New 1,2-Dihydroazocine Synthesis

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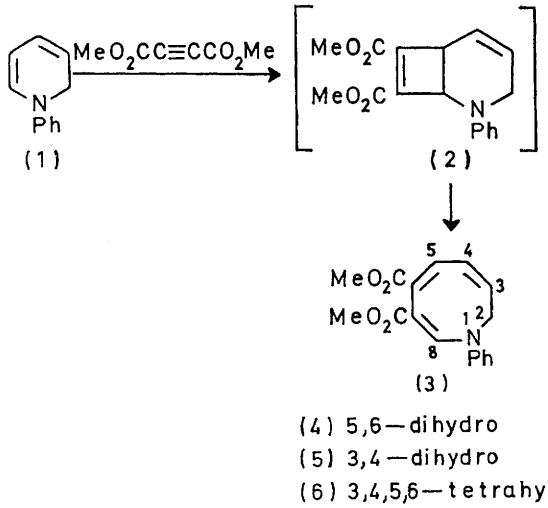
Summary 1,2-Dihydro-1-phenylpyridine with dimethyl acetylenedicarboxylate gave dimethyl 1,2-dihydro-1-phenylazocine-6,7-dicarboxylate, the n.m.r. spectrum of which showed a flexible ring at room temperature.

1,2-DIHYDRO-1-PHENYLPYRIDINE (**1**) with *N*-phenylmaleimide gives a normal Diels–Alder adduct,[1] but we have now found that with dimethyl acetylenedicarboxylate in ether the dihydroazocine (**3**) is obtained in 70% yield. This appears to be the first ring expansion of a simple dihydropyridine to the corresponding dihydroazocine, and it probably takes place through the cyclobutene (**2**) in a similar way to the recently reported[2] conversion of 1-methyl-1,4-dihydroquinoline into dimethyl 1-methyl-1,6-dihydrobenzo[*b*]azocine-3,4-dicarboxylate. In complete contrast with these results a number of 1,4-dihydropyridines with dimethyl acetylenedicarboxylate give[3] cyclobuta-[*b*]pyridines which do not yield azocines on heating or pyrolysis, while a number of azocines are in equilibrium with the corresponding dihydrocyclohexa-azetidines or -azetines at room temperature.[4]

The n.m.r. spectrum of (**3**) at 35° and 60 and 100 MHz showed equivalent methylene protons τ 5·5 (d, J 7 Hz, 2 × 2-H), 3·66 (dt, J 7, 7, and 10 Hz, 3-H), 3·41 (dd, J 10 and 3 Hz, 4-H), 3·18 (d, J 3 Hz, 5-H), and 2·12 (s, 8-H). The relationships between the coupled protons were confirmed by double-resonance experiments. The 8-H resonance, which is very similar for compounds (**4**)—(**6**), is close to that of the 3-H (τ 2·07) of methyl *trans*-3-anilinoacrylate.[5] It is at lower field than the corresponding proton (τ 3·46) of 8-methoxyazocine[6] because of the deshielding neighbouring ester group. On lowering the temperature the methylene resonance of (**3**) broadened, and in both CS_2 and $CDCl_3$ split into quartets centred on τ 4·83 (J 14 and 8 Hz) and 6·07 (J 14 and 5·5 Hz), the change being complete at −40°; the rest of the spectrum was essentially unchanged. This is a complete contrast to the behaviour of 1,2-dihydro-1-phenylpyridine, the n.m.r. spectrum of which does not alter between +35° and −40° and shows equivalent methylene protons. The protons in (**3**) became non-equivalent at *ca.* −10°. There was no evidence from the n.m.r. spectra that intramolecular cyclisation, *e.g.* to (**2**), was taking place to a significant extent.

Reduction of (**3**) by sodium borohydride gave (**4**), the n.m.r. spectrum of which showed τ 5·44 (q, J 16 and 8 Hz, 2-H), 6·00 (q, J 16 and 8 Hz, 2-H), 3·9—4·65 (m, 3- and 4-H), 7·15 (m, 2 × 5-H), and 5·57 (t, J 8 and 8 Hz, 6-H) at 35°. The ring flexibility was reduced slightly at −50° as the 6-H had split into a quartet (J 6 and 9·5 Hz), but there were no other significant changes. Hydrogenation of (**3**) gave (**5**), and of (**4**) gave (**6**).



(4) 5,6—dihydro
(5) 3,4—dihydro
(6) 3,4,5,6—tetrahydro

The u.v. spectra (MeOH) of (**4**) [242 (infl) (10^{-4} ϵ 0·41) and 308 nm (2·38)] and (**6**) [256 (0·24) and 307 nm (3·09)] are similar to that[5] of methyl *trans*-*N*-methylanilinoacrylate [220 (0·68) and 297 nm (2·95)], while the resemblance is not so close for (**3**) [253 (1·40) and 297 nm (1·90)] and (**5**) [286 (1·20) and 326 nm (1·46)]. The u.v. spectra for (**3**)—(**6**) are hardly changed by acid, and that of (**3**) is not affected by the addition of *N*-bromosuccinimide (NBS). 1,2-Dihydro-1-phenylpyridine is oxidised very rapidly by air in the presence of acid, or by NBS, to the rather different 1-phenylpyridinium chromophore, and the absorption of *NN*-dimethylaniline at 299 nm is very greatly reduced in

intensity by protonation. These data, coupled with the variable-temperature n.m.r. observations, exclude structures based on the dihydropyridine nucleus for compounds (**3**)—(**6**). Cold alkaline hydrolysis of (**3**) hydrolysed one ester group, while hot refluxing 2N-sodium hydroxide yielded some aniline.[7]

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