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NEW SYNTHESIS OF BENZO[a]QUINOLIZINES BY THE [3+3]CYCLOCONDENSATION OF 1-ALKYL-3,4-DIHYDROISOQUINOLINES WITH AMINOMETHYLENEMALONATES

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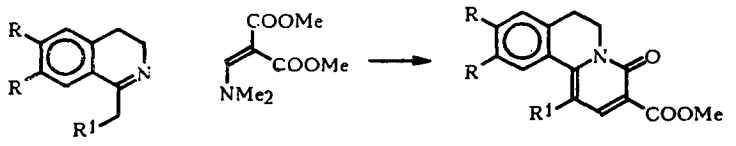
The interaction of 1-alkyl-3,4-dihydroisoquinolines with dimethyl dimethylaminomethylenemalonate has been studied.

The tricyclic benzo[a]quinolizine molecular fragment is a key part of the structure of a number of important natural [1, 2] and synthetic [3, 4] bioregulators, which is responsible for interest in the study of physicochemical, medicobiological, and other questions connected with this molecular structure. Progress in the chemistry and biochemistry of the benzo[a]-quinolizines is determined to a considerable degree by advances in the development of new effective schemes for their chemical synthesis and transformations. The arsenal of methods for the formation of the benzo[a]quinolizine tricyclic backbone that has been developed at the present time numbers several tens but, nevertheless, investigations in this direction are not ceasing [5-7], which, on the one hand, shows an unsatisfied demand for such compounds and, on the other hand, demonstrates new possibilities of organic synthesis.

Within the framework of the realization of a program on the synthesis of condensed azines and, in particular, those including a benzo[a]quinolizine tricyclic fragment by the reactions of cyclic Schiff bases and azomethines with 1,3-dicarbonyl compounds and their enolic enone derivatives, we have studied the interaction of the 1-alkyl-3,4-dihydroisoquinolines (**1a, b**) with the dimethylaminomethylenemalonate (**2**).

The condensation of the azomethines (**1a, b**) with the aminomethylenemalonate (**2**) was effected by heating equimolar mixtures of the reactants in DMF in an atmosphere of argon at 150-160°C for 6-24 h. The yields of the desired benzo[a]quinolizines (**3a, b**) amounted to 77-86% for the isolated and purified product.



1a,b **2** **3a,b**

R=R1=H(a); R=OMe: R1=Me(b)

This reaction, represented by two individual examples undoubtedly has a more general nature and can be extended to other cyclic azomethines (1-alkyl-3,4-dihydro-β-carbolines) and β-aminovinyl carbonyl compounds (β-aminoacrylates) as a simple one-stage approach to various — including natural — condensed azines with a nitrogen atom at a ring junction such as, for example, indolo[a]quinolizines.

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EXPERIMENTAL

The course of the reactions and the purity of the products were monitored by TLC on Silufol UV-254 plates. Melting points were determined on a Boetius heated stage. IR spectra were taken on a UR-20 instrument, and UV spectra were recorded on a Varian MAT-311 spectrophotometer at an energy of the ionizing electrons of 70 eV [sic]. The elementary analyses of compounds (**3a, b**) agreed with the calculated values.

4*H*-3-Methoxycarbonyl-6,7-dihydrobenzo[1]quinolizine-4-one (3a). A mixture of 1.1 g (7.5 mmole) of the azomethine (**1a**) and 1.42 g (7.5 mmole) of the aminomethylenemalonate (**2**) in 5 ml of DMF was heated at 150-160°C in an atmosphere of argon for 6 h. Then the reaction mixture was evaporated, and the residue was subjected to flash chromatography on silica gel 5/40 μ, with elution by $CHCl_3$. This gave 1.64 g of the benzo[a]quinolizine (**3a**). Yield 85.9%, mp 169-169.5°C (chlf–hexane). IR spectrum (KBr, ν_{max}, cm^{-1}): 1722, 1683, 1570, 1485, 1275, 1260, 1135. UV spectrum (EtOH, λ_{max}, nm) (ε): 263.1 (9220), 370 (15870).

4*H*-9,10-Dimethoxy-3-methoxycarbonyl-1-methyl-6,7-dihydrobenzo[a]quinolizin-4-one (3b). In a similar way to that described above, 1.1 g (5 mmole) of the azomethine (**1b**) and 0.95 g (5 mmole) of the aminomethylenemalonate (**2**) were heated for 24 h, to give 1.27 g of the benzo[a]quinolizine (**3b**). Yield 77%, mp 204-206°C (alcohol–ether).

IR spectrum (KBr, ν_{max}, cm^{-1}): 1737, 1641, 1611, 1507, 1470, 1279, 1218, 1156, 1134. UV spectrum (EtOH, λ_{max}, nm) (ε): 246.9 (14220), 385.4 (20300).

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