syn-Selectivity in the Reaction of 1,3-Dipoles with *cis*-Cyclobut-3-ene-1,2-diol

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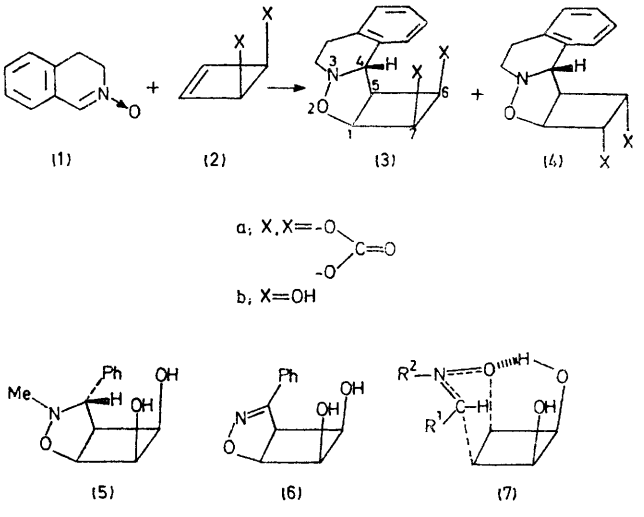
Summary Cyclic nitrones, *C*-phenyl-*N*-methylnitrone, benzonitrile oxide, and 2,4,6-trimethylbenzonitrile oxide react in benzene with *cis*-cyclobut-3-ene-1,2-diol to give as the sole or the dominant products the sterically disfavoured *syn*-adducts.

STERICALLY dis-favoured *syn* stereoselectivity in 1,3-dipolar cycloadditions has been reported only for the reactions of 1,3-dipoles (diazoalkanes,[1] nitrile oxides,[2] nitrones[3]) with *cis*-3,4-dichlorocyclobutene. We now report reactions of *cis*-cyclobut-3-ene-1,2-diol (**2b**), m.p. 110 °C [prepared by $LiAlH_4$ reduction (ether, room temperature) of the carbonate (**2a**)[4]] in which the sole or the major adducts formed were the sterically dis-favoured *syn* adducts.

The 3,4-dihydroisoquinoline *N*-oxide (**1**) reacted with (**2a**) in anhydrous benzene at room temperature to give as dominant product the *anti*-adduct (**4a**) (75%), m.p. 146—147 °C, with minor amounts of (**3a**) (3·5%), m.p. 190—191 °C; with (**2b**) the cycloaddition was highly stereoselective, giving the *syn*-adduct (**3b**) (92%), m.p. 88—90 °C, as the sole isolated product even though t.l.c. analyses of the crude reaction mixture showed traces of the *anti*-isomer (**4b**). The adducts (**3b**) and (**4b**), m.p. 147—149 °C, can be prepared easily by gentle heating in water of (**3a**) and (**4a**) respectively. The adduct (**4b**) was also prepared in low yield by $LiAlH_4$ reduction (ether, room temperature) of (**4a**).

Comparable results were also observed for the reaction of 5,5-dimethyl-Δ^1-pyrroline *N*-oxide with (**2a**) in anhydrous benzene at reflux [*syn*-adduct (8%), m.p. 122—123 °C, *anti*-adduct (65%), m.p. 126—128 °C] and with (**2b**) at room temperature (87% yield of *syn*-adduct, m.p. 109—110 °C).



In addition to the conversion of (**3a**) and (**4a**) into (**3b**) and (**4b**), structural assignments relied upon elemental analyses, and i.r. and ^{1}H n.m.r. data. The n.m.r. data (Table) for

TABLE

^{1}H N.m.r. [δ (C_6D_6)] data and (in parentheses) $\Delta\delta = \delta(CDCl_3) - \delta(C_6D_6)$[a,b]

	1-H	4-H	5-H	$J_{4,5}$	$J_{5,6}$
(**3b**)	4·08(m) (0·31)	4·73br (s) (0·05)	3·17(m) (0·43)	<1·0	5·0
(**4a**)	3·87(d) (0·65)	3·72br (s) (0·76)	3·02(d) (0·67)	<0·5	<0·5

[a] Other Δδ values: 0·31 for 6- and 7-H in (**3b**), 0·84 for 6-H and 0·58 for 7-H in (**4a**). [b] J in Hz.

adducts (**3b**) and (**4a**) are typical for *anti*- and *syn*-adducts.[3] In particular, the *trans* relationship of 4- and 5-H in (**3b**) and (**4a**), and 5- and 6-H in (**4a**) is supported by the low coupling constants found.[3,5] Moreover, the lower aromatic solvent induced shift observed for 4-H of the *syn*-adduct (**3b**) compared with that found for (**4a**), is attributed to the *syn*-disposition of the groups at positions 6 and 7 which makes solvation of 4-H difficult.

The reaction of *C*-phenyl-*N*-methylnitrone and (**2b**) in benzene at reflux was slow, and gave only the *syn*-adduct (**5**) (38%), m.p. 104 °C. The latter adduct was shown (i.r., t.l.c., ^{1}H n.m.r.) to be different from the other three possible stereoisomers which have been synthesized by a different route.[6] We assume that compound (**5**) is formed through an *exo* addition of the *E*-isomer of *C*-phenyl-*N*-methylnitrone to (**2b**). The latter isomer, although present in very low concentrations in the equilibrium $E \rightleftharpoons Z$ would be the most reactive form of the *C*-phenyl-*N*-methylnitrone.[7]

Benzonitrile oxide generated *in situ* was similarly treated with (**2b**) in benzene at room temperature; the adduct (**6**) (65%), m.p. 147—148 °C, was isolated and here too t.l.c. analyses of the crude reaction mixture showed minor amounts of the known *anti*-isomer.[8]

Experiments with diazoalkanes (diazomethane, diazoethane, 2-diazopropane and phenyldiazomethane) and (**2b**) in ether yielded insoluble materials, probably polymeric, which were not studied further.

In our opinion, a rationalization of the clear *syn*-selectivity observed for the reactions studied involves, besides the possible interactions already invoked in the case of *cis*-3,4-dichlorocyclobutene,[2,3,9] the formation of a hydrogen bond between the hydroxylic hydrogen of the dipolarophile and the oxygen atom of the 1,3-dipole, *e.g.* (**7**).[10]

In accordance with this view, 2,4,6-trimethylbenzonitrile oxide adds (**2b**), yielding a predominance of the *syn*-adduct, m.p. 117—119 °C (*syn*:*anti* ratio 9:1) in benzene solution, and comparable amounts of the *syn* and *anti*, m.p. 154 °C, adducts in methanol solution.†

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† Structures of these adducts have been assigned by comparison of their ^{1}H n.m.r. spectra with those of the adducts from benzonitrile oxide.

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