

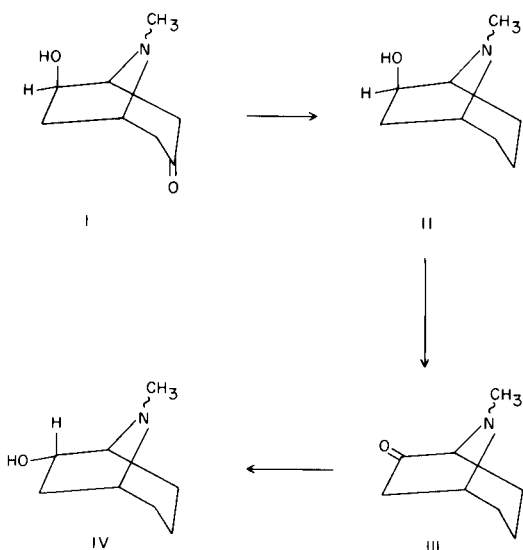
Synthesis of 6 α -Tropanol

Herbert S. Aaron and Louis P. Reiff

Chemical Research Laboratory, Research Laboratories

Apart from optical isomers, there are six possible secondary hydroxytropanes. Of these, the 3-hydroxy epimers have long been known (1), and more recently, both of the 2-hydroxy (2) and one (β) of the 6-hydroxy (3) epimers have been described. We report here the synthesis of 6 α -tropanol (IV) as the final member of this series. In addition, an improved synthesis of 6-tropanone is also reported.

The synthetic route that was followed is illustrated below:



By this route, 6 β -hydroxytropan-3-one (4) (I) was catalytically hydrogenolyzed (5) in 94% yield to 6 β -tropanol (II). Previously, the latter had been obtained from I by a Wolff-Kishner reduction (3). Chromic acid oxidation of II by a modification of the earlier procedure (3), which had given a 25% yield, resulted in a 70% yield of 6-tropanone (III). Catalytic hydrogenation of III gave 6 α -tropanol, m.p. 67°, epimerically pure by g.l.c. analysis. These results are in agreement with the expectation that hydrogenation should take place from the relatively

unhindered top (exo) side of the molecule. In view of these results, the identity of a compound, m.p. 91°, indirectly reported (6) to be 6 β -tropanol, later suggested (3) to be 6 α -tropanol, continues to remain in doubt.

EXPERIMENTAL

6 β -Tropanol (II).

6 β -Hydroxytropan-3-one (4) (I) (2.00 g., 12.9 mmoles) in 50 ml. of 1 *N* hydrochloric acid was hydrogenated (7) over 2.0 g. of platinum dioxide for 90 minutes. The mixture was filtered to remove the catalyst, and the filtrate was made basic with excess sodium carbonate and continuously extracted overnight with chloroform. The chloroform solution was dried over magnesium sulfate, then concentrated under reduced pressure. A colorless oil was obtained that crystallized when triturated under pentane to give 1.7 g. (94%) of product, shown to be a single component by g.l.c. analysis (8). Recrystallization from petroleum ether (b.p. 30-60°) gave II, m.p. 65° (lit. (3) 65°), pK_a 10.22 (0.0050 ionic strength) (9). The infrared spectrum (10) in 0.002 *M* carbon tetrachloride solution revealed a free O-H band at 3627 cm^{-1} and an intramolecular bonded O-H band at 3586 cm^{-1} . The mass spectral data have been reported (11).

6-Tropanone (III).

6-Tropanol (2.50 g., 17.7 mmoles) was dissolved in 25 ml. of glacial acetic acid at 15°. Chromic acid (3.54 g., 35.4 mmoles) in acetic acid (15 ml. plus 3 ml. of water) was added dropwise during 1 hour with stirring and cooling. When the addition was completed, the mixture was heated to 90° for 16 hours. The acetic acid was removed under reduced pressure, and the residue was made basic with saturated potassium carbonate solution and continuously extracted overnight with ether. The ether solution was dried over magnesium sulfate, then concentrated to give 1.8 g. (73%) of product, which was found to be about 95% pure by g.l.c. analysis (8). Distillation gave 1.54 g. of III, b.p. 93-95° (20 mm.), ν (carbon tetrachloride)C=O 1750 cm^{-1} , pK_a 7.05 (0.0050 ionic strength) (9), picrate, m.p. 270° (ethanol) (lit. (3) 269°). The mass spectral data have been reported (11).

6 α -Tropanol (IV).

6-Tropanone (1.2 g., 8.6 mmoles) was dissolved in 25 ml. of absolute ethanol and hydrogenated (7) over 0.2 g. of platinum dioxide for 2 hours, then filtered to remove the catalyst. The solvent was removed under reduced pressure to give an oil, 1.2 g. (99%), which was revealed to be a single component by g.l.c. analysis (8). Distillation gave IV, b.p. 100-103° (2 mm), which

crystallized spontaneously, m.p. 67° , pK_a 9.91 (0.0050 ionic strength) (9). The infrared spectrum (10) in 0.002 *M* carbon tetrachloride solution showed only a free O-H band at 3634 cm^{-1} .

Anal. Calcd. for $C_8H_{15}NO$: C, 68.0; H, 10.7; mol. wt. 141.2. Found: C, 67.9; H, 10.5; mol. wt. 141 (mass spectral (11)), 142 (neut. equiv.) (9).

A picrate was prepared in and recrystallized from ethanol, m.p. 272° .

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.4; H, 4.9; N, 15.1. Found: C, 45.3; H, 4.6; N, 14.9.

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- (7) Catalytic hydrogenations were performed in a rocking Parr apparatus at 50 p.s.i.g. hydrogen pressure and room temperature.
- (8) Conditions: 10 ft. by 0.25 in. column of Carbowax 20 M (15%) on 60/80 Gas-Chrom P at 226° and 120 ml./minutes. (He). Relative retention times: 6 α -tropanol, 7.9 minutes; 6 β -tropanol, 6.2 minutes; 6-tropanone, 4.2 minutes.
- (9) We thank Mr. C. A. Andreasen for the titration data.
- (10) Dilute solution infrared spectra were recorded on a Perkin-Elmer model 521 grating spectrophotometer, using 2 cm quartz infrared grade cells. We thank Mr. C. P. Ferguson for these data.
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Edgewood Arsenal, Md. 21010