SYNTHESIS OF 6-METHYL-2-METHOXY-5-NITRO-4-PHENYL-1,4-DIHYDROPYRIMIDINE

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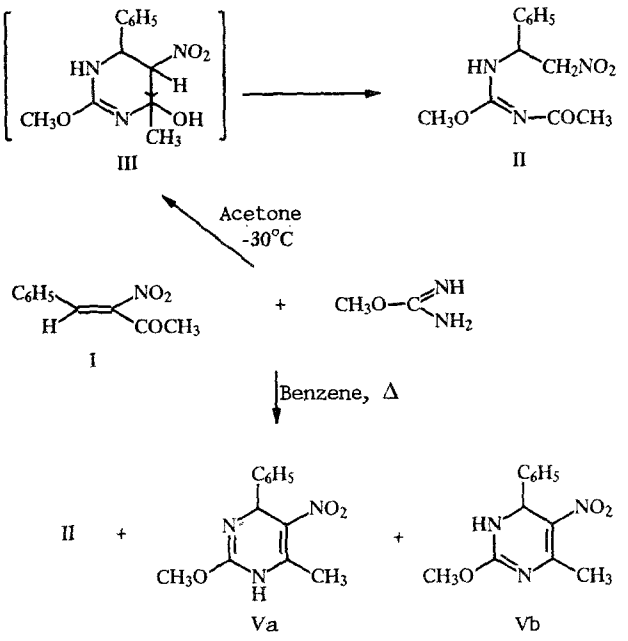
The literature contains comprehensive studies of 5-alkoxycarbonyl-4-aryl-1,4(3,4)-dihydropyrimidines, which are synthons for obtaining calcium intake antagonists [1-3]. However, information is absent from the literature on 4-aryl-1,4-dihydropyrimidines containing a nitro group ortho to the geminal center.

We isolated the isourea (II) after treatment of 1-benzilidine-1-nitropropanone-2 (I) with O-methylisourea in acetone at a temperature of —30°C (method A) as the only product from the reaction mixture. The reaction evidently proceeds through the formulation of the corresponding unstable substituted 3,4,5,6-tetrahydropyrimidine (III), which is transformed into the isourea II by cleavage of the pyrimidine ring at the $C_{(5)}$—$C_{(6)}$ bond. Attempts to cyclize II were not successful. In particular, heating II in benzene in the presence of para-toluene sulfonic acid for 9 h formed the urea (IV). Boiling a mixture of ketone I and O-methylisourea in benzene for 4 h under a Dean—Stark trap (method B) gave the acyclic product I and a mixture of the substituted 1,4- and 3,4-dihydropyrimidines (Va and Vb, respectively), which was confirmed by the presence of a double set of signals in the ^1H NMR spectrum. The dihydropyrimidines V upon treatment with 2,3-dichloro-5,6-dicyanobenzoquinone in benzene at room temperature dihydrogenated to the corresponding substituted pyrimidine (VI).



EXPERIMENTAL

Elemental analysis data for compounds III-VI corresponded with the calculated values.

N-Acetyl-N′-[(1-phenyl-2-nitro)ethyl]-O-methylisourea (II, $C_{12}H_{15}N_3O_4$). mp 77-79°C (from hexane). ^1H NMR spectrum (in $CDCl_3$): 2.15 (3H, s, CH_3), 3.84 (3H, s, OCH_3), 4.68 (2H, m, CH_2), 5.61 (1H, m, CH), 7.24-7.41 (5H, m,

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C_6H_5), 10.62 ppm (1H, d, NH). ^{13}C NMR (in DMSO-D_6): 27.80 (CH_3), 52.7 (OCH_3), 54.59 (CH), 78.76 (CH_2), 126.00-135.93 (C_6H_5), 161.24 (C=N), 185.35 ppm (CO). Yield 67.5% (method A), 84.7% (method B).

N-Acetyl-N'-[(1-phenyl-2-nitro)ethyl]-urea (IV, $C_{11}H_{13}N_3O_4$). mp 129-131°C (from ethanol). ^1H NMR spectrum (in $CDCl_3$): 2.17 (3H, s, CH_3), 4.81 (2H, m, CH_2), 5.72 (1H, m, CH), 7.38 (5H, m, C_6H_5), 9.40 (1H, d, NH), 9.90 ppm (1H, s, NH). Yield 84.5%.

1,4- and 3,4-Dihydro-6-methyl-2-methoxy-5-nitro-4-phenylpyrimidines (V, $C_{12}H_{13}N_3O_3$). mp 151-153°C (from ethanol). ^1H NMR spectrum (in $CDCl_3$): Va — 2.50 (3H s, CH_3), 3.72 (3H, s, OCH_3), 5.90 (1H, s, CH), 6.36 (1H, b.s, NH); Vb — 2.59 (3H, s, CH_3), 3.93 (3H, s, OCH_3), 5.78 (1H, b.s, NH), 5.83 (1H, d, J = 3.2 Hz, CH). Both with multiple signals 7.27-7.62 ppm (m, C_6H_5). Yield 11.1%.

6-Methyl-2-methoxy-5-nitro-4-phenylpyrimidine (VI), $C_{12}H_{11}N_3O_3$). mp 93-95°C (from hexane). ^1H NMR spectrum (in $CDCl_3$): 2.58 (3H, s, CH_3), 4.12 (3H, s, OCH_3), 7.47-7.67 ppm (5H, m, C_6H_5). Yield 77%.

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