ALKYLATION OF 2-HYDROXYPYRIMIDINES BY ETHYL BROMOACETATE

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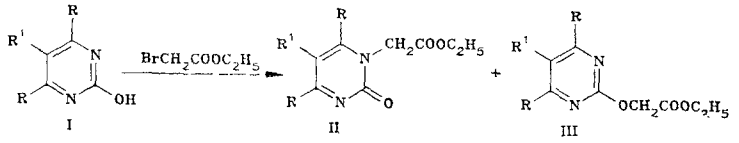
Studying the conditions for the alkylation of 2-hydroxypyrimidines (I) by ethyl bromoacetate, we found that the use of potassium carbonate in acetonitrile as a condensing agent makes it possible to avoid the secondary reactions associated with the conversions of esters of haloacetic acids under the action of the strong bases usually used in the alkylation of 2-hydroxypyrimidines.



I—III a R=R'=H; b R=H, R'=Cl; c R=CH_3, R'=H; d R=C_6H_5, R'=H

Under these conditons compounds Ia and b form esters of (1,2-dihydro-2-oxo-1-pyrimidinyl) acetic acids (IIa and b) with 30 and 80% yields, respectively, Ic forms a mixture of N and O isomers (46 and 13%), and compound Id forms only the ether IIId (57%). The structure of the N derivative IId was erroneously assigned to the latter in [1]. Therefore, the nature of the substitutent in positions 4 and 6 of the pyrimidine ring strongly influences the direction of the reaction; however, in the case of compound Id, N-carbethoxymethylation does not take place, apparently due to the steric hindrances.

A mixture of 5 mmole of compound I and 0.4 g (0.29 mmole) of potassium carbonate in 20 ml of dry acetonitrile is boiled for 45 min with stirring, a solution of 0.92 g (5.5 mmole) of ethyl bromoacetate in 20 ml of acetonitrile is added over the course of 1-3 h, and the mixture is boiled for an additional 1 h. The hot solution is filtered, the filtrate is evaporated in a vacuum, and II and III are extracted from the residue by boiling ethyl acetate.

Compound IIa: mp 110-112°C (from ethanol). UV spectrum (in ethanol, λ_{max} (log ε): 216 (3.93), 311 nm (3.68). PMR spectrum (CDC_3): 1.19 (3H, t, J = 7 Hz, CH), 4.18 (2H, q, J = 7 Hz, CH_3), 4.58 (2H, s, NCH_2), 6.28 (1H, d. d, J_{54} = 4 Hz, J_{56} = 6 Hz, 4-H), 7.72 (1H, d. d, J_{64} = 3 Hz, J_{65} = 6 Hz, 6-H), 8.49-8.60 ppm (1H, m, 4-H). IIb: mp 175-177°C [2]. UV spectrum (in ethanol), λ_{max} (log ε): 208 (sh), 226 (4.04), 332 nm (3.60). PMR spectrum ($CDCl_3$): 1.22 (3H, t, J = 7 Hz, CH_3), 4.20 (2H, q, J = 7 Hz, CH_2), 4.55 (2H, s, NCH_2), 7.66 (1H, d, J = 3 Hz, 6-H), 8.51 ppm (1H, d, J = 3 Hz, 4-H). IIc: mp 119-121°C (from carbon tetrachloride). UV spectrum (in ethanol), λ_{max} (log ε): 208 (sh), 2.17 (3.86), 306 nm (3.81). PMR spectrum ($CDCl_3$): 1.19 (3H, t, J = 7 Hz, CH_3), 2.19 (3H, s, 4-CH_3), 2.24 (3H, s, 6-CH_3), 4.14 (2H, q, J = 7Hz, CH_2), 4.68 (2H, s, NCH_2), 6.05 ppm (1H, s, 5-H). IIIc: mp 56-57°C [3]. UV spectrum (in ethanol), λ_{max} (log ε): 210 (3.76), 263 nm (3.78). PMR spectrum ($CDCl_3$): 1.18 (3H, t, J = 7 Hz, CH_3), 2.31 (6H, s, 4,6-CH_3), 4.15 (2H, q, J = 7Hz, CH_2), 4.81 (2H, s, OCH_2), 6.62 ppm (1H, s, 5-H). IIId: mp 100-100.5°C (95-97°C, according to the data in [1]). UV spectrum (in ethanol), λ_{max} (log ε): 204 (4.61), 244 (sh), 252 (4.34), 313 nm (4.33). PMR spectrum ($CDCl_3$): 1.16 (3H, t, J = 7 Hz, CH_3), 4.18 (2H, q, J = 7Hz, CH_2), 4.96 (2H, s, OCH_2), 7.74 (1H, s, 5-H), 7.37-8.12 ppm (10 H, m, aromatic protons).

The UV spectrum of compound IIId is similar to the spectrum of 2-methoxy-4,6-diphenylpyrimidine [4]. The data from the elemental analysis of the compounds obtained correspond to the calculated values.

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UNEXPECTED FORMATION OF 2,4-QUINAZOLINEDIONE IN THE REACTION OF α-CYANO-β-DIMETHYLAMINOCROTONAMIDE WITH ETHYL ANTHRANILATE

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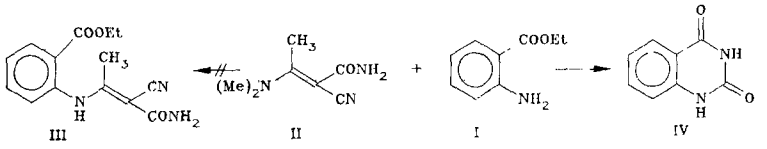
When aromatic amines are reacted with enamines in the presence of acetic acid, transamination reaction with the formation of N-arylenamines is observed [1].

However, when we attempted to carry out the reaction of ∿0.03 mole of ethyl anthranilate (I) with ∿0.01 mole of the enaminoamide α-cyano-β-dimethylaminocrotonamide (II) in 15 ml of acetic acid with boiling for 5 h, instead of α-cyano-β-(N-ethoxycarbonylphenyl)aminocrotonamide (III) we unexpectedly obtained 2,4-quinazolinedione (IV) with a 50% yield and mp 350°C (from DMFA), which was identical to a sample obtained by a back synthesis according to the method in [2].



The formation of compound IV may be a consequence of the elimination of HNCO from enaminoamide II under these conditions followed by its addition of amino ester I at the amino group and the subsequent irreversible cyclization to bicycle IV. Such elimination of HNCO was previously postulated for N-carbamidoamidines with the general formula RRNC=N–$CONH_2$ upon heating [3]. The data from the elemental analysis of compound IV for C, H, and N and the molecular weight (mass-spectrometrically) correspond to the calculated values.

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