THE SYNTHESES OF 2-METHYL-3-(p-TOLYLAZO)-PYRIMIDO [1,2-*a*]BENZIMIDAZOLE-4-ONE, 7-HYDROXY-5-METHYL-6-(p-TOLYLAZO)-[1,2,4]-TRIAZOLO[1,5-*a*]PYRIMIDINE, 2-METHYLPYRAZOLO [1,5-*a*] PYRIDINE-5,7(4H,6H)-DIONE AND ARYLAZOTHIOPYRIMIDINES≠

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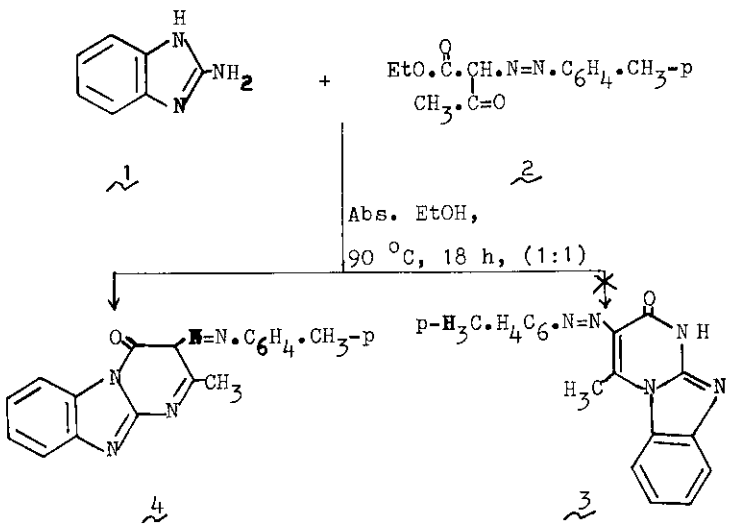
Abstract——Condensation of 2-aminobenzimidazole (1) with ethyl α-(p-tolylazo)-β-oxobutyrate (2) in absolute EtOH (molar ratio) afforded 2-methyl-3-(p-tolylazo)-pyrimido [1,2-*a*]benzimidazole-4-one (4). The reaction of 3-amino-1,2,4-triazole (5) with (2) in the same reaction medium for 16 h gave 7-hydroxy-5-methyl-6-(p-tolylazo)-[1,2,4]triazolo [1,5-*a*]pyrimidine (6). 2-Methylpyrazolo [1,5-*a*]pyridine-5,7(4H,6H)-dione (9) was obtained by the fusion of 3-methyl-2-pyrazolin-5-one (8) with ethyl acetoacetate at 120 °C for 6 h. The condensation of ethyl α-(arylazo)-β-oxobutyrate (2a-e) with thiourea in methanolic sodium methoxide afforded the arylazothiopyrimidines (11a-e) in quantitative yield.

The demonstration of potent biological activity in different substituted-2-aminobenzimidazoles and the development of various drugs like mebenazole[1,2] and astemazole[3,4] support the importance of this nucleus in generating better chemotherapeutic agents[5]. Also a considerable attention has been drawn to the synthesis of several condensed heterocyclic systems, especially derived from triazole[6].

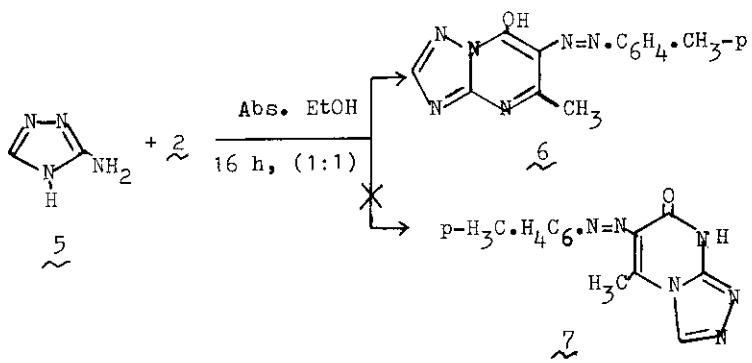
The condensation of 2-aminobenzimidazole (1) with ethyl α-(p-tolylazo)-β-oxobutyrate (2) in absolute ethanol (molar ratio) gave a product, mp 90 °C in 60% yield. The IR spectrum of this product does not show any ester carbonyl or methyl ketone absorption; it thus appears that the product has either (3) or (4), both consistent with molecular formula $C_{18}H_{15}N_5O$, obtained by elemental analysis and mass spectrum.

≠ Part 1 in the series of heterocyclic compounds with bridgehead nitrogen.

The IR spectrum of the condensation product (4) exhibits no absorption due to a CONH group of cyclic structure 3. The assignment of the structure (4) is consistent with the observation, that, in β-keto ester, the amino group attacks the methyl ketone first, then the ester group, and also supported by ^{1}H NMR spectrum, which exhibits signal at δ = 6.35 (s, 1H, -COCH-)[7].

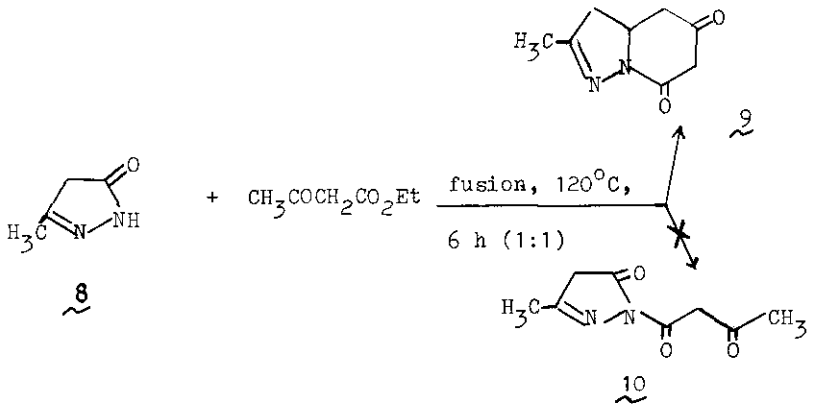


The reaction of aminotriazole with arylazo-β-keto esters has not yet been fully exploited and we report in this paper the compound which is formed by the reaction of (2) and 3-amino-1,2,4-triazole (5). Thus, when (5) and (2) were refluxed in absolute ethanol (molar ratio) for 16 h, 7-hydroxy-5-methyl-6-(p-tolylazo)-[1,2,4]-triazolo[1,5-a]pyrimidine (6)[8], rather than (7) was obtained. No carbonyl absorption due to CO, but instead a sharp and clear band at 3570 Cm^{-1} (OH) was observed. The ^{1}H NMR spectrum displayed signals due to two methyl groups in addition to the

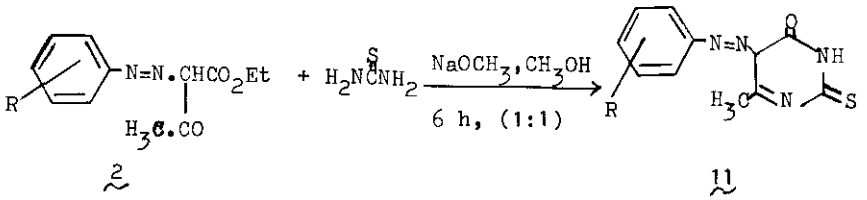


aromatic protons[8].

It is intersting to synthesize 2-methylpyrazolo[1,5-*a*]pyridine-5,7(4H,6H)-dione (9)[9] in connection with the above mentioned condensation. Two possible structures (9) or (10) may be anticipated from fusion of ethyl acetoacetate with 3-methyl-2-pyrazolin-5-one (8). The ^{1}H NMR and mass spectra favours structure (9) rather than (10). The presence of an olefinic proton at δ 5.53 supported structure (9). No signals for the methyl ketone (structure 10) was observed Thus the methyl ketone moiety was involved in the cyclisation.



One of the most intersting synthesis of the arylazothiopyrimidine (11a-e)[10] was gained upon treatment of 2 with thiourea in methanolic sodium methoxide. The ^{1}H NMR spectra of (11a-e) displayed signals due to CONH but no signal for (NH-N=). The IR spectra showed absorptions due to -CONH-, C=S and C=N. Further evidence was obtained from the mass spectra.



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a; R=H, b; R=o-CH_3

c; R=p-CH_3, d; R=o-OCH_3

e; R=p-OCH_3

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7. 4: Brown crystals (EtOH), mp 90 °C, 60% yield, IR (KBr) cm^{-1}: 1680 (CO), 1580 (C=N), NMR (CD_3COCD_3) δ: 2.9 (3H,s, $-CH_3$ aromatic), 1.8 (3H, s, CH_3-C=N-), 6.2-6.8 (8H, m, Ar-H), MS m/z (rel. int.): 317.36 $[M]^+$ (4) (calc. for $C_{18}H_{15}N_5O$: 317.36), 234 $(M-C_7H_7N_2)^+$ (3), 197 $(234-C_3H)^+$ (2), 106 (100).
8. 6: Yellow crystals (EtOH), mp 194 °C, 80% yield, IR (KBr) cm^{-1}: 3570 (OH), 1600 (C=N), NMR ($CDCl_3$) δ: 2.7 (3H, s, $-CH_3$ aromatic), 1.5 (3H, s, CH_3-C=N-), 5.7 (1H, s, -CH=N), 6.4-6.8 (4H, m, Ar-H), MS m/z (rel. int.): 268.28 $[M]^+$ (43) (calc. for $C_{13}H_{12}N_6O$: 268.28), 177 $(M-C_7H_7)^+$ (13), 149 $(177-N_2)^+$ (42), 109 $(149-C_3H_4)^+$ (100).
9. 9: Orange crystals (EtOH), mp 242 °C, 85% yield, IR (KBr) cm^{-1}: 1735 (β-diketone) 1605 (C=N), NMR (DMSO-d_6) δ: 3.3 (2H,s, $-NCOCH_2-$), 1.9 (2H, s, $=C-CH_2-CO$), 5.53 (1H, s, -C-CH=C-), 2.1 (3H, s, H_3C-C=N), MS m/z (rel. int.): 164.164 $[M]^+$ (100) (calc. for $C_8H_8N_2O_2$: 164.164), 136 $(M-CO)^+$ (44), 121 (15), 107 (37), 77 (53).
10. 11a-e: IR (KBr) cm^{-1}: 1375-1385 and 1450-1510 (C=S), 1630-1675 (CO-amide), 3100-3350 (NH-amide), NMR (DMSO-d_6) δ: 1.6-1.8 (3H, s, H_3C-C=N), 6.6-7.5 (5H and 4H, m, Ar-H).

    11a. Yellow crystals, mp 201 °C, 70% yield (satisfactory elemental analysis).

    11b. Brown crystals, mp 202 °C, 60% yield (satisfactory elemental analysis).

    11c. Deep brown crystals, mp 212 °C, 70% yield (satisfactory elemental analysis).

    11d. Reddish brown crystals, mp 205 °C, 60% yield (satisfactory elemental analysis).

    11e. Brownish black crystals, mp 250 °C, 80% yield, MS m/z (rel. int.): 276.316 $[M]^+$ (21) (calc. for $C_{12}H_{12}N_4SO_4$: 276.316), 258 (4), 157 (14), 123 (79), 108 (100), 80 (89).

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