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LETTERS TO THE EDITOR

SYNTHESIS OF 11-N-ARYLAMINOMETHYLENE DERIVATIVES OF 8-AZASTEROIDS. A NEW REACTION OF CYCLIC SCHIFF'S BASES

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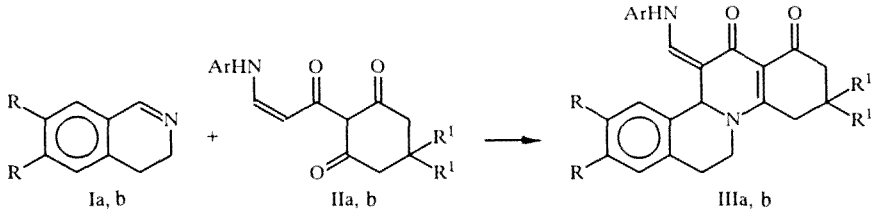
Benzo[*a*]-, dibenzo[*a,f*]- and other derivatives of quinolizine usually have valuable physiological activity [1, 2] which explains the considerable interest in the study of their properties [2-4] and synthetic methods for similar heterocyclic compounds [3-6]. The most useful of the current synthetic methods is the block technique, which is a one-stage process with regio- and stereo-selectivity (see [3, 4]).

During a study of the reactions of cyclic Schiff's bases with β-dicarbonyls and their derivatives [3-6], we observed that the 3,4-dihydroisoquinolines Ia and b reacted with 2-[3-(N-arylamino)acryloyl]cyclohexan-1,3-diones (IIa and b) to give the 8-aza-D-homogonane ABCD tetracycles IIIa and b in one step. From an examination of the literature on the reactions of Schiff's bases, β-di- and tri-carbonyl compounds, it appears that this reaction, although formally similar to one described earlier [3-6] is a new annelation reaction of cyclic Schiff's bases:



Ia, b IIa, b IIIa, b

I, IIIa R = H; I, IIIb R = OMe; IIa, IIIb R^1 = H; IIb, IIIa R^1 = Me; IIb, IIIa Ar = Ph; IIa, IIIb Ar = C_6H_4Me-*p*

The most important feature of this process is the introduction of the aminomethylene group at position 11, a group which has considerable synthetic potential, at the same time as the 8-azasteroidal tetracycle is formed. Compounds IIIa and b are clearly of theoretical and practical interest for the study of the interconnection between structure and biological activity, particularly in the immunotropic properties of 8-azasteroids [2, 7].

The reaction of the azomethines Ia and b with the enaminotriketones IIa and b was carried out by heating an equimolar mixture in a suitable organic solvent. The 8-aza-D-homogonanes IIIa and b were formed in yields of up to 60%. The mechanism of the reaction has been studied. IR spectra of KBr discs were recorded with a UR-20 spectrometer, UV spectra of ethanol solutions were recorded with a Specord M-400, mass spectra were obtained with a Varian MAT-311 mass spectrometer and melting points were determined with a Boetius block heater.

C, H, and N elemental analyses for compounds IIIa and b corresponded to theoretical values.

16,16-Dimethyl-11-N-phenylaminomethylene-8-aza-D-homogona-1,3,5(10),13-tetraen-12,17α-dione (IIIa, $C_{26}H_{26}N_2O_2$). A mixture of 3,4-dihydroisoquinoline Ia (0.34 g, 2.7 mmol) and the enaminotriketone IIb (0.76 g, 2.7 mmol) in ethanol (20 ml) was boiled under argon for 5 h. The reaction was monitored by TLC (Silufol UV-254, 9:1 chloroform-methanol). The reaction mixture was evaporated to dryness and the residue was recrystallized from 1:3-4 ethanol-ether to give yellow needles of the 8-aza-D-homogonane (IIIa) (0.7 g, 64.8%), M 398.50, m.p. 132-136°C, M^+ 398. IR spectrum: 3280, 1658, 1625, 1600, 1550, 1525, 1450, 1370, 1281, 760 cm^{-1}. UV spectrum (λ_{max},(ε)): 268 (11990), 310 (21860), 387 (19160) nm.

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2,3-Dimethoxy-11-N-p-tolylaminomethylene-8-aza-homogona-1,3,5(10),13-tetraen-12,17α-dione (IIIb, $C_{27}H_{28}N_2O_4$) was obtained analogously by boiling a mixture of 3,4-dihydroisoquinoline Ib (0.64 g, 3.3 mmol) and the enaminotriketone IIa (0.9 g, 3.3 mmol) in methanol (50 ml) for 7 h. Yellow plates of the 8-aza-D-homogonane IIIb were obtained (0.93 g). M 444.51, m.p. 149-152°C, M^+ 444. IR spectrum: 3300, 1658, 1630-1610, 1555, 1520, 1460 cm^{-1}. UV spectrum: (λ_{max} (ε): 230 (18070), 294 (14530), 385 (18020) nm.

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