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LETTERS TO THE EDITOR

SYNTHESIS OF 5-ARYLSULFONYL-1,2,3,4-TETRAHYDROPYRIMIDINE-2-THIONES

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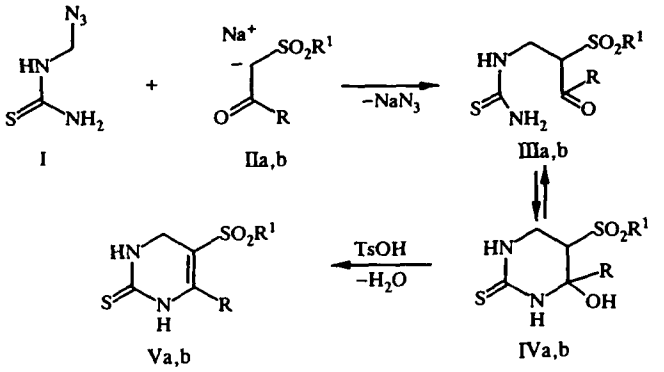
Previously [1, 2] we developed a new general method for the synthesis of 5-acyl substituted 1,2,3,4-tetrahydropyrimidine-2-thiones, which are of considerable interest as potential calcium ion antagonists [3]. The synthesis is based on the interaction of readily obtained α-azides or α-tosyl substituted thiourea or urea with the sodium enolates of 1,3-dicarbonyl compounds with subsequent dehydration of the 5-acyl-4-hydroxyhexahydropyrimidine-2-thione or -2-one products. This method is considerably better than the Biginelli condensation [4] which is normally used for the synthesis of compounds of this type. It is more general and makes possible the synthesis of valuable products which cannot be obtained by the Biginelli reaction. In this paper we report the synthesis using our method of some previously unknown 5-arylsulfonyl-1,2,3,4-tetrahydropyrimidine-2-thiones.

We have shown that N-(azidomethyl)thiourea (I) reacts readily with the sodium enolate of tosylacetone IIa, generated by treatment of the corresponding CH acid with sodium hydride, in acetonitrile (20°C, 6 h) to give 4-hydroxy-4-methyl-5-tosylhexahydropyimidine-2-thione (IVa) in 92% yield. This is the result of spontaneous heterocyclization of the initially formed N-(3-oxo-2-tosyl-1-butyl)thiourea (IIIa).



II–V a R = Me, R^1 = C_6H_4Me-4; b R = R^1 = Ph

Under the conditions described above, the final product of the reaction of azidomethylthiourea I with the sodium enolate of phenylsulfonylacetophenone IIb is N-(3-oxo-3-phenyl-2-phenylsulfonyl-1-propyl)thiourea (IIIb) in a yield of 98%. An intense carbonyl stretching bands is observed at 1669 cm^{-1} in its IR spectrum. The acyclic structure of this compound is retained in solution as shown by hydrogens corresponding to IIIb alone in the ^1H NMR spectrum. That compound IIIb does not heterocyclize spontaneously may result from the reduced electrophilicity of the carbonyl group and also to steric hindrance by the tosyl group.

6-Methyl-5-tosyl-1,2,3,4-tetrahydropyrimidine-2-thione (Va) was produced in 86% yield by boiling a solution of compound IVa in ethanol or acetonitrile with 0.1 equivalent of TsOH for 1 h. Under analogous conditions, (3-oxopropyl)thiourea IIIb was not converted to 6-phenyl-5-phenylsulfonyl-1,2,3,4-tetrahydropyrimidine-2-thione (Vb). However, if more than 0.5 equivalent of TsOH was used (ethanol or acetonitrile, boiling), compound IIIb was converted in 80% yield to the tetrahydropyrimidine Vb, presumably via formation of the cyclic isomeric form IVb.

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6-Methyl-5-tosyl-1,2,3,4-tetrahydropyrimidine-2-thione (Va). M.p. 229°C (dec., ethanol). IR spectrum: 3187, 3137 (N–H), 1667 (C=C), 1604 (thioamide-II), 1298, 1143 (SO_2), 812 (C–H_{arom}), 1219 cm^{-1}. ^1H NMR spectrum: 10.21 (1H, br.s., $N_{(1)}$–H), 9.10 (1H, br.s., $N_{(3)}$–H), 7.74 (2H, d, J = 8.3 Hz, H_{arom}), 7.43 (2H, d, H_{arom}), 3.87 (2H, s, 4-H), 2.40 (3H, s, CH_3 in tosyl), 2.17 ppm (3H, s, 6-CH_3). Found, %: C 51.15, H 4.95, N 9.78. Calc. for $C_{12}H_{14}N_2O_2S_2$, %: C 51.04, H 5.00, N 9.92.

6-Phenyl-5-phenylsulfonyl-1,2,3,4-tetrahydropyrimidine-2-thione (Vb). M.p. 238-238.5°C (dec., ethanol). IR spectrum: 3389, 3162 (N–H), 1663 (C=C), 1568, 1548 (thioamide-II), 1294, 1137 (SO_2), 726 (C–H_{arom}), 1208 cm^{-1}. ^1H NMR spectrum: 10.46 (1H, br.s., $N_{(1)}$–H), 9.23 (1H, br.s., $N_{(3)}$–H), 7.12-7.68 (10H, m, 6-Ph and 5-SO_2Ph), 4.13 ppm (2H, d, $J_{NH,4\text{-}H}$ = 2.0 Hz, 4-H). Found, %: C 58.01, H 4.14, N 8.62. Calc. for $C_{16}H_{14}N_2O_2S_2$, %: C 58.16, H 4.27, N 8.48.

IR spectra of Nujol mulls were recorded on a Shimadzu IR-435 spectrophotometer. ^1H NMR spectra of DMSO-D_6 solutions were recorded with a Bruker MSL-200 spectrometer.

The C, H, and N elemental analysis data for compounds Va and Vb agreed with the calculated values.

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