Bicyclic Bishydrazines: A New Class of Heterocycle by a Double Diene Synthesis

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Summary Double diene synthesis from α-pyrone and azodicarboxylic esters gives monocyclic hydrazine di-esters and bicyclic bishydrazine tetra-ester; the latter, a new class of heterocycle, show two pairs of non-equivalent ester groups in the room temperature n.m.r. spectrum.

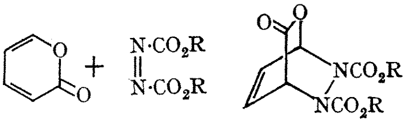
α-PYRONES have frequently been used in Diels–Alder reactions with olefins to give mono-adducts which may then decarboxylate, spontaneously or on heating, to give dienes capable of further addition;[1] the bis-adducts formed are bicyclo[2,2,2]octene derivatives. We report the analogous reaction of α-pyrone with azo-esters to give mixtures of the 1,2-dihydropyridazine esters (II) presumably from the lactones (I), and the bis-adducts (III) which are derivatives of the new heterocyclic system 1,2,3,4-tetrazabicyclo-[2,2,2]oct-5-ene.

α-Pyrone and dimethyl azodicarboxylate (0·1M each) reacted slowly (refluxing benzene, 10 d.) Chromatography of the solution on silica gel gave (IIa), an oil identical (i.r., n.m.r., g.l.c.) with authentic ester[2] and (IIIa) (26%, based on azo-ester), m.p. 200—201°, $\nu_{C=O}$ (CCl_4) 1762, 1728 cm.$^{-1}$, u.v. end absorption only, n.m.r. ($CDCl_3$, 50°) τ 3·3 (AA′) and 3·6 (BB′) (2t, 4H, vinyl and tertiary, $|J_{AB} + J_{AB'}|$ = 7·0 c./sec.), 6·1 (s, 6H, Me); dihydro-derivative (Pd–H_2), m.p. 165·5°.

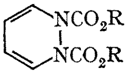
Under similar reaction conditions diethyl azodicarboxylate in 7 days gave (IIb) (16% by g.l.c., not isolated) and (IIIb) (22%), m.p. 149—150°, $\nu_{C=O}$ (CCl_4) 1767, 1722 cm.$^{-1}$, n.m.r. ($CDCl_3$, 50°) vinyl and tertiary H as for (IIIa), τ 5·77 (q, CH_2, J = 6·8 c./sec.), 8·73 (t, CH_3); dihydro-derivative, m.p. 111—113·5°. Diphenyl azodicarboxylate reacted more rapidly to give (IIIc) (3 d., 60%), m.p. 171—171·5°, $\nu_{C=O}$ (CCl_4) 1775, 1742 cm.$^{-1}$, n.m.r. ($CDCl_3$) complex, between τ 2·2—2·9.

In the room temperature, 60 Mc./sec. n.m.r. spectrum of (IIIa) the methyl group appears as a doublet of equal intensities ($\Delta\nu$ = 4·2 c./sec.) with no accompanying change in the ring hydrogens. Further cooling leads to broadening of all absorptions. Likewise the room temperature spectrum of (IIIb) shows two equal intensity methyl triplets ($\Delta\nu$ = 1·3 c./sec., J = 6·8 c./sec. in each) and two methylene quartets ($\Delta\nu$ = 4·1 c./sec.) and unaffected ring hydrogens.

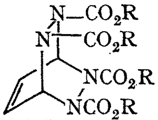
These observations can be accommodated by an extension of the "slow bridge flipping" hypothesis of Anderson and Lehn,[3] who found that the non-equivalence of the ester groups in the room temperature spectrum of the bicyclic esters (IV) and their dihydro-derivatives could be interpreted on the basis of a dissymmetric twist conformation (IV, as shown) having planar or near-planar nitrogens and interconverting by slow N–N bond rotation into its mirror image; the ester groups, which are in different environments, then exchange their identities. The planarity of the nitrogens, attributable to partial double bond character between N and CO, was concluded to be general for a wide range of mono- and bi-cyclic esters. Pyramidal nitrogen, permitting slow inversion of the ester groups was in no case thought to be involved.† Application of a *double* bridge flipping



(Ia) R=Me
(Ib) R=Et
(Ic) R=Ph

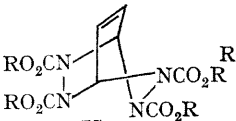


(II)

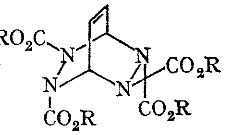


(III)

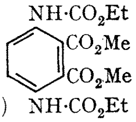
(IV)



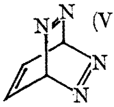
(V)



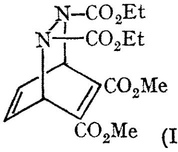
(VI)



(VIII)



(VII)



(IX)

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† Whether nitrogen in hydrazine esters is pyramidal or planar had been the subject of some controversy. The literature pertinent to this, and to conformational effects in hydrazines in general, can be found from ref. 3.

concept to (III) gives the dissymmetric structure (V) with planar nitrogens. Models show that large twist angles lead to two pairs of ester groups in slightly different environments, thus giving a possible explanation for the chemical shift differences.

Alternatively, a dissymmetric non-twist form with pyramidal nitrogens could be considered having the ester substituents in a staggered arrangement of two non-equivalent pairs (VI). Of seven possible non-twist forms (three of them dissymmetric) with pyramidal nitrogens, (VI) is likely the most stable, being the only one with neither eclipsing nor 1,3-diaxial interactions. At higher temperatures coalescence of the ester signals would be expected from either (V), by synchronous double bridge flipping, or (VI) by nitrogen inversion, both processes now being rapid and leading to the enantiomers, and hence to equivalence of the ester groups. Which, if either, of these rate processes is operative is being investigated.

Decarboxylative hydrolysis of hydrazine ester groups [$\text{-N(CO}_2\text{R)-N(CO}_2\text{R)-} \longrightarrow \text{-NH-NH-}$] is a general reaction, and applied to (III) should give a bis-hydrazine easily susceptible to oxidation to the unknown and probably unstable tetrazabarrelene (VII), which would be of interest with respect to the cyclobutadiene problem. However under a variety of conditions of hydrolysis with acid or alkali the adducts either failed to react (IIIc) or underwent C–N bond cleavage (IIIa, b) to give the hydrazinedicarboxylic esters or their hydrolysis products. The use of more labile ester groups (*e.g.* R = CH_2CCl_3[4]) may prove successful.

Compound (IIb), more efficiently made by Altman's method[2] (40%), m.p. 69·5—70°, $\nu_{C=O}$ (CCl_4) 1775, 1742 cm.$^{-1}$, λ_{max} (EtOH) 298 nm. (ϵ 3150), n.m.r. ($CDCl_3$, 25°) τ 3·2 (br, 2H, vinyl), 4·3 (br, 2H, vinyl),‡ 2 vinyl H, 5·71 (*q*, CH_2, *J* = 7·5 c./sec.), 8·66 (t, CH_3), is a sluggish diene in the Diels–Alder reaction. Refluxed with diethyl azodicarboxylate in benzene for 10 days it gave (IIIb) (60%), and with dimethyl acetylenedicarboxylate in toluene for one day it gave dimethyl *N,N'*-dicarbethoxy-3,6-diaminophthalate (VIII), m.p. 184—185°, (30%; structure confirmed by independent synthesis) presumably by way of (IX) which would aromatise readily.

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‡ Altman (ref. 2) observed multiplicity for the vinyl hydrogens of (IIa); the temperature was not specified.

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