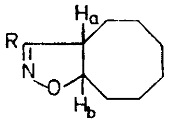
1,3-Dipolar Cycloaddition of Mesitonitrile Oxide to *cis*- and *trans*-Cyclo-octene. A Kinetic Investigation

By **Giorgio Bianchi** * and **Domenico Maggi**, Istituto di Chimica Organica dell'Università, Via Taramelli 10, 27100 Pavia, Italy

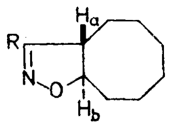
Rate constants and activation parameters for the addition of mesitonitrile oxide to *cis*- and *trans*-cyclo-octene have been determined. It is concluded that the high reactivity of *trans*-cyclo-octene with mesitonitrile oxide and other 1,3-dipoles is due to distortions of the double bond.

REACTIVITY in 1,3-dipolar cycloadditions has been extensively studied and now seems well understood.[1] According to perturbation theory,[2-4] the basic elements to be considered in order to evaluate and rationalize reactivity in 1,3-dipolar cycloadditions are the coefficients and energies of the frontier orbitals (HOMO and LUMO) of the reactants. However, in several instances, it has been found that dipolarophiles with very similar frontier orbital energies showed quite different dipolarophilic activities towards 1,3-dipoles.[3,5] Consequently other factors can influence reaction rates in 1,3-dipolar cycloadditions, *e.g.*, the stability of reactants and products, steric hindrance, and electrostatic interactions.

This paper reports kinetic data obtained for the 1,3-dipolar cycloadditions of mesitonitrile oxide (MNO) to *cis*- and *trans*-cyclo-octene to give adducts (1) and (2), respectively, whose homogeneity was checked by n.m.r. spectra.



(1)



(2)

$R = 2,4,6\text{-}Me_3C_6H_2$

In line with quantitative and qualitative data reported in the literature for reactions of the same dipolarophiles with azides [6] and diazomethane,[7] the rate constant found for the two cycloadditions studied turned out to be different in spite of the similar HOMO energies of the two cycloalkenes (see Table 4). A property of some alkenes defined as 'bond distortion' [8,9] is considered to be the factor determining reactivity in this and other similar cases of 1,3-dipolar cycloadditions.

RESULTS

Kinetic data (Table 1) obtained by following reactions up to 60—80% completion by quantitative u.v. analysis, gave results fitting the second-order rate equation (1). The effect of solvent polarity on the rate of MNO addition to

$$\mathrm{d\,[product]/d}t = k\mathrm{[MNO][cyclo\text{-}octene]} \qquad (1)$$

trans-cyclo-octene is given in Table 2. All the k_2 values reported are the average of three or more independent runs.

TABLE 1

Second-order rate constants ($1\ mol^{-1}\ s^{-1}$) for cycloadditions of MNO to *cis*- and *trans*-cyclo-octene in absolute ethanol

cis-Cyclo-octene		*trans*-Cyclo-octene	
t/°C	10^4k_2	t/°C	k_2
25.0	0.657	20.0	0.342
30.4	1.066	25.0	0.481
35.4	1.470	30.0	0.647
40.1	3.710	35.0	0.816
44.7	4.200		
50.0	6.540		

TABLE 2

Rates of addition of MNO with *trans*-cyclo-octene in various solvents at 25.0 °C

Solvent	E_T *	Dielectric constant	k_2/ $1\ mol^{-1}\ s^{-1}$
Ethanol	51.9	24.3	0.481
Acetonitrile	46.0	37.5	0.236
Chloroform	39.1	4.7	0.119
Ethyl acetate	38.1	6.0	0.196
Cyclohexane	31.2	2.0	0.363

* E_T = empirical solvent polarity parameter (see C. Reichardt and K. Dimroth, *Fortschr. Chem. Forsch.*, 1968, **11**, 1).

TABLE 3 [a]

Thermodynamic parameters

Reaction	E_a	log A	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$
MNO + *cis*-cyclo-octene	18.60	9.9	−16.6	23.07
MNO + *trans*-cyclo-octene	10.60	7.4	−25.2	17.41

[a] log A, $\Delta S^{\ddagger}$ (±1.0; cal mol^{-1} K^{-1}), and $\Delta G^{\ddagger}$ (kcal mol^{-1}) are for reactions at 25 °C; E_a (±0.3) values are expressed as kcal mol^{-1}.

Activation parameters for the two reactions are given in Table 3.

---

[1] (*a*) R. Huisgen, R. Grashey, and J. Sauer in 'The Chemistry of Alkenes,' ed. S. Patai, Interscience, New York, 1964, p. 806; (*b*) G. Bianchi, C. De Micheli, and R. Gandolfi, *ibid.*, supplementary volume, in the press.

[2] R. Sustmann, *Tetrahedron Letters*, 1971, 2717.

[3] R. Sustmann and H. Trill, *Angew. Chem. Internat. Edn.*, 1972, **11**, 838.

[4] K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Amer. Chem. Soc.*, 1973, **95**, 7301.

[5] K. Bast, M. Christl, R. Huisgen, and W. Mack, *Chem. Ber.*, 1973, **106**, 3312.

[6] A. S. Bailey and J. E. White, *J. Chem. Soc.* (*B*), 1966, 819; L. W. Boyle, M. J. Peagram, and G. H. Whitham, *ibid.*, 1971, 1728.

[7] T. Aratani, Y. Nakanisi, and H. Nozaki, *Tetrahedron*, 1968, **26**, 4339.

[8] W. L. Mock, *Tetrahedron Letters*, 1972, 475.

[9] L. Radom, J. A. Pople, and W. Mock, *Tetrahedron Letters*, 1972, 479.

TABLE 4

Strain energy differences (alkene minus alkane; see ref. 10), ionization potentials (IP_v),[a,b] and relative rate constants for cycloadditions of MNO (this work), benzonitrile oxide (BNO),[c] and PhN_3 (from ref. 1*b*) with cycloalkenes

Alkene	IP_v(eV)	Strain energy difference	$k_{rel.}$ MNO	$k_{rel.}$ BNO	$k_{rel.}$ PhN_3
cis-Cyclo-octene	8.98	−2.71	1.00		0.355
trans-Cyclo-octene	8.69	6.33	7 300		3 655
Cyclohexene	9.12	0.86		0.012	0.017
Cyclopentene	9.18	−0.60		1.00	1.00
Norbornene	8.97	5.72		71.00	101.00

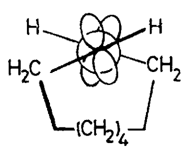
[a] P. Bischof and E. Heilbronner, *Helv. Chim. Acta*, 1970, **53**, 1677; P. Bischof, J. A. Hashmall, E. Heilbronner, and V. Hornung, *ibid.*, 1969, **52**, 1745. [b] C. Batic, O. Ermer, E. Heilbronner, and J. R. Wiseman, *Angew. Chem. Internat. Edn.*, 1973, **12**, 312. [c] W. Fliege and R. Huisgen, *Annalen*, 1973, 2038.

DISCUSSION

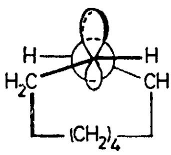
The data reported in Tables 1 and 3 reveals that the reaction leading to compound (2) is favoured. The difference in $\Delta S^{\ddagger}$ values found for the two reactions, although greater than that expected for a statistical factor of 2, mostly originates from the fact that only one face of *trans*-cyclo-octene is attacked, whereas attack can occur with equal probability on either side of *cis*-cyclo-octene. The relative indifference to solvent polarity found in the present investigation (Table 2) parallels the insensitivity reported for the majority of 1,3-dipolar cycloadditions.[1]

Comparison of relative rate constants with ionization potentials and strain energy differences for dipolarophiles for the reactions reported in Table 4, reveals how both the frontier orbital energies of the reactants and strain energy variations implicated in 1,3-dipolar cycloadditions, fail to explain the different reactivities of the dipolarophiles considered. Particularly notable is the lack of correlation between strain energy variation and relative rate constants for all the 1,3-dipolar cycloadditions reported in Table 4. However, the experimental kinetic data found can be understood on the basis of work by Mock and his co-workers.[8,9] According to these authors rehybridization occurring at the carbon atoms of double bonds subject to torsional strain is responsible for some aspects of double bond reactivity such as 1,3-dipolar cycloadditions. In fact, as a consequence of the well known non-planarity of the double bond of *trans*-cyclo-octene [10,11] considerable bond distortion is present in the unsaturated part of the molecule. Such distortion is accompanied by significant bending of the bonds at the unsaturated carbon atoms which eventually tends to produce a pyramidal structure (4) instead of (3) in which the twisted double bond will retain complete sp^2 hybridization.

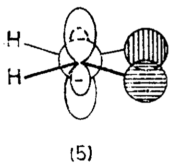
The particular shape of the π orbitals in (4), which incorporate some *s* character, allows quite favourable overlap with the lobes of the two ends of the 1,3-dipoles, according to the two parallel planes reaction scheme proposed by Huisgen.[12] This favourable situation for a suprafacial reaction,[13] evidently cannot occur in all the dipolarophiles possessing high energy strain. For example norbornene, in which rehybridization is presumably absent, shows lower reactivity than expected from its strain energy (see Table 4).* On the other hand bond distortion which causes pyramidalization at the carbon atoms of the double bond on opposite faces of the molecule will also result in low reactivity. Typical examples of this type of dipolarophile with low activity are represented by the *cis*-alkene (5) and cyclohexene (6).



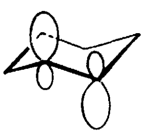
(3)



(4)



(5)



(6)

EXPERIMENTAL

Preparation of Materials.—*cis*-Cyclo-octene (Fluka) was purified by distillation. *trans*-Cyclo-octene was obtained as described in the literature.[14]

Isolation and Characterization of Adducts (1) *and* (2).—(a) *cis*-Cyclo-octene (1.61 g, 0.014 mol) in benzene (10 ml) and MNO (1.10 g, 0.0062 mol) were left at room temperature until MNO had disappeared as shown by t.l.c. The solution was then evaporated to dryness and the residue crystallized from ethanol to give cis-11-*mesityl*-10-*aza*-9-*oxabicyclo*-[6.3.0]*undec*-10-*ene* (1) as plates (2.1 g, 77%), m.p. 87—89°, $\lambda_{max.}$ (EtOH) 260 nm (ε 1 960), δ 3.27 (1 H, m, H_a), 4.58 (1 H, m, H_b), 1.00—2.22 (12 H, m, $[CH_2]_6$), 2.22 (9 H, s, Me_3), and 6.84 (2 H, s, ArH); H_a and H_b collapsed to two doublets (*J* 10 Hz) on irradiation of the methylene groups (Found: C, 79.65; H, 9.1; N, 5.2. $C_{18}H_{25}NO$ requires C, 79.65; H, 9.3; N, 5.15%).

(b) *trans*-Cyclo-octene (0.80 g, 0.007 mol) in benzene (10 ml) and MNO (0.86 g, 0.005 3 mol) were left at room temperature for 30 min. The solution was evaporated to give an oil which crystallised from light petroleum on cooling. Further purification by sublimation (110—120° at 2.5 mmHg) gave the trans-*isomer* (2) as crystals, m.p. 41.5—

---

* As suggested by a referee, the case of norbornene reactivity should be considered with caution as a simple correlation between cyclo-alkene strain and dipolar reactivity is not expected here because of unfavourable interactions between the bridging methylene group and the approaching 1,3-dipole.

[10] N. L. Allinger and J. T. Sprague, *J. Amer. Chem. Soc.*, 1972, **94**, 5734.

[11] O. Ermer, *Angew. Chem. Internat. Edn.*, 1974, **13**, 604.

[12] R. Huisgen, *Angew. Chem. Internat. Edn.*, 1963, **2**, 633.

[13] R. B. Woodward and R. Hoffmann, 'The Conservation of Orbital Symmetry,' Academic Press, New York, 1970, p. 65.

[14] A. C. Cope and R. D. Bach, *Org. Synth.*, 1969, **49**, 39.

42.5°, $\lambda_{max.}$ (EtOH) 260 nm (ε 3 150), δ 3.30 (1 H, m, H_a), 4.50 (1 H, m, H_b), 1—2.26 (12 H, m, $[CH_2]_6$), 2.26 (9 H, m, Me_3), and 6.87 (2 H, m, ArH). On irradiation of the methylene groups, H_a and H_b collapsed to two doublets (*J* 12 Hz) (Found: C, 79.15; H, 9.25; N, 5.3%).

Kinetics.—Kinetic data for MNO addition to *cis*-cyclo-octene were obtained for solutions containing an excess of olefin by following spectrophotometrically the disappearance of the nitrile oxide. Kinetic runs for reactions of MNO with *trans*-cyclo-octene were for solutions containing nearly equal amounts of the two reactants. The samples were accurately weighed into standard flasks and made up to 50 ml with spectroscopic grade ethanol, then placed in a thermostatted bath at the required temperature. After the two solutions were mixed together in a 100 ml volumetric flask, portions (1 ml) were pipetted at suitable intervals into ethanol (50 ml) and cooled to prevent further reaction. The second-order rate constants were determined in the usual way from expression (2) where *a* is the initial concentration

$$k_2t = \frac{2.303}{b - a} \log \frac{a(b - x)}{b(a - x)} \qquad (2)$$

of MNO, *b* that of the cyclo-octene, *x* the concentration of MNO at time *t*, and k_2 the second-order rate coefficient in l mol^{-1} s^{-1}. The amount of MNO at any time was determined from the u.v. absorption, $\lambda_{max.}$ 260 nm (ε 16 500), and the concentration in the original reaction solution was calculated.

[5/1285 *Received*, 30*th June*, 1975]