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Ternary condensation of cyclic azomethines, aromatic aldehydes, and barbituric acid: a new approach to the synthesis of 8,15,17-triaza-D-homogonanes

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New fused heterocyclic compounds of the 8,15,17-triaza-D-homogonane series have been obtained by ternary condensation of cyclic azomethines (1-methyl-3,4-dihydroisoquinolines) with aromatic aldehydes and barbituric acid in DMF.

Key words: azomethines, aldehydes, barbituric acid, ternary condensation; azasteroids, 8,15,17-triaza-D-homogonanes; benzo[*a*]pyrimido[4,5-*f*]quinolizines.

The reactions of cyclic azomethines and Schiff's bases with β-dicarbonyl and β-tricarbonyl compounds[1,2] and their enol derivatives[3,4] are widely used in the syntheses of fused nitrogen-containing heterocyclic compounds. They serve as the final stages of synthetic schemes in which the preliminarily built blocks are combined in a target molecular structure.[5] Multicomponent one-pot processes that make it possible to perform a sequence of reactions and to obtain a product with the required structure and stereochemistry over a single synthetic cycle are the most effective.

In a continuation of the studies dealing with the synthesis of fused nitrogen-containing heterocyclic compounds structurally related to steroids,[6—8] we found that heating equimolar mixtures of cyclic azomethines (**1a,b**), aromatic aldehydes (**2a,b**), and barbituric acid (**3**) in DMF (Scheme 1) affords previously unknown 12-aryl-substituted derivatives of 8,15,17-triaza-D-homogonane (**4a—c**).

The compounds obtained are of considerable interest in the search for new biologically active compounds with immunotropic properties.[6] There are grounds to believe that this reaction can be extended to other azomethines, methylene-active compounds, and aldehydes and can be used for the synthesis of quinolizine derivatives including those used in medicine.

Experimental

Melting points of 8,15,17-triaza-D-homogonanes **4a—c** were determined using a Boetius hot-stage apparatus. UV spectra were recorded on a Specord M-400 spectrophotometer,

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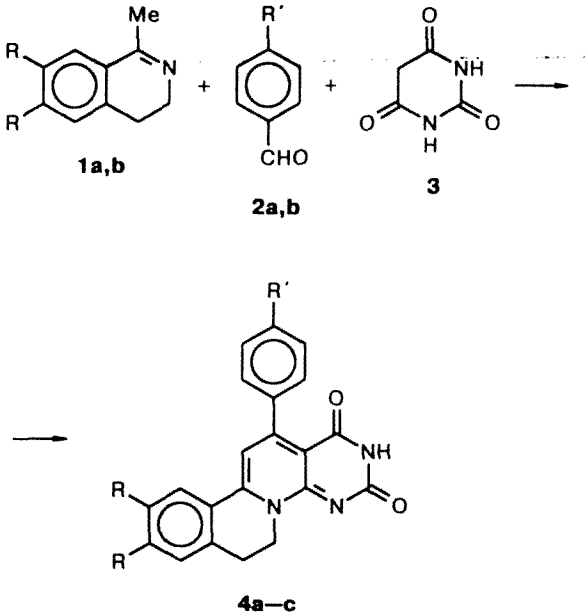
Scheme 1



R = H (**1a**, **4a**), OMe (**1b**, **4b**,**c**);

R' = H (**2a**, **4a**,**b**), OMe (**2b**, **4c**)

IR spectra were measured on a UR-20 instrument, and mass spectra were obtained on a Varian MAT-311 mass spectrometer.

12-Phenyl-8,15,17-triaza-D-homogona-1,3,5(10),9(11),12,14-hexaene-16,17a-dione (4a). A mixture of azomethine **1a** (0.87 g), aldehyde **2a** (0.61 mL), and barbituric acid **3** (0.77 g) in 7 mL of anhydrous DMF was heated for 15—20 min at 50—80 °C. After 3—5 min, the reaction mixture became homogeneous, and later it turned turbid, and some amount of a crystalline solid precipitated. When the temperature was increased to 100—110 °C, the mixture became again homogeneous, and at 150—160 °C, a plentiful crystalline precipitate formed. The mixture was cooled, diluted with water, kept for 3 h at ~20 °C, and filtered. The precipitate was washed on the filter successively with water, ethanol, and ether and dried first in air and then in a vacuum desiccator over anhydrone to give compound **4a** (1.75 g, 85.4%) as bright-yellow crystals, m.p. 212—215 °C (decomp.). Found (%): C, 73.75; H, 4.29; N, 12.07. $C_{21}H_{15}N_3O_2$. Calculated (%): C, 73.89; H, 4.43; N, 12.31. MS, *m/z*: 341 $[M]^+$. UV (EtOH), λ_{max}/nm (ε): 260 (21200), 295 (7000), 360 (6950). IR (KBr), ν/cm^{-1}: 3260, 3080—2880, 1660, 1617 sh, 1600—1550, 1445, 1380—1345.

2,3-Dimethoxy-12-phenyl-8,15,17-triaza-D-homogona-1,3,5(10),9(11),12,14-hexaene-16,17a-dione (4b). A reaction of azomethine **1b** (1.03 g), aldehyde **2a** (0.51 mL), and acid **3** (0.64 g) similar to that described for the preparation of compound **4a** gave **4b** (1.8 g, 90%) as yellow crystals, m.p. 252—255 °C (decomp.). Found (%): C, 68.66; H, 4.54; N, 10.22. $C_{23}H_{19}N_3O_4$. Calculated (%): C, 68.82; H, 4.77; N, 10.47. MS, *m/z*: 401 $[M]^+$. UV (EtOH), λ_{max}/nm (ε): 250 (23000), 295 (8750), 361 (8250). IR (KBr), ν/cm^{-1}: 3270, 3080—2880, 1660, 1642 1599 sh, 1560, 1512, 1462, 1395, 1377, 1340, 1295, 1280, 1269, 1245, 1220, 1145.

2,3-Dimethoxy-12-(4-methoxyphenyl)-8,15,17-triaza-D-homogona-1,3,5(10),9(11),12,14-hexaene-16,17a-dione (4c). A similar reaction of azomethine **1b** (0.82 g), aldehyde **2b** (0.49 mL), and acid **3** (0.51 g) gave compound **4c** (1.55 g, 89.6%) as yellow crystals, m.p. 242—248 °C (decomp.). Found (%): C, 66.59; H, 4.75; N, 9.54. $C_{24}H_{21}N_3O_5$. Calculated (%): C, 66.81; H, 4.91; N, 9.74. MS, *m/z*: 431 $[M]^+$. UV (EtOH), λ_{max}/nm (ε): 218 (18500), 251 (18900), 359 (6300). IR (KBr), ν/cm^{-1}: 3250—2700, 1710 sh, 1695—1645, 1595 sh, 1575—1540, 1512, 1470—1430, 1390, 1375, 1340, 1295, 1270, 1215, 1175, 1145.

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