boiled another 5 min. Ethanol was removed *in vacuo* and the residue extracted with boiling benzene (160 ml.). Evaporation of the benzene solution left a residue which crystallized from benzene–petroleum ether (b.p. 60–90°) to give *trans*-1,2,-di(carbethoxyamino)-cyclohexane, (1.3 g.; 67%) m.p. 142° lit.,[14] m.p. 145°.

Hydrolysis of the urethan with concentrated hydrochloric acid according to the method of Wieland gave *trans*-1,2-diaminocyclohexane dihydrochloride in 80% yield, m.p. 300–303°, lit. m.p. 303°.[14]

(b) *With sodium hydroxide. trans*-3-Benzenesulfonyloxydecahydroquinazoline (2.43 g.) was dissolved in aqueous sodium hydroxide solution (0.3 g. in 10 ml. water) and was boiled for 45 min. A small amount of solid was filtered and the filtrates concentrated to a very small volume. Concentrated hydrochloric acid (20 ml.) was added and the solution refluxed for 6 hr. The solution was made alkaline with sodium hydroxide and benzoyl chloride (4 ml.) were added. The derivative (1.1 g.; 46%) which formed crystallized from acetic acid, m.p. 350°.

Anal. Calcd. for $C_{20}H_{22}N_2O_2$ (322.2): C, 74.50; H, 6.88; N, 8.69. Found: C, 74.55; H, 6.93; N, 8.59.

In an experiment similar to that above, benzenesulfonyl chloride (3.0 ml.) was added instead of benzoyl chloride. On acidification of the basic medium *trans*-1,2-di(phenylsulfonamido)cyclohexane (1.0 g.; 35%) was obtained, which recrystallized from benzene–petroleum ether (b.p. 60–90°), m.p. 155–156°, lit.[15] m.p. 153–155°.

trans-1,2-Diaminocyclohexane dihydrochloride was made recently by the reduction of 1,2-cyclohexanedionedioxime by sodium in ethanol[16] but no melting point of this salt was recorded. These authors characterized the free bases by its boiling point. The over-all yield of the base from ethyl 2-oxocyclohexanecarboxylate was stated to be 0–20%. In another recent attempt to prepare *trans*-1,2-diaminocyclohexane, the product of the catalytic hydrogenation of methyl phthalate was subjected to the Curtius rearrangement.[17] The base was obtained by these authors in unspecified yield and was characterized by a hydrochloride, m.p. 322–326°, a benzoyl derivative, m.p. 340–343°, and a benzenesulfonyl derivative, m.p. 153–154°.

Methyl 5-norbornene-endo-cis-2,3-dicarboxylate. This ester was prepared in 76% yield according to the method of Morgan, *et al.*,[18] b.p. 71–73° (0.25 mm.) n_D^{23} 1.4846.

Isomerization of the cis to the trans ester. The *cis* ester (26.25 g.; 0.125 mole) was refluxed in methanol containing sodium methoxide (0.6 g. sodium in 20 ml. methanol). After

(13) E. Beckmann, *Ber.*, **23**, 3334 (1890).

(14) H. Wieland, O. Schlichting, and W. v. Langsdorff, *Z. physiol. Chem.*, **161**, 74 (1926).

(15) F. M. Jaeger and L. Bijkerk, *Proc. Acad. Sci. Amsterdam*, **40**, 12 (1937).

(16) H. S. Broadbent *et al.*, *J. Am. Chem. Soc.*, **82**, 189 (1960).

(17) V. G. Iashunskil and M. N. Shchukina, *J. Gen. Chem., USSR, Engl. Transl.*, **28**, 230 (1958).

(18) M. S. Morgan, R. S. Tipson, A. Lowry, and W. E. Baldwin, *J. Am. Chem. Soc.*, **66**, 404 (1944).

1.25 hr., the solution was cooled, diluted with water (150 ml.), and the ester extracted into a benzene-ether (1:1) mixture (100 ml.). The organic layer was washed with water, with dilute sulfuric acid, and then again with water. Distillation of the organic layer afforded the *trans* ester (23.0 g.; 87%), b.p. 68–69° at 0.2 mm. On cooling, the distillate solidified m.p. 29.5–30°, lit.[19] b.p. 119–120° at 4 mm., m.p. 37–39°. The infrared spectra (10% chloroform solution) of the *cis* and *trans* esters showed notable differences:

cis Ester (in cm.$^{-1}$): 3000 (s); 1742 (vs); 1430 (s); 1358 (m); 1335 (s); 1250 (s); 1195 (s); 1165 (s); 1118 (w); 1092 (w); 1075 (m); 1040 (m); 942 (w); 908 (m); 848 (w).

trans Ester (in cm.$^{-1}$): 3000 (s); 1732 (vs); 1430 (s); 1368 (m); 1310 (s); 1260 (s); 1242 (w); broad absorption between 1210–1170 (s); 1110 (s); 1070 (w); 1022 (s); 990 (w); 910 (m); 878 (w); 862 (m).

5-Norbornene-endo-trans-2,3-dicarbo(benzoylhydroxamic) acid. The *trans* ester (21.0 g.; 0.1 mole) was treated with hydroxylamine and sodium ethoxide as described above. As the salt did not precipitate after 3 hr., the solvents were removed *in vacuo*. The residual sodium salt was dissolved in water (200 ml.) containing sodium acetate trihydrate (16.2 g.) and treated dropwise with benzoyl chloride (40 ml.) at 0°. After 2.0 hr. the mixture was acidified, with concentrated hydrochloric acid (20 ml.) and the solid filtered, washed with water, then with benzene (100 ml.) and then with ether (20 ml.). The crude solid (22.5 g.) was recrystallized from 80% ethanol (250 ml.) and it formed fine needles which weighed 21.0 g. (50%) m.p. 187° with dec.

Anal. Calcd. for $C_{23}H_{20}N_2O_6$ (420.2): C, 65.71; H, 4.77; N, 6.67. Found: C, 65.32; H, 4.78, N, 6.98.

The *cis* ester when carried through this reaction sequence afforded only 30% of the *trans*-benzoylhydroxamic acid.

Rearrangement of trans-benzoylhydroxamic acid, VI. The hydroxamic acid (4.2 g.; 0.01 mole) was dissolved in potassium hydroxide solution (1.12 g. in 26.4 ml. of water). The solution was warmed on a steam bath and within 5 min. a solid commenced to precipitate. After 1 hr. the product (2.25 g.) was collected, washed with water. It decomposed above 300°. The product was boiled with methanol (100 ml.) and refiltered. The solid decomposed above 340°.

Anal. Calcd. for $C_8H_{10}N_2O$: C, 64.00; H, 6.66; N, 18.66. Found: C, 63.71; H, 6.87; N, 18.32.

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(19) The *trans* ester was prepared by refluxing the anhydride in methanol in the presence of dry hydrogen chloride. A. T. Blomquist and E. C. Winslow, *J. Org. Chem.*, **10**, 149 (1945).

[Contribution from the Department of Chemistry, University of Delaware]

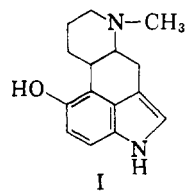
The Synthesis of 6-Hydroxy-1,3,4,5-tetrahydrobenz [cd] indole[1]

JAMES A. MOORE and MICHAEL RAHM

Received July 25, 1960

5,8-Dimethoxy-1-tetralone (IV) was converted to the aminomethyltetralin (VIII) *via* the cyanohydrin (V) and nitrile (VII). Demethylation and ferricyanide oxidation led to the 6-hydroxytetrahydrobenzindole (IX).

The importance of both 5-hydroxytryptamine (serotonin) and of lysergic acid derivatives in pyschopharmacology, and the biochemical interactions of these substances,[2] suggest that derivatives of 12-hydroxyergoline (I) might be of considerable pharmacological interest. This possibility has prompted us to undertake synthetic efforts designed to furnish access to the 12-hydroxyergoline system.



I

Most of the previous synthetic approaches to reduced benz[*cd*]indole or ergoline derivatives have involved the elaboration of rings C and D on a preformed indole nucleus[3]; an exception has very recently been described by Walker and Weaver.[4] The presence of the 12-hydroxy group in II, however, lends a rather broader scope to the synthetic possibilities. One attractive approach permitted by this substituent is embodied in the elegant synthesis of 5-hydroxyindole, described by Cromartie and Harley-Mason,[5] in which β-(2,5-dihydroxyphenyl)ethylamine is cyclized directly to the indole by mild oxidation. As an initial stage in the adaptation of this route to the ergoline system I, the preparation of the model tricyclic compound IX has been accomplished and is described in the present paper.

The required aminomethyltetralin was obtained from 5,8-dimethoxy-1-tetralone (IV)[6] by the reaction sequence shown in Fig. 1. In the preparation of the ketone IV, the procedure of Momose *et*

(1) Supported by a grant from the Geschickter Fund for Medical Research.

(2) For a review, *cf. Ann. N. Y. Acad. Sci.*, **66**, 417–480 (1957).

(3) *Inter alia:* F. C. Uhle and W. A. Jacobs, *J. Org. Chem.* **10**, 76 (1945); A. Stoll and J. Rutschmann, *Helv. Chim. Acta* **33**, 67 (1950); E. C. Kornfeld, E. J. Fornefeld, G. B. Kline, M. J. Mann, D. E. Morrison, R. G. Jones, and R. B. Woodward, *J. Am. Chem. Soc.* **78**, 3087 (1956); H. Plieninger, M. Schach v. Wittenau and B. Kiefer, *Chem. Ber.* **91**, 2095 (1958).

(4) G. N. Walker and B. N. Weaver, *J. Org. Chem.* **35**, 484 (1960).

(5) R. J. T. Cromartie and J. Harley-Mason, *J. Chem. Soc.* 2525 (1952).

(6) T. Momose, H. Oya, Y. Ohkura, and M. Iwasaki, *Pharm. Bull.* (Tokyo), **2**, 119 (1954); *Chem. Abstr.* **50**, 911 (1956).