Formation of Benzazepines from Indoles by Ring Expansion with Dimethyl Acetylenedicarboxylate Confirmed by an *X*-Ray Structure Determination

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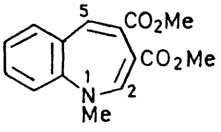
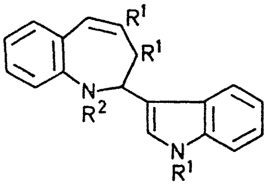
Summary. 1-Methylindole with dimethyl acetylenedicarboxylate in acetonitrile yields dimethyl 1-methylbenz[*b*]azepine-3,4-dicarboxylate which adds a further mole of the indole to give the 2,3-dihydro-2-(3-indolyl) derivative, the structure of which has been established by *X*-ray diffraction.

1-METHYLINDOLE and dimethyl acetylenedicarboxylate in acetonitrile, which had been distilled from P_2O_5, gave the benz[*b*]azepine (**1**) but if the acetonitrile employed had not been specially purified the major product from the reaction was the dihydrobenz[*b*]azepine (**3**). The last compound (**3**) was also obtained from the acid-catalysed addition of 1-methylindole to the benzazepine (**1**) and is identical to a compound previously assigned structure (**6**)[1] and structure (**7**).[2] The benzazepine (**1**) is probably formed by the stepwise addition of the indole, behaving initially as an enamine, to the acetylene followed by cyclisation to a cyclobutene and ring opening, as proposed for a similar reaction of 2-ethoxyindole[3] and established in the case of 1-acetyl-3-(*N*-piperidino)indole and methyl propiolate.[4]

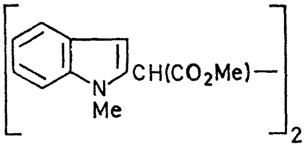
The n.m.r. spectrum of the diol (**5**), obtained from the ester (**3**) with $LiAlH_4$, showed a non-equivalent methylene group (position 3) and the four proton aliphatic proton system which includes this group has been accurately simulated by computer.[5] Although the diester (**3**) was stable to catalytic hydrogenation the diol (**5**) gave the 4,5-dihydro derivative (**9**). Reduction of the diester (**3**) in methanol with sodium amalgam gave the azepine (**8**). The u.v. spectra of (**8**) and (**9**) were very similar, and in the mass spectrometer both compounds lost a fragment containing the 3- and 4-carbon atoms with their substituents. The adduct (**2**), obtained from indole, was stable to $LiAlH_4$ in ether but with sodium dihydrobis(2-methoxyethoxy)-aluminate in hot benzene gave a mixture of the lactone (**10**), identified from its spectra, and the diol (**4**).



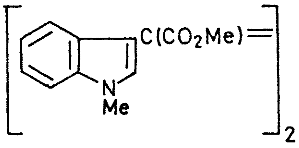
(1)



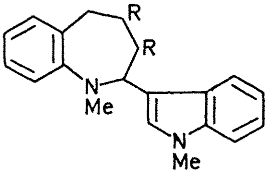
(2) $R^1 = CO_2Me$, $R^2 = H$
(3) $R^1 = CO_2Me$, $R^2 = Me$
(4) $R^1 = CH_2{\cdot}OH$, $R^2 = H$
(5) $R^1 = CH_2{\cdot}OH$, $R^2 = Me$



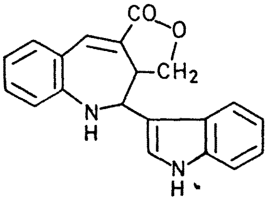
(6)



(7)



(8) R = CO_2Me
(9) R = $CH_2{\cdot}OH$



(10)

An *X*-ray crystallographic examination of the diester (**3**) confirmed the structure proposed and showed that in the crystal the carbocyclic ring, the nitrogen atom, the 3-, 4-, and 5-carbon atoms and the 4-methoxycarbonyl group are nearly co-planar. Some resonance delocalisation could therefore occur along the extended vinylogous amide system between the nitrogen atom and the carbonyl oxygen atom of the 4-methoxycarbonyl group leading to the development of partial positive and negative charges at these nitrogen at oxygen atoms respectively. This suggestion is consistent with the small deviations in the observed bond lengths from those anticipated for a non-interacting system, and is noteworthy in that one benzenoid double bond is involved. It is also in agreement with the observations that while the reduced azepines (**4**), (**5**), (**8**), and (**9**), like 2-aminocinnamic esters,[6] are basic the esters (**2**) and (**3**) do not dissolve in aqueous acid and their u.v. spectra show no change on addition of $HClO_4$. In contrast to the dihydrobenz[*b*]azepine (**3**), 1-*p*-bromobenzenesulphonylazepine adopts a boat-like structure in the crystal in which the 2-, 3-, 6-, and 7-carbon atoms are co-planar.[7]

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