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 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-14,3b-indazole (III), mp 134-135°C, 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 (CD66) δ: 2.17 (3H, s, -CO-CH3), 3.26 (3H,
s, -N-CH$_3$), 6.61 (1H, s, 8a-H), 6.35-7.10 (9H, m, Ar-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 ($\nu$ 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-methylaminophenyl]-1,2,4-triazole (IV), in almost quantitative yield. The structure of (IV), mp 201-202$^\circ$, was deduced on the basis of the following evidence: $\nu$ max (nujol mull) 3322, 1690 cm$^{-1}$; nmr (DMSO-d$_6$) $\delta$: 2.63 (3H, s, -CO-CH$_3$), 2.68 (3H, d, -N-CH$_3$, J=4.5), 6.03 (1H, br q, NH, J=4.5), 6.20-7.70 (4H, m, Ar-H), 7.39 (5H, s, N-C$_6$H$_5$); $\nu$ max EtOH nm (log $\epsilon$): 221sh (4.37), 258sh (4.06), 3.44 (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). 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


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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