REACTION OF 8-AZA-D-HOMOGONA-1,3,5(10),13-TETRAENE-12,17a-DIONES WITH N-BROMOSUCCINIMIDE

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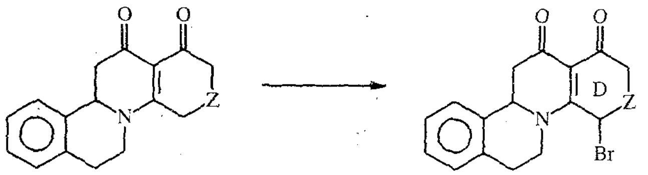
The halogen derivatives of 8-azasteroids are of interest as intermediates for planned transformations. We have shown earlier [1] that the bromination of 8-aza-D-homogonanes by means of cupric bromide is initially directed to the C_{11} carbon atom of the C ring. The halogen derivatives of this series, in particular the C_{17}-bromo- and chloro derivatives, were also obtained by annelation of 3,4-dihydroisoquinolines by 4-halogen derivatives of 2-acetyldimedone [2].

We found that the reaction of 8-aza-D-homogonanes (Ia, b) with N-bromosuccinimide is directed to the C_{15} carbon atom of the D ring with the formation of 15-bromo derivatives of 8-aza-D-homogonanes (IIa, b) previously unknown and unobtainable using other methods.



Ia,b IIa,b

I,II a Z = CH_2; b Z = CMe_2

15-Bromo-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIa, $C_{17}H_{16}BrNO_2$). A suspension of 2.13 g (12 mmoles) of N-bromosuccinimide in 20 ml of methylene chloride was added at 0°C, with stirring, to a solution of 2.68 g (10 mmoles) of 8-aza-D-homogonane (Ia) [3] in 40 ml of methylene chloride. The reaction mixture was stirred for 2 h at 0°C, and then for a further 2 h at room temperature. The reaction mixture was then washed with a 5% solution of sodium thiosulfate, water, dried over sodium sulfate, and the solvent was evaporated. The residue was dissolved in chloroform and filtered through 5 g of silica gel 5/40μ. The combined filtrate was evaporated, and the residue recrystallized from a chloroform–hexane (3:1) mixture. Bromide IIa was obtained in the form of white crystals, mp 84-87°C (dec.). M^+ 345 and 347. IR spectrum (ν, cm^{-1}): 1704-1665, 1640-1610, 1548-1512, 1500, 1370-1340, 1330-1310, 1192, 1155, 770, 760. UV spectrum [λ_{max}, nm (ε)]: 261 (8470), 312 (7930). Yield, 2.1 g (60.7%).

15-Bromo-16,16-dimethyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIb, $C_{19}H_{20}BrNO_2$). A solution of 1.78 g (10 mmoles) of N-bromosuccinimide in 2 ml of DMFA was added at 0°C, with stirring, to a solution of 2.95 g (10 mmoles) of 8-aza-D-homogonane Ib [3] in 20 ml of DMFA, the mixture was stirred at 0°C for 3 h, and then for a further 2 h at room temperature. The reaction mixture was diluted with water and 30 ml of a 1% solution of sodium thiosulfate was added. The precipitate that separated out was filtered off, washed with water, dried, and dissolved in chloroform, and the solution was chromatographed on a column with silica gel 100/160μ, eluting with chloroform. The combined eluates were evaporated and by crystallization of the residue from a chloroform–ether (2:3) mixture, the bromo derivatives IIb were obtained in the form of white crystals, mp 156-162°C (dec.), M^+ 373 and 375. IR spectrum (ν, cm^{-1}): 1680, 1617, 1592, 1530, 1495, 1440, 1350, 1338, 1293, 1195, 1084, 760, 745. UV spectrum [λ_{max}, nm (ε)]: 202 (19060), 264 (12900), 331 (12460). Yield, 2 g (53.5%).

The elemental analysis data of compounds IIa, IIb corresponded to the calculated values.

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