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Azasteroids. I. A Convenient Synthesis of Ethyl 1,2,3,3-Tetrahydrobenzo[f]quinoline-3-carboxylate (1)

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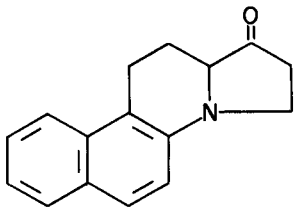
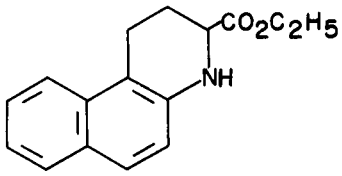
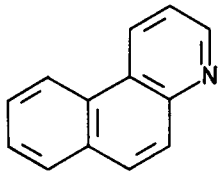
In view of the fact that a synthesis of 3-desoxy-18-nor-14-azaequilenin (I) has recently been reported (3) we wish to report on our synthetic path to this azasteroid. In this work the intermediate ethyl 1,2,3,4-tetrahydrobenzo[f]quinoline-3-carboxylate (II) was conveniently synthesized from commercially available benzo[f]quinoline (III). Compound III was converted to the Reissert compound (IV) (4), which on hydrolysis (5) gave the acid V. Catalytic hydrogenation of V gave poor results when carried out in glacial acetic acid or 15% hydrochloric acid at room temperature. However, the reduction proceeded smoothly and quantitatively by the procedure indicated in the experimental. Esterification of the crude, reduced acid hydrochloride (VI) proceeded to give II which can be converted into I as described (3).



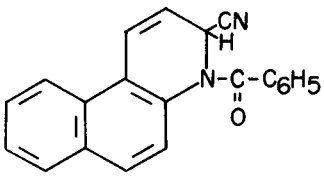
I



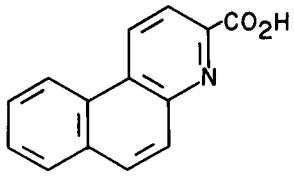
II



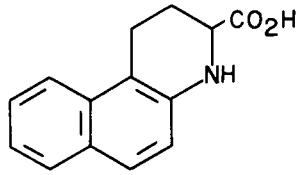
III



IV



V



VI

EXPERIMENTAL

3-Cyano-4-benzoyl-3,4-dihydrobenzo[f]quinoline (IV).

This compound was prepared from benzo[f]quinoline, benzoyl chloride and potassium cyanide in methylene chloride-water as previously described (4).

Benzo[f]quinoline-3-carboxylic acid (V).

To 31.0 g. (0.1 mole) of finely powdered Reissert compound (IV) in 25 ml. of glacial acetic acid was added 25 ml. of 48% hydrobromic acid. The mixture was refluxed for 24 hrs., cooled and filtered. The solid product was washed with ether, dried, and recrystallized from a small volume of methanol to give a quantitative yield of acid. Recrystallization of a sample from 95% ethanol gave material with m.p. 187-188°. Reported (6) for hemihydrate from ethanol, m.p. 188°.

1,2,3,4-Tetrahydrobenzo[f]quinoline-3-carboxylic acid (VI).

A mixture of 4.6 g. (0.02 mole) of acid V, 0.2 g. of platinum oxide and 100 ml. of 15% hydrochloric acid was hydrogenated at 50-60° and at 3 to 4 atmospheres pressure. The theoretical amount of hydrogen was taken up in about 2 hrs. and the mixture was filtered and concentrated to dryness to give a quantitative yield of the hydrochloride of VI. A small sample was recrystallized from methanol-ethyl acetate to give material, m.p. 217°.

Anal. Calcd. for $C_{14}H_{14}ClNO_2$: C, 63.76; H, 5.35; N, 5.31. Found: C, 63.56; H, 5.56; N, 5.20.

Ethyl 1,2,3,4-Tetrahydrobenzo[f]quinoline-3-carboxylate (II).

A mixture of 5.3 g. (0.02 mole) of the crude hydrochloride of VI in 150 ml. of absolute ethanol was brought to reflux and dry hydrogen chloride gas was passed through the mixture for 30 min. The mixture was then refluxed for 6 hrs. and concentrated to yield a white solid which was collected by filtration. The solid was dissolved in water, treated with excess potassium carbonate and the mixture extracted with ether. Concentration of the dried ether extract followed by recrystallization from 95% ethanol (m.p. 69-72°) or by distillation at reduced pressure gave 3.2 g. (63%) of the desired ester. A small sample was redistilled, b.p. 192-194°/0.3 mm.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.14; H, 7.02; N, 5.81.

The picrate was prepared in the usual manner, m.p. 157-159°.

Anal. Calcd. for $C_{22}H_{20}N_4O_9$: C, 54.54; H, 4.16; N, 11.57. Found: C, 54.27; H, 4.32; N, 11.42.

REFERENCES

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(2) U. S. Public Health Service Predoctoral Fellow.

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