1,4-Dipolar Cycloadditions as Trapping Reactions for Zwitterionic Intermediates of 2+2 Cycloadditions

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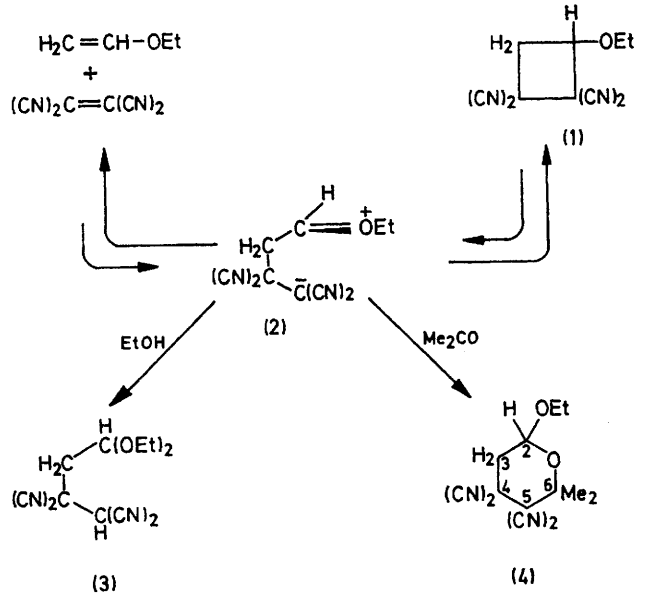
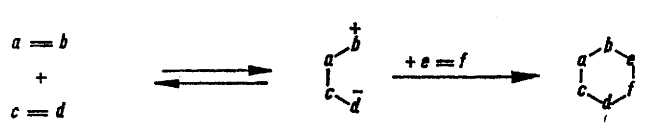
Summary The zwitterionic intermediate in the 2+2 cycloaddition of tetracyanoethylene to ethyl vinyl ether behaves as a 1,4-dipole and can be intercepted by cycloadditions to heteromultiple bonds producing six-membered heterocycles.

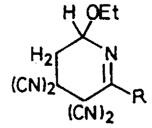
The 2+2 cycloadditions of tetracyanoethylene (TCNE) to enol ethers take place *via* reversibly formed zwitterions of type (**2**),[1] which can be trapped by alcohols with formation of acetals, *e.g.*, (**3**).[2] The stereospecificity of the alcohol addition to the zwitterions from TCNE and *cis*- and *trans*-propenyl alkyl ethers offered conclusive evidence for the 'U'-conformation of the intermediate.[3]

When TCNE is treated with ethyl vinyl ether in acetone at room temperature, after 10 min 6% of the oxan derivative (**4**) is obtained along with 94% of the cyclobutane (**1**) under conditions of kinetic control. A quantitative yield of the three-component adduct (**4**) was isolated when the acetone solution of (**1**) was kept for one week at room temperature. The four-membered ring adduct (**1**) in polar solvents is in equilibrium with a small concentration of the zwitterion (**2**) which is irreversibly captured by acetone. A slow *cis,trans* isomerisation of the TCNE adducts of enol ethers in acetonitrile[4] and the alcoholysis of tetracyanoalkoxycyclobutanes[2] indicated earlier the reversibility of the ring closure to cyclobutanes of type (**1**).



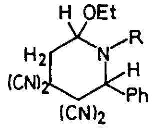
Earlier a general scheme of 1,4-dipolar cycloaddition was introduced.[5] A nucleophilic multiple bond system *a*=*b* combines with an electrophilic system *c*=*d*, sometimes in equilibrium, to give a 1,4-dipole (**5**) which undergoes a two-step cycloaddition to a third multiple bond system *e*=*f*. A variety of six-membered rings (**6**) can be produced by this principle.[6] The combination of the 1,4-dipole (**2**) with acetone is recognized as a new example of this general scheme.





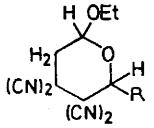
(7) R = Me

(8) R = Ph



(9) R = Me

(10) R = Et



(11) R = Ph

(12) R = Et

The oxan (**4**), m.p. 155—156°, shows an ABX system for 3-H_2 and 2-H at τ 7·00, 7·22, and 4·68 with J_{AB} 15·0 Hz and $J_{AX} + J_{BX}$ 9·6 Hz. The ethoxy group at the chiral centre forms an ABX_3 spectrum, while two 6-methyls occur as singlets at τ 8·08 and 8·17.

The tetrahydropyridine derivative (**7**), m.p. 106—107°, is formed with 99% yield when a solution of (**1**) in acetonitrile is kept for three weeks at room temperature; the C=N frequency is 1675 cm^{-1}. The less reactive benzonitrile needs 3 days at 60° to provide a 40% yield of (**8**), m.p. 99—101°. Elemental analyses, osomometric molecular weight determinations, n.m.r. and i.r. spectra provided evidence for the structure of the three-component cycloadducts (**7**)—(**12**).

The reaction of (**1**) with benzylidene-methylamine and -ethylamine proceeds at room temperature in 3 days; 63% each of (**9**), m.p. 146—147°, and (**10**), m.p. 140—141·5°, were isolated. Benzaldehyde reacts in one week at 20° to give the oxan (**11**), m.p. 149—150°, in 95% yield. The reaction with propionaldehyde is accompanied by polymerisation of the latter; due to isolation difficulties, only 28% of (**12**), m.p. 118—117°, was obtained. Only one of the two conceivable diastereomers of adducts (**9**)—(**12**) appears to form.

Experiments to react the 1,4-dipole (**2**) with olefins or acetylenes to produce carbocyclic six-membered rings have so far not been successful.

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[4] R. Huisgen and G. Steiner, *J. Amer. Chem. Soc.*, **1973**, **95**, 5054.

[5] R. Huisgen and K. Herbig, *Annalen*, **1965**, **688**, 98; R. Huisgen, M. Morikawa, K. Herbig, and E. Brunn, *Chem. Ber.*, 1967, **100**, 1094, and later papers.

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