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UNUSUAL CONDENSATION OF 6,7-DIMETHOXY-1,3,3-TRIMETHYL-3,4-DIHYDROISOQUINOLINE WITH 4-ANTIPYRYLIDENEBARBITURIC ACID

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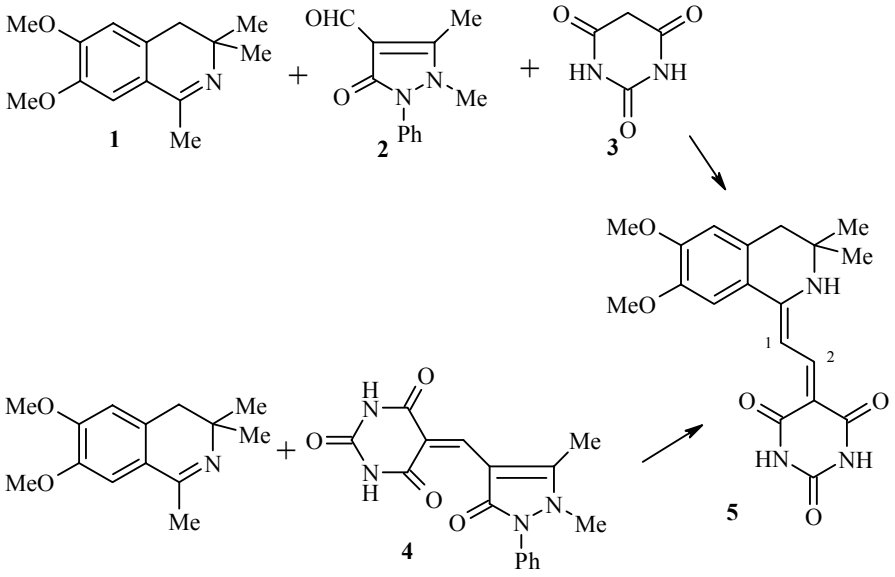
Keywords: antipyrin-4-carbaldehyde, barbituric acid, 6,7-dimethoxy-1,3,3-trimethyl-3,4-dihydroisoquinoline.

The reaction of arylidene barbituric acids with 1-methyl-3,4-dihydroisoquinolines, leading to the corresponding 8-azasteroid derivatives, has been described [Ref. 1, p. 208]. This reaction can be carried out both with the arylidene barbituric acid itself and in the three-component variant: by heating a mixture of the aldehyde, barbituric acid, and 1-methyl-3,4-dihydroisoquinoline in DMF [Ref. 1, p. 426].

Since 8-azasteroids with substituents in the 7 position have not yet been described, it was of interest to carry out the analogous reaction with 6,7-dimethoxy-1,3,3-trimethyl-3,4-dihydroisoquinoline.

However, as we have established, the reaction of 6,7-dimethoxy-1,3,3-trimethyl-3,4-dihydroisoquinoline (**1**) with a mixture of 4-antipyrin aldehyde **2** and barbituric acid **3**, or with the product **4** obtained by condensation of compounds **2** and **3**, leads to formation of only 1-(6,7-dimethoxy-3,3-dimethyl-1,2,3,4-tetrahydro-1-isoquinolylidene)-2-(3,5-diaza-2,4,6-trioxo-1-cyclohexylidene)ethane (**5**), which judging from the spin–spin coupling constant of the vicinal protons (~15 Hz), exists in the *trans* conformation.



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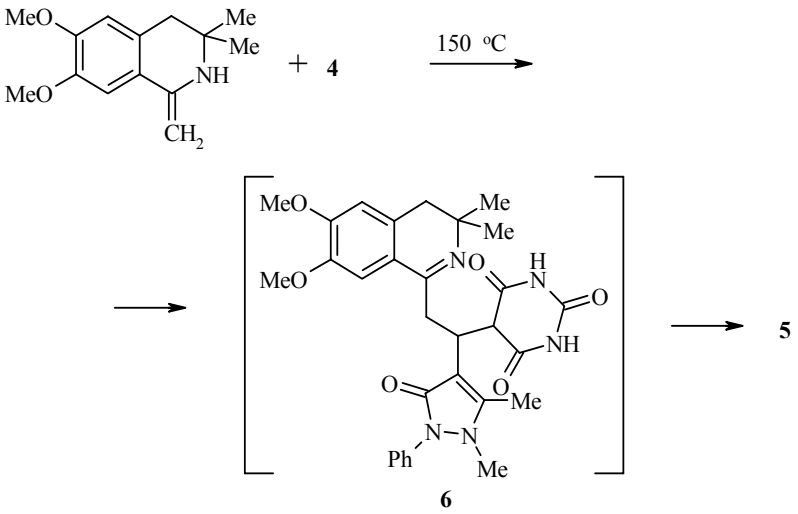
Probably in the first step of the reaction, the antipyrylidene barbituric acid **4** undergoes Michael addition to the enamine form of 3,4-dihydroisoquinoline **1**, but the product **6** proves to be unstable under the reaction conditions and eliminates the antipyrin moiety.



1-(6,7-Dimethoxy-3,3-dimethyl-1,2,3,4-tetrahydro-1-isoquinolylidene)-2-(3,5-diaza-2,4,6-trioxo-1-cyclohexylidene)ethane (5). Dry DMF (10 ml) was added to a mixture of compound **1** (2.21 g, 0.01 mol), barbituric acid (1.28 g, 0.01 mol), and antipyrin carbaldehyde (2.16 g, 0.01 mol); the mixture was heated to boiling. The mixture become homogeneous at first, but after 1-2 min abundant precipitation began. The mixture was heated for 15 min, cooled down, and poured into 100 ml water; the red precipitate was collected, dried, and crystallized from alcohol. Yield 59%, decomposes at ~217°C. IR spectrum, ν, cm^{-1}: 3300 (NH); 1730, 1660 (C=O); 1615 (C=N). The ^1H NMR spectrum was taken on a Bruker AM 300 (300 MHz) in DMSO-d_6, internal standard Me4Si, δ, ppm: 1.31 (6H, s, *gem*-CH_3); 2.87 (2H, s, CH_2-4); 3.83 (3H, s, OCH_3-6); 3.89 (3H, s, OCH_3-7); 6.96 (1H, s, 5-H); 7.28 (1H, s, 8-H); 7.55 (1H, d, H(1) vinyl); 8.30 (1H, d, H(2) vinyl); 9.70 (1H, s, $NH_{isoquin}$); 10.01 (1H, br. s, NH_{barb}); 10.12 (1H, br. s, NH_{barb}). The mass spectrum was taken on a Finnigan MAT under standard conditions (electron impact, 70 eV), *m/z* (I_{rel}, %): 371 $[M]^+$ (100); 356 [M - Me] (90); 341 [M - 2Me] (23); 296 (68); 283 [M-NHCONH] (20); 270 (45); 244 [M - barbituric acid] (50); 233 (60); 218 [M - barbituric acid CH=CH] (70); 191 [methoxy-3,3-dimethyl-1,2,3,4-tetrahydroisoquinoline] (40); 128 [barbituric acid] (38).

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REFERENCES

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