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Reactions of 1*H*-1,2- and 1*H*-1,3-Diazepines with Dimethyl Acetylenedicarboxylate

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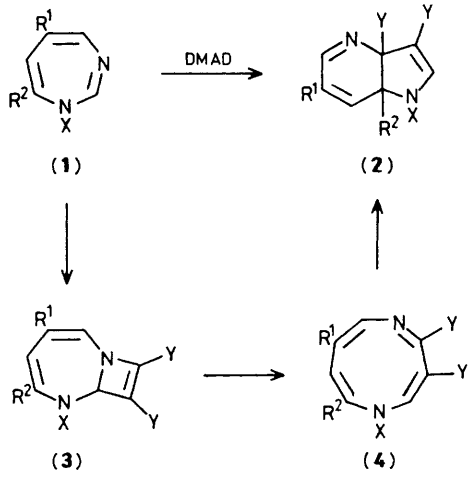
The title reactions yield the 3a,7a-dihydropyrrolo[3,2-*b*]pyridines (**2**) and 3a,7a-dihydroindazoles (**9**), respectively, probably *via* the diazonine intermediates (**4**) and (**8**) derived from the initially formed [2 + 2] π cycloadducts; the indazoles (**9**) further react with the reagent to give the dimethyl phthalates (**6**) and the pyrazoles (**7**) *via* the [4 + 2] π cycloadducts (**10**).

Fully unsaturated seven-membered heterocyclic compounds are known to react with a variety of dienophiles and dienes, because they possess many reaction sites and can undergo intermolecular cycloadditions as monoenes, dienes, or trienes, in addition to norcaradiene forms.[1] Cycloadditions of seven-membered heterocyclic rings containing two heteroatoms, such as 1,2-diazepines,[2] 1,3-diazepines,[3] and 1,3-oxazepines,[4] have also been well studied. However, these compounds have appeared[2—4] to be unreactive with acetylenes, even activated acetylenecarboxylic acid esters, which are known to react with a variety of heterocycles.[5] We report here that 1,2- and 1,3-diazepines can be forced to react with dimethyl acetylenedicarboxylate (DMAD) by prolonged heating.

Treatment of the 1*H*-1,3-diazepines (**1a—c**)[6] with DMAD (1.5 mol. equiv.) in benzene at 60—70 °C until almost all of the starting diazepines had been consumed (for 6—7 days)† gave the corresponding 3a,7a-dihydropyrrolo[3,2-*b*]pyridines (**2**)‡ in 40—60% yields, as the sole characterizable products.

The formation of (**2**) from (**1**) may proceed by initial addition of DMAD to the imine double bond of (**2**) to give the cycloadducts (**3**). The adducts (**3**) may undergo ring expansion to the 1,5-diazonines (**4**), which then cyclize to give the products (**2**), although attempts to isolate the key intermediates (**3**) and (**4**) have been unsuccessful. In all cases, the formation of the other possible cycloadducts was not observed.

However, the reaction of the 1*H*-1,2-diazepines (**5a—c**)[7] with DMAD (2.5 mol. equiv.) under similar conditions resulted in the formation of the dimethyl phthalates (**6**) (20—40%) and the 3,4-bismethoxycarbonylpyrazoles (**7**) (20—40%). This reaction may involve the 1,2-diazonine intermediates (**8**), by analogy with the case of (**1**). The diazonines (**8**) might undergo intramolecular cyclization to give the 3a,7a-



X = CO_2Et
Y = CO_2Me

a; R^1 = Me, R^2 = H
b; R^1 = R^2 = Me
c; R^1 = H, R^2 = Me

Scheme 1

† Reaction times shorter than 6—7 days resulted in a decrease in the amount of products (**2**) and an increase in starting diazepines; the yields of (**2**) calculated from the consumed (**1**) are nearly constant (40—60%), indicating that the formation of the cycloadduct (**3**) is the rate-determining step for this reaction.

‡ Satisfactory elemental analyses and spectral data were obtained for all new compounds reported; *e.g.*, (**2a**): m.p. 145—146 °C; i.r. $\nu_{max.}$ (KBr) 1744 and 1710 cm^{-1} (C=O); ^1H n.m.r.: δ ($CDCl_3$) 1.36 and 4.28 (3H, t, and 2H, q, CO_2Et), 1.96 (3H, dd, 6-Me), 3.76 and 3.82 (each 3H, s, CO_2Me), 4.95 (1H, m, 7a-H), 6.2—6.4 (1H, m, 7-H), 7.70 (1H, s, 2-H), 7.81 (1H, d, 5-H), $J_{5,7}$ 2, $J_{6\text{-Me},7}$ 1.5, $J_{6\text{-Me},7a}$ 1.5, and $J_{7,7a}$ 5 Hz; ^{13}C n.m.r.: δ (ring carbons) 58.4 (d), 71.6 (s), 115.6 (s), 121.6 (d), 128.7 (s), 142.6 (d), 157.4 (d).

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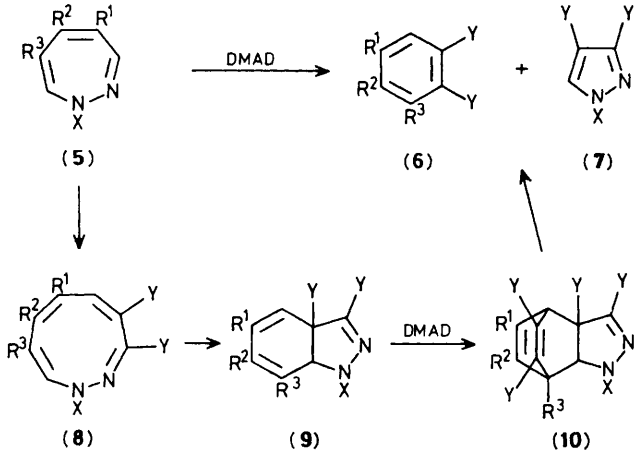

X = CO_2Et
Y = CO_2Me

a; $R^1 = R^2 = R^3 = H$
b; $R^1 = R^3 = H, R^2 = Me$
c; $R^1 = R^3 = Me, R^2 = H$

Scheme 2

dihydroindazoles (**9**), which further react with DMAD to afford the products (**6**) and (**7**) *via* the [4 + 2] π cycloadducts (**10**). This mechanistic assumption is confirmed by the following facts. When the reaction of (**5b**) with DMAD (1.1 mol. equiv.) was carried out at 40 °C for 10 days, the indazoles (**9b**) could be isolated in *ca.* 5% yield,§ together with (**6**) (10%), (**7**) (10%), and the starting diazepine (**5b**) (55%). The key intermediate (**9b**) was isolated, and when treated with DMAD at 60 °C for 20 h it gave (**6**) and (**7**) quantitatively. In addition, 3-methyl-1*H*-1,2-diazepines did not react with DMAD, even when heated for 2 weeks, suggesting that the methyl group blocks the initial cycloaddition to DMAD.

Although the stereochemistry of these reactions is not clear at present, the products (**2**) and (**9b**) are assumed to be *cis*-fused compounds from their ^1H n.m.r. data,¶ and so the intermediates (**4**) and (**8**) might be all-*cis* diazonines. It is known that the thermal isomerization of all-*cis* cyclononatetraene and its hetero analogues gives the corresponding *cis*-fused bicyclic compounds.[8]

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§ Compound (**9b**): m.p. 98—99 °C; i.r., $\nu_{max.}$ (KBr) 1740 and 1710 cm^{-1} (C=O); ^1H n.m.r.: δ ($CDCl_3$) 1.36 and 4.36 (3H, t, and 2H, q, CO_2Et), 1.80 (3H, br., 6-Me), 3.77 and 3.85 (each 3H, s, CO_2Me), 5.24—5.36 (1H, m, 7a-H), 5.78—5.92 (1H, m, 7-H), 5.94 (1H, d, *J* 9 Hz, 4-H), 6.12 (1H, d, *J* 9 Hz, 5-H); ^{13}C n.m.r.: δ (ring carbons) 59.0 (s), 64.3 (d), 113.9 (d), 119.5 (d), 127.7 (d), 132.5 (s), 144.9 (s).

¶ It is known[9] that the 7a-proton of *cis*-1-ethoxycarbonyl-3a,7a-dihydroindole resonates at much lower field (δ 5.05) than that of its *trans*-isomer (δ 3.93). Therefore, the chemical shifts of 7a-H in (**2a**) (δ 4.95) and (**9b**) (δ *ca.* 5.3) suggest that (**2a**) and (**9b**) are *cis*-fused isomers.

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