A 1,3-DIPOLAR CYCLOADDITION REACTION OF 1-METHYLINDAZOLE

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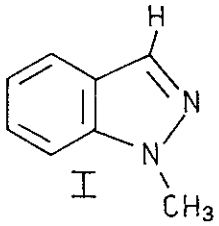
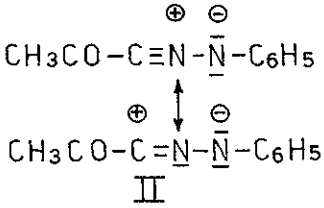
A 1,3-dipolar cycloaddition reaction of 1-methylindazole with C-acetyl-N-phenyl-nitrilimine was performed. The cycloadduct could be used to synthetize 1,2,4-triazole derivatives.

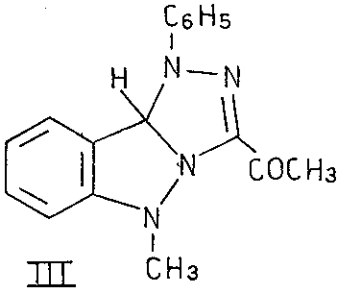
In the framework of our studies[1] on the behaviour of heterocyclic systems towards nitrilimines, we have carried out the reaction between 1-methylindazole (I) and C-acetyl-N-phenyl-nitrilimine (II), prepared in situ. Treatment of (I) with stoichiometric amount of α-chloro-(N-phenylhydrazone)acetone and three-fold excess of triethylamine (THF, 20 days, room temperature) gave a reaction mixture which, after triethylamine hydrochloride being filtered off and the solvent evaporated under vacuum, afforded 1-phenyl-3-acetyl-5-methyl-1,9b-dihydro-5H-1,2,4-triazol-[4,3b]-indazole (III), mp 134-135°, in 40% yield. The structure of the cycloadduct (III) was assigned on the basis of elemental analysis, spectroscopic data and chemical transformation. An examination of the nmr spectrum [(C_6D_6) δ: 2.17 (3H, s, -CO-CH_3), 3.26 (3H,



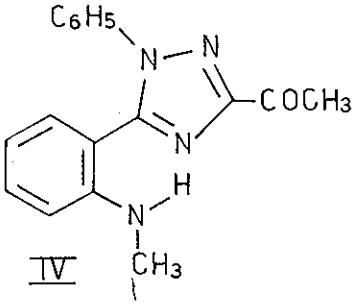
I



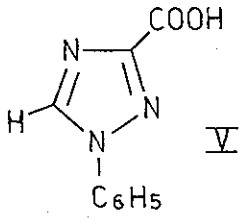
II



III



IV



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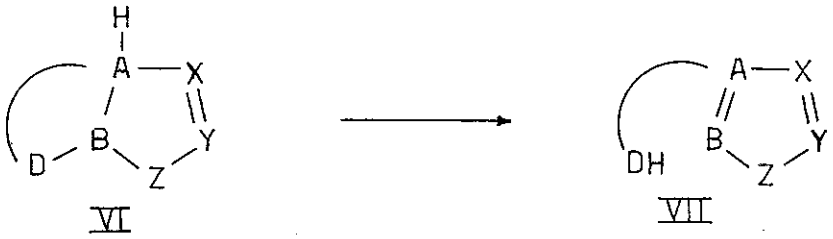

VI VII

s, -N-$\underline{CH}_3$), 6.61 (1H, s, 8a-$\underline{H}$), 6.35-7.10 (9H, m, Ar-$\underline{H}$)] revealed large shielding effect on 9b-H and -N-CH_3 protons with respect to 3-H and -N-CH_3 protons of (I) ($\Delta\delta$ = -1.30 and -0.27 respectively). This shielding effect substantiated the absence of ring current clearly supporting the structure proposed. The carbonyl frequency [ν max (nujol mull) 1666 cm^{-1}] observed is also consistent with (III). A sample of (III) with catalytic amount of conc. HCl (THF, 24 hr, room temperature) gave, after evaporation of the solvent under vacuum, 1-phenyl-3-acetyl-5-[o-methyl aminophenyl]-1,2,4-triazole (IV), in almost quantitative yield. The structure of (IV), mp 201-202°, was deduced on the basis of the following evidence: ir ν max (nujol mull) 3322, 1690 cm^{-1} ; nmr (DMSO-d_6) δ : 2.63 (3H, s, -CO-$\underline{CH}_3$), 2.68 (3H, d, -N-$\underline{CH}_3$, J=4.5), 6.03 (1H, br q, N$\underline{H}$, J=4.5), 6.20-7.70 (4H, m, Ar-$\underline{H}$), 7.39 (5H, s, N-$C_6\underline{H}_5$); uv $\overset{EtOH}{\underset{max}{}}$ nm (log ε): 221sh (4.37), 258sh (4.06), 344 (3.65). Moreover, a suspension of (IV) in a warm solution of sodium hydroxide treated with $KMnO_4$, afforded 1-phenyl-1,2,4-triazol-3-carboxylic acid (V)[2].

The results obtained give further information on the behaviour, as dipolarophiles, of the nitrogen heteroaromatic compounds putting in evidence the tendency of C=N bond of 1-methylindazole (I) to react towards nitrilimines so as the C=N bond of some mono[3] and diazines[4], azomethines[5], oximes[6], etc.. As expected, the unsubstituted nitrogen controls the orientation of the dipole. Furthermore the transformation of (III) into (IV) furnishes an interesting alternative route to synthetize 1,2,4-triazole derivatives. This behaviour is similar to that of other non aromatic cycloadducts[7,8]

which, by treatment with acids, give aromatic compounds through an elimination reaction, e.g.scheme (VI → VII).

REFERENCES AND FOOTNOTES

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8 Likewise, we have observed that cycloadduct obtained from N-methylindole and diphenyl-nitrilimine gives 1,3-diphenyl-4- o-methylaminophenyl pyrazole by treatment with HCl in ethanolic solution at room temperature, through a fission of D-B bond (unpublished results). A different behaviour showed cycloadducts obtained from N-substituted indole derivatives and C-acetyl or C-carbethoxy-N-phenyl-nitrilimines. In these cases, in fact, under similar experimental conditions we have observed the cleavage of the B-Z bond[1a,1d].

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