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REACTIONS OF 3-DIAZOPYRAZOLO(3,4-b)PYRIDINE WITH SOME REACTIVE METHYLENE COMPOUNDS AND CYCLOADDITIONS[1]

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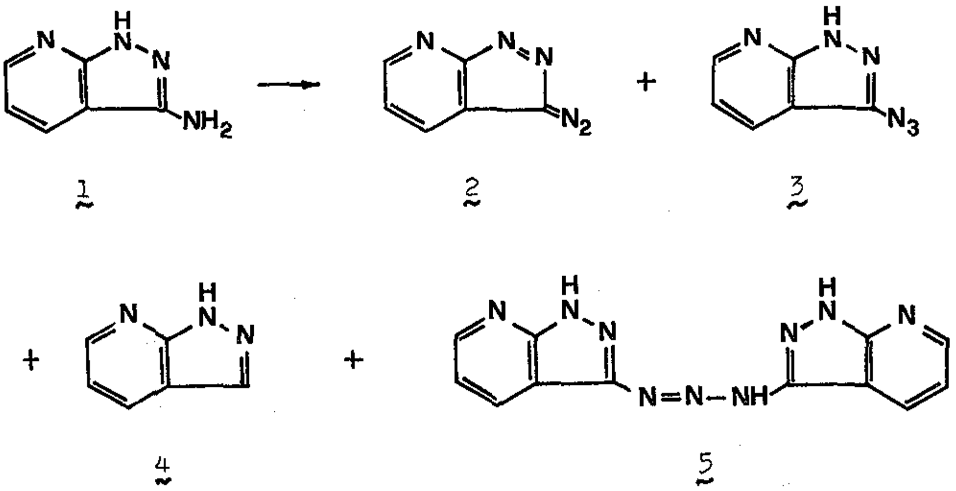
3-Diazopyrazolo(3,4-b)pyridine is transformed with reactive methylene compounds into polycyclic 1,2,4-triazine derivatives *via* the coupling products. A cycloaddition reaction and reaction with 2,5-dimethylfuran are also described.

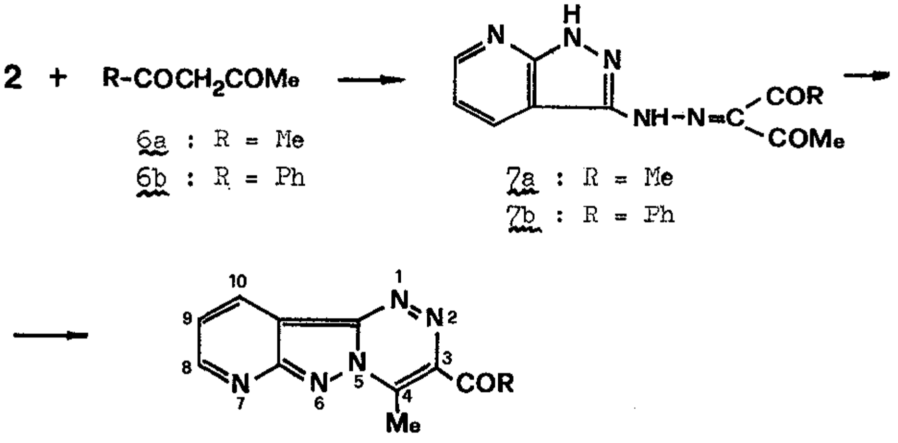
Heterocyclic diazo compounds are valuable synthons for the preparation of heterocyclic systems.[2] One of little investigated aspects is their reaction with reactive methylene compounds and formation of new heterocyclic systems. Recently, we have described some reactions of diazoazoles and their ability to form condensed 1,2,4-triazines.[3-5] We now report some interesting reactions of 3-diazopyrazolo(3,4-b)pyridine (2) with some reactive methylene compounds as well as some transformations of the cyclic products.

3-Aminopyrazolo(3,4-b)pyridine (1) when diazotized with sodium nitrite in water-hydrochloric acid, afforded a mixture of the anticipated diazo compound (2), 3-azidopyrazolo (3,4-b)-pyridine (3, m.p. 178-180°, dec.), the parent pyrazolo (3,4-b)pyridine (4, m.p. 97-99°) and the corresponding triazene (5, m.p.

252-254°) as the main product. The presence of all these products can be explained by the formation of the triazene from the diazo compound (2) and the starting amine (1) during the diazotization process and subsequent decomposition into the above mentioned products. Supporting evidence for the proposed decomposition of 5 was obtained when pure diazo compound (2) and the amine (1) were allowed to react in an ethanolic solution at 0°. From the resulting reaction mixture in addition to the triazene (5) also the azide (3) and the parent system (4) were isolated. However, if the amine (1) was diazotized very slowly (2-3 hours) in a 50% tetrafluoroboric acid solution with isoamyl nitrite, the corresponding diazonium tetrafluoroborate was obtained in 57% yield. Upon neutralization, extraction with chloroform and crystallization from chloroform and petroleum ether the pure diazo compound (2, m.p. 150-152°,dec.) was obtained.



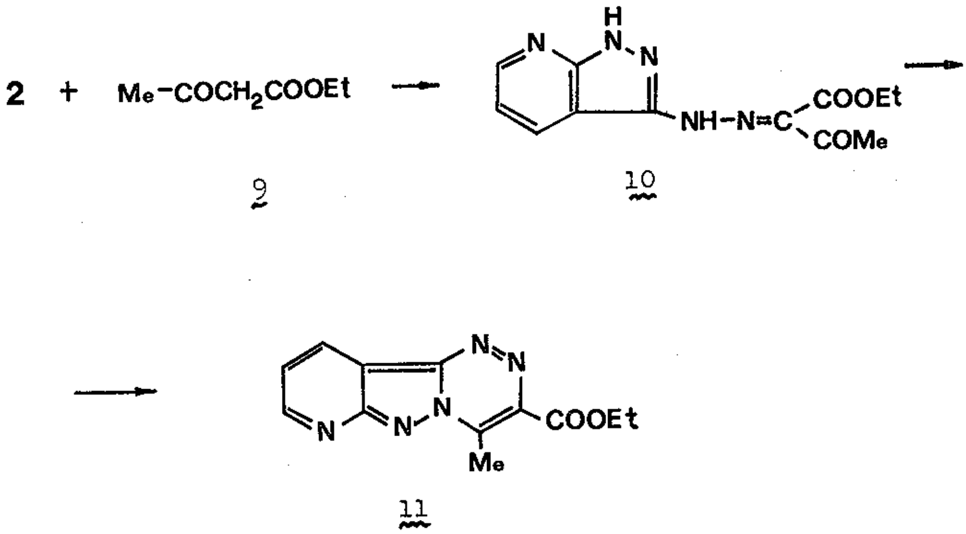
3-Diazopyrazolo(3,4-b)pyridine (2) reacted with acetylacetone (6a) or benzoylacetone (6b) in ethanolic solution at 0° to give the corresponding coupling products 7a (m.p. 180-184°, 90% yield), and 7b (m.p. 159-162°, 85% yield), respectively. Both compounds, when heated in ethanol under reflux for 1 hour, were transformed into the corresponding pyridopyrazolotriazines 8a (m.p. 174-175°, 50% yield) and 8b (m.p. 180-182°, 66% yield). The structure of 8b as 3-benzoyl-4-methyl derivative and not as the isomeric 3-acetyl-4-phenyl derivative follows from its nmr spectrum revealing (in DMSO-d_6) a singlet for the methyl group at $\tau = 6.87$ and a multiplet at 1.9-2.35 corresponding to the aromatic protons of the benzoyl group. A similar structural problem was encountered with the cyclic product 11 (m.p. 142-143°, 58% yield), obtained from 2 and ethyl acetoacetate (9) *via* the coupling product 10 (m.p. 174-176°, 90% yield). The nmr spectrum of 11 revealed a singlet at $\tau = 6.8$, corresponding to the



6a : R = Me
6b : R = Ph

7a : R = Me
7b : R = Ph

8a : R = Me
8b : R = Ph



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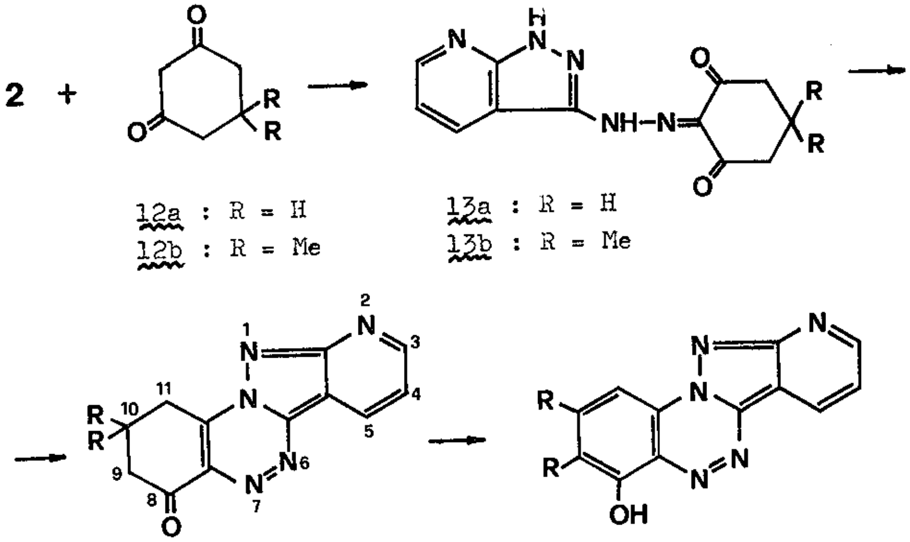


12a : R = H
12b : R = Me

13a : R = H
13b : R = Me

14a : R = H
14b : R = Me

15a : R = H
15b : R = Me

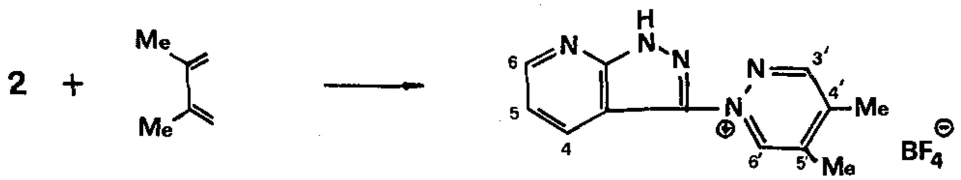
methyl group and signals at 5.45 (q) and 8.55 (t)assignable to a carbethoxy group, thus excluding an alternative pyridopyrazolotriazinone structure.

An interesting case was found with 1,3-cyclohexanedione (12a) and its 5,5-dimethyl derivative (12b). Both were converted in the presence of 2 into the corresponding hydrazones 13a (m.p. 252-257°, 86 % yield, nmr (DMSO-d_6, 60°): τ = -5.1 (s,NH), -3.5 (s, NH), 1.45 (m, H_4 and H_6), 2.76 (dd, H_5), 7.4 (m, 4'- and 6'-CH_2), 7.95 (m, 5'-CH_2), $J_{4,5}$ = 8.0, $J_{5,6}$=5.0 Hz) and 13b (m.p. 195-198°, 56% yield, nmr (DMSO-d_6): τ = -6.3 (s, NH), -3.75 (s, NH), 1.32 (m, H_4 and H_6), 2.64 (m, H_5), 7.35 (s, 4'- and 6'-CH_2), 8.92 (s, 5'-Me). The hydrazone and diketone structure is substantiated by their nmr spectra. Cyclization of 13 to 14 could be accomplished in hot dimethylformamide (for 13a) or in polyphosphoric acid (1 hour at 60-70° in the case of 13b). Compound 14a (m.p. 207-211°, 55% yield, nmr (DMSO-d_6, 90°): τ = 1.0 (m,H_3 and H_5),2.46 (dd,H_4), 6.35 (t, 11-CH_2), 7.1 (m, 9- and 10-CH_2), $J_{3,4}$ = 4.4, $J_{4,5}$ = 8.0 Hz) could exist in several alternative isomeric or enolic forms, but on hand of the recorded nmr spectrum the structure 14a is only adequate. The same structural analogy exists for compound 14b (m.p. 282-284°, 67% yield, nmr (DMSO-d_6, 120°): τ = 1.0 (m, H_3 and H_5), 2.43 (dd, H_4), 6.38 (s, 11-CH_2), 7.16 (s, 9-CH_2), 8.74 (s, 10-Me), $J_{3,4}$ = 4.6, $J_{4,5}$ = 8.0 Hz).

Compound 14a when heated at 210-220° for 10 minutes is transformed into the fully aromatic tetracycle 15a(m.p. 252-257°, 58%yield, nmr (DMSO-d_6): τ =0.91 (dd, H_5), 1.72(dd, H_3), 3.17 (dd, H_4), 2.0 (deg.dd, H_{10}), 2.45 (dd, H_{11}), 2.75 (dd, H_9), $J_{3,4} = 4.6$, $J_{3,5} = 2.0$, $J_{4,5} = 8.0$, $J_{9,10} = 7.5$, $J_{9,11} = 1.0$ Hz).

Although the geminal methyl groups in 14b do not allow such aromatization, this could be achieved after a methyl group has migrated to a neighbouring position. In this manner, compound 14b when heated in concentrated sulfuric acid for 3 hours at 100° was transformed into 15b (m.p. 292-296°, nmr (DMSO-d_6, 110°): τ = 1.1 (m, H_3 and H_5), 2.16 (s, H_{11}), 2.52 (dd, H_4), 7.46 (s, 10-Me), 7.67 (s, 9-Me), $J_{3,4} = 4.6$, $J_{4,5} = 8.0$ Hz). It should be mentioned that the methyl group could migrate either at position 9 or at position 11. The proposed structure, corresponding to methyl group migration at position 9, is evident from the chemical shifts for proton C_{11}-H and the 9-methyl group. If the methyl group would be attached at position 11 as consequence of steric effect a strong deshielding effect would be observed.

Diazoazoles with the diazo group attached at ortho position to a ring nitrogen atom can be regarded as 1,2-, 1,3- or 1,4-dipoles. In fact, they react to give cycloaddition products and in most reactions investigated they reacted as 1,3-dipoles.[2] So far, the only reported case of a heterocyclic diazo compound reacting as a 1,2-dipolar species is the reaction between 3-diazo-4,5-dicyanoimidazole and butadiene.[6] It was therefore of interest to establish if the investigated diazo compound 2 also undergoes a similar cycloaddition reaction. A solution of pyrazolo(3,4-b)pyridine-3-diazonium tetrafluoroborate in acetonitrile was treated with 2,3-dimethylbutadiene (16) at 0° and from the reaction mixture a product could be isolated to which on hand of analytical and spectroscopic data the structure of the cycloadduct 17 (m.p. 236-239°, 28% yield, nmr (DMSO-d_6): τ = -5.13 (s, NH), -0.63 (s, $H_{6'}$), 0.22 (s, $H_{3'}$), 1.05 (dd, H_6), 1.18 (dd, H_4), 2.37 (dd, H_5), 7.3 (s, 4'- and 5'-Me), $J_{4,5}$ = = 8.4, $J_{4,6}$ = 1.6, $J_{5,6}$ = 4.5 Hz) could be assigned. A similar reaction was attempted with 2,5-dimethylfuran. An ethanolic solution of the latter, when treated with the diazo compound 2 at 0° and then heated under reflux for 1 hour afforded a pro-



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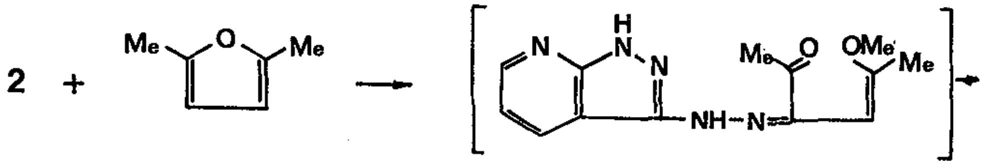

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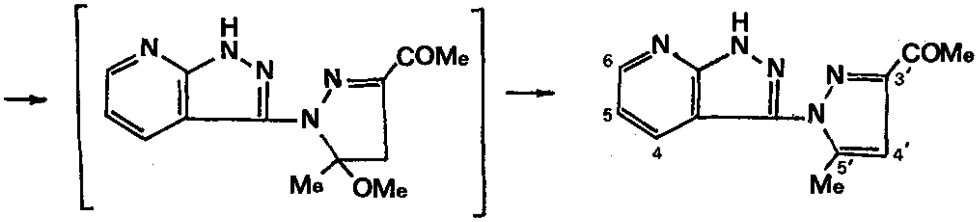

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duct to which structure 19 was assigned (m.p. 270-273°, 42% yield, *nmr* (DMSO-d_6): $\tau = 1.37$ (dd, H_6), 1.52 (dd, H_4), 2.72 (dd, H_5), 3.32 (s, H_4), 7.41 (s, 5'-Me, 3'-COMe), $J_{4,5} = 8.1$, $J_{5,6} = 4.6$, $J_{4,6} = 1.6$ Hz). Apparently, no cycloaddition occured and the reaction can be interpreted as to proceed via the ring opened intermediate (18).

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