Tetracyanoethylene and Enol Ethers. A Model for 2 + 2 Cycloadditions via Zwitterionic Intermediates

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Thermal 2 + 2 cycloadditions leading to four-membered rings are less frequently encountered than Diels–Alder reactions (4 + 2 → 6) or 1,3-dipolar cycloadditions (2 + 3 → 5). They are restricted to certain classes of unsaturated compounds, e.g., allenes, ketenes, polyhaloethylenes, conjugated dienes, and strained hydrocarbons.[1]

The principle of conservation of orbital symmetry[2,3] forbids concerted thermal 2 + 2 cycloadditions. How then do they occur?

1
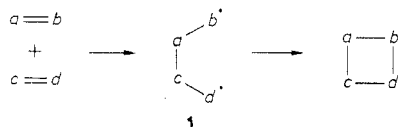
The pathway via a biradical intermediate (1) offers an alternative. Despite a favorable reaction enthalpy, $\Delta H = -19$ kcal/mol,[4] and an equilibrium concentration of 99.76 mol % at 25 °C and 760 Torr,[5] cyclobutane cannot be prepared on a preparative scale by dimerization of ethylene. To overcome the activation barrier, $E_A = 44$ kcal/mol, a high temperature is required; due to an unfavorable dimerization entropy ($\Delta S = -46$ eu), the equilibrium concentration of cyclobutane amounts to only 0.01 mol % at 500 °C and 760 Torr.[5]

For 2 + 2 cycloadditions to be feasible, the activation energy must be decreased. Polyhaloolefins are able to dimerize by the *biradical* route because fluorine destabilizes the π bond and chlorine stabilizes the terminal centers of the intermediate 1. Conjugated dienes dimerize via a tetramethylene derivative of type 1 in which the terminal radicals are allylic. Bartlett's masterful investigation of cyclobutane formation from 1,1-dichloro-2,2-difluoroethylene and from the cis,trans isomeric hexa-2,4-dienes demonstrated the biradical course to be operative.[6]

2   **3**
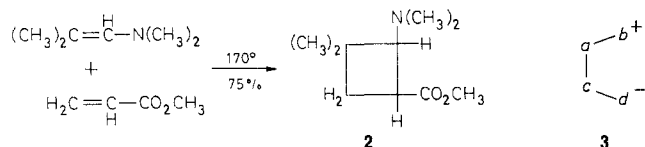
2 + 2 cycloaddition of an electron-rich to an electron-poor olefin has only moderate activation energy demands, as testified by the formation of **2** from an enamine and methyl acrylate.[7] A zwitterion of type **3**

would be an attractive intermediate. This mechanism for the process 2 + 2 → 4 appears likewise to be a general one.[8]

Tetracyanoethylene (TCNE) possesses a highly electron-deficient C=C bond with low-lying MO's. TCNE is not only a potent dienophile in the Diels–Alder reaction,[9] it is also amenable to 2 + 2 cycloadditions. Characteristically, vinyl ethers and even *p*-methoxystyrene are sufficiently electron rich to yield

4   **5** (90 %)
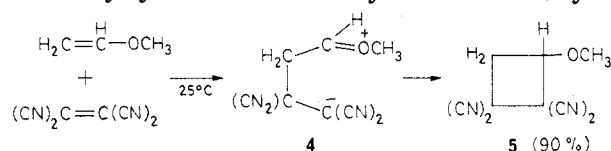
cyclobutane derivatives with TCNE at room temperature, as discovered by Williams, Wiley, and McKusick.[10]

The fact that simple alkenes and the double bond of acrylic ester are inert to TCNE argues against a biradical intermediate of type 1, but in favor of a zwitterion 3; formula 4 illustrates the efficient charge stabilization of the presumed intermediate from methyl vinyl ether and TCNE. 1,3-Dienes which are either trans fixed[11,12] or are sterically hindered at one of the terminal carbon atoms[13] likewise undergo 2 + 2 cycloadditions with TCNE. Here the zwitterion should be of the allyl cation type. The stability of the cyclopropylcarbinyl cation makes cyclopropyl-substituted ethylenes prone to add TCNE.[14]

(1) Reviews: (a) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962); (b) R. Huisgen, R. Grashey, and J. Sauer, "The Chemistry of Alkenes", S. Patai, Ed., Interscience, London–New York, 1964, p 739.

(2) R. Hoffmann and R. B. Woodward, *J. Am. Chem. Soc.*, **87**, 2046 (1965).

(3) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

(4) S. W. Benson, "Thermochemical Kinetics", Wiley, New York, N.Y., 1968, Table A11.

(5) L. M. Quick, D. A. Knecht, and M. H. Back, *Int. J. Chem. Kinet.*, **4**, 61 (1972), and references therein.

(6) (a) P. D. Bartlett, L. K. Montgomery, and B. Seidel, *J. Am. Chem. Soc.*, **86**, 616 (1964); (b) L. K. Montgomery, K. Schueller, and P. D. Bartlett, *ibid.*, **86**, 622 (1964); (c) P. D. Bartlett and L. K. Montgomery, *ibid.*, **86**, 628 (1964), and later papers.

(7) K. C. Brannock, A. Bell, R. D. Burpitt, and C. A. Kelly, *J. Org. Chem.*, **26**, 625 (1961); **29**, 801 (1964).

(8) Review: D. Seebach, *Methoden Org. Chem.*, (*Houben-Weyl*) 4th Ed., 4/4, 278 (1971).

(9) Review: E. Ciganek, W. J. Linn, and O. W. Webster, "The Chemistry of the Cyano Group", Z. Rappoport, Ed., Interscience, London–New York, N.Y., 1970, p 423–638.

(10) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Am. Chem. Soc.*, **84**, 2210 (1962).

(11) (a) A. T. Blomquist and Y. C. Meinwald, *J. Am. Chem. Soc.*, **81**, 4013 (1959); (b) J. K. Williams, *ibid.*, **81**, 4013 (1959); (c) R. Criegee, J. Dekker, W. Engel, P. Ludwig, and K. Noll, *Chem. Ber.*, **96**, 2362 (1963); (d) G. W. Griffin and L. I. Peterson, *J. Am. Chem. Soc.*, **85**, 2268 (1963).

(12) P. D. Bartlett, *Q. Rev., Chem. Soc.*, **24**, 473 (1970).

(13) (a) C. A. Stewart, *J. Org. Chem.*, **28**, 3320 (1963); (b) J. J. Eisch and G. R. Husk, *ibid.*, **31**, 589 (1966).

(14) (a) F. Effenberger and W. Podszun, *Angew. Chem., Int. Ed., Engl.*, **8**, 976 (1969); (b) S. Nishida, I. Moritani, and T. Teraji, *Chem. Commun.*, 501 (1970); 36 (1971); (c) F. Effenberger and O. Gerlach, *Chem. Ber.*, **107**, 278 (1974).

Woodward and Hoffmann[3] concluded that although concerted thermal four-membered ring formation by the suprafacial combination of two $_\pi2$ units is prohibited, the process $[_\pi2_a + _\pi2_s]$ should be orbital symmetry allowed. However, the steric congestion which occurs in the antarafacial approach of two olefins appears to be hard to surmount. No example of a thermal reaction $[_\pi2_a + _\pi2_s]$ of two ethylene-like bond systems has been established so far.[15] There is good evidence, however, that cyclobutanone formation from ketenes and alkenes follows this rare mechanistic pathway.[16,17]

We chose the virtually quantitative cycloaddition of TCNE to enol ethers as a model for mechanistic investigation. This system allows various criteria for a zwitterionic intermediate to be applied. Other conceivable pathways would be stepwise addition via a biradical (1) and concerted antarafacial addition. Furthermore, it has been suggested that in polar 2 + 2 cycloadditions configuration interaction makes the Woodward–Hoffmann forbidden s + s process "effectively allowed".[18]

Stereoselectivity

Retention of olefinic configuration in cycloadditions is a necessary but not sufficient condition for concertedness, whereas lack of stereospecificity points to a stepwise process. Proskow, Simmons, and Cairns[19] showed that 2 + 2 cycloadditions of *cis*- and *trans*-1,2-dicyano-1,2-bis(trifluoromethyl)ethylene to electron-rich olefins are not wholly stereospecific, allowing the conclusion that at least part of the reaction occurs in a stepwise manner.

6

7 (29%)　　　**8** (4%)　　　**9** (37%)
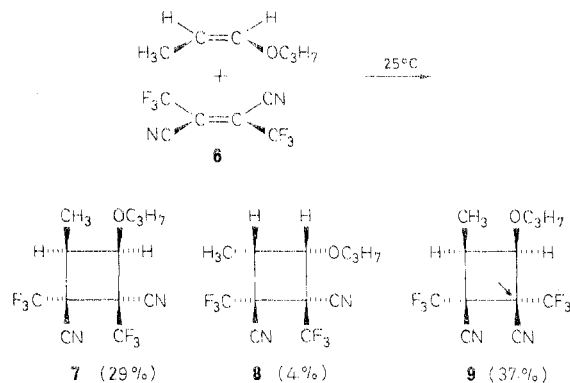
For instance, trans isomer **6** combined with *cis*-propenyl propyl ether to give cycloadducts **7** and **8** with retention and **9** with inversion at the center marked in **9** by the arrow. The stereochemistry of the electron-rich olefin was assumed not to be lost. In contrast, structural retention at the electron-deficient bond was postulated in all additions to simple vinyl ethers and

(15) The 2 + 2 cycloaddition of tetrafluoroethylene with *cis*- and *trans*-1,2-dideuterioethylene was originally suggested to be concerted. The lack of stereoselectivity revealed a stepwise addition: P. D. Bartlett, G. M. Cohen, S. P. Elliott, K. Hummel, R. A. Minns, C. M. Sharts, and J. Y. Fukunaga, *J. Am. Chem. Soc.*, 94, 2902 (1972).

(16) (a) P. R. Brook, J. M. Harrison, and A. J. Duke, *Chem. Commun.*, 589 (1970); (b) M. Rey, S. Roberts, A. Dieffenbacher, and A. S. Dreiding, *Helv. Chim. Acta*, 53, 417 (1970); (c) T. DoMinh and O. P. Strausz, *J. Am. Chem. Soc.*, 92, 1766 (1970); (d) W. T. Brady and R. Roe, *ibid.*, 93, 1662 (1971).

(17) (a) R. Huisgen, L. A. Feiler, and G. Binsch, *Chem. Ber.*, 102, 3460 (1969); (b) R. Huisgen and H. Mayr, *Tetrahedron Lett.*, 2965, 2969 (1975).

(18) (a) N. D. Epiotis, *J. Am. Chem. Soc.*, 94, 1924 (1972); (b) N. D. Epiotis, R. L. Yates, D. Carlberg, and F. Bernardi, *ibid.*, 98, 453 (1976).

(19) S. Proskow, H. E. Simmons, and T. L. Cairns, *J. Am. Chem. Soc.*, 88, 5254 (1966).

Scheme I
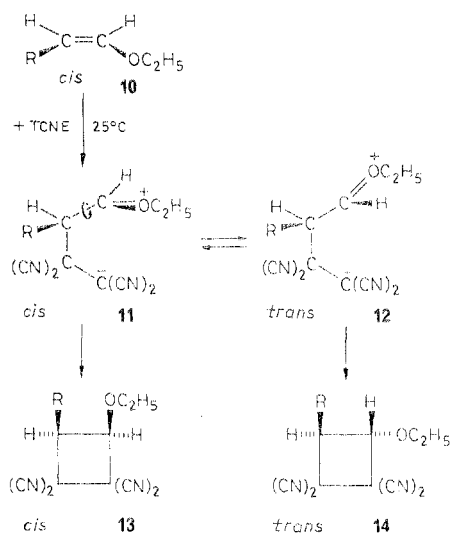
sulfides. Also the observed solvent dependence of the steric course does not form a consistent pattern. The model is a very demanding one, because the four asymmetric centers in 7–9 allow eight racemic diastereomers. We agree with the authors that the structural assignments of the cycloadducts are not unequivocal.[19]

Simpler models compel the conclusion that TCNE cycloaddition is *not stereospecific* with respect to the electron-rich double bond.[20,21] The facile reaction of TCNE with ethyl *cis*-1-alkenyl ether (10) produced quantitatively two cyclobutane derivatives. The configuration of the alkenyl ether is retained in the major product 13, while the NMR chemical shifts of the minor component leave no doubt that it has the trans structure 14. In terms of the zwitterion mechanism, *rotation* about the marked bond of 11 starts to compete with the cyclization of the zwitterion (Scheme I). Numerous zwitterion conformations are imaginable. With respect to the ring closure, we can deal with the question *as if* only the two idealized conformations 11 and 12 exist; these may be designated as cis and trans.

The stereochemical leakage increases with solvent polarity. Thus, starting from 10, R = C_2H_5, one obtains 2% of "leakage" product 14, R = C_2H_5, in benzene, 7% in dichloromethane, 10% in ethyl acetate, and 18% in acetonitrile. On starting with the ethyl *trans*-1-butenyl ether, one encounters in the cis adduct 13, R = C_2H_5, the nonstereospecific product; its share rises again from 2% in benzene, 3% in dichloromethane, and 5% in ethyl acetate to 16% in acetonitrile. A longer lifetime for intermediates 11 and 12 in a more polar solvent, owing to better solvation and diminished Coulomb attraction of the charge centers (due to higher dielectric constant), appears to be responsible for this outcome. The cycloadditions of alkyl *cis*- and *trans*-propenyl ethers and of *cis*- and *trans*-diethoxyethylene to TCNE show a similar dependence of stereoselectivity on solvent polarity. Product ratios after short reaction times are kinetically controlled.
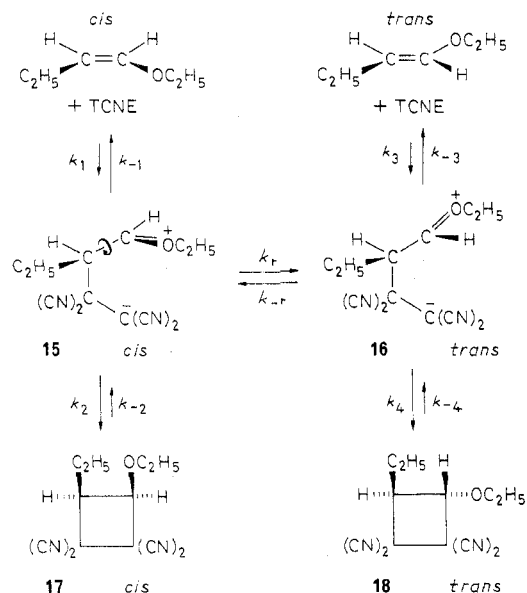
For TCNE cycloaddition to *cis*-anethole, Bartlett and Kramer[22] observed 10–15% of nonstereospecific product (trans adduct) in benzene and 49% in aceto-

(20) R. Huisgen and G. Steiner, *J. Am. Chem. Soc.*, 95, 5054 (1973).
(21) G. Steiner, Ph.D. Thesis, University of Munich, 1972.
(22) P. D. Bartlett and B. D. Kramer, quoted in ref 12.

Scheme II

Equiv of enol ether	Unconsumed enol ether		% Cycloadducts ($R = C_2H_5$)	
	Found (equiv)	cis:trans	17 (cis)	18 (trans)
1.11 cis	0.14	82:18	82	18
1.29 cis	0.28	86:14	85	15
2.02 cis	0.97	92:8	88	12
4.12 cis	3.05	96:4	89	11
0.85 trans			16	84
1.16 trans	0.20	16:84	15	85
2.12 trans	1.08	6:94	10	90
3.73 trans	2.61	3:97	9	91

nitrile. That no cis adduct was found starting with *trans*-anethole offers an interesting contrast to our results as just described. It was also reported that *cis-* and *trans*-1-ferrocenylpropene provide one and the same TCNE cycloadduct.[23]

Reversibility of Zwitterion Formation

Cis–trans isomeric enol ethers are thermostable at room temperature for several days. The reaction of TCNE with 1.1 equiv of *cis*-1-butenyl ethyl ether (≥99.5% configurational purity) in acetonitrile was complete in a few seconds; the 0.1 equiv of unconsumed enol ether turned out to be cis → trans isomerized to the extent of 18%.[24] Not the cycloadduct, but rather TCNE is the "catalyst" for geometrical isomerization of the butenyl ether. The simplest mechanism is formation of zwitterion **15**, rotation to **16** and dissociation to the unsaturated reactants (Scheme II). Thus, the zwitterion enters into three competing processes: ring closure to the cyclobutane derivative, rotation around the former double bond of the enol ether, and dissociation to starting materials.

The kinetic system of Scheme II involves ten rate constants. The experimental quantities are insufficient for a solution. However, approximate rate ratios for the competing steps can be derived from our data by neglecting double conformational rotation. Rotation never amounted to more than 20% of ring closure; therefore, double rotation would come at most to 20% of 20%, i.e., only 4%. Under this premise the proportion of cis:trans adduct, observed without excess of enol ether, becomes the ratio of ring closure to rotation (k_2/k_r) for the cis zwitterion **15**, and the ratio of trans adduct to *trans*-butenyl ether for large excess of *cis*-butenyl ether is identical with the quotient of ring closure to dissociation (k_4/k_{-3}) of the trans zwitterion **16**.

The data of Table I reveal that in acetonitrile ring closure is five times faster than rotation for the cis and trans zwitterions of Scheme II ($k_2/k_r = 4.6$, $k_4/k_{-r} =$

5.3). The two zwitterionic comformers undergo ring closure and reversal to olefin with practically the same rates; 0.9 and 1.1 are the pertinent ratios of the rate constants (k_2/k_{-1}, k_4/k_{-3}).[24] In nonpolar solvents the ratio of ring closure to rotation is larger, i.e., much less material isomerizes through rotation.

2 + 2 cycloadditions via biradicals and via zwitterions display similarities as well as differences. Bartlett found the additions of 1,1-dichloro-2,2-difluoroethylene to hexa-2,4-dienes[25] and 1,4-dichlorobuta-1,3-dienes[26] likewise to be reversible. For the biradical systems rotation is faster; these cycloadditions are less stereoselective than those with zwitterionic intermediates. The biradical from 1,1-dichloro-2,2-difluoroethylene and *cis,cis*-hexa-2,4-diene underwent rotation 10 times faster than ring closure,[6] whereas a factor of 4 was found for the biradical from tetrafluoroethylene and *cis*-2-butene.[27] The 2 + 2 cycloadditions of benzyne to *cis-* and *trans*-propenyl ethyl ether[28] as well as to *cis-* and *trans*-dichloroethylene,[29] both supposedly proceeding via biradicals, show substantial nonstereospecific portions.

On the other hand, the reactions of TCNE with enol ethers appear to rank at the lower end of the stereoselectivity scale among 2 + 2 cycloadditions via zwitterions. The additions of fumaro- and maleonitrile to tetramethoxyethylene gave pure **19** and **20** within the

analytical limits.[30] The relative conformational inflexibility of the zwitterion compared with the biradical

(23) K. R. Berger, E. R. Biehl, and P. C. Reeves, *J. Org. Chem.*, **39**, 477 (1974).
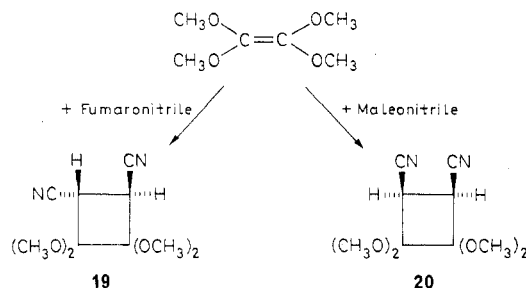(24) R. Huisgen and G. Steiner, *J. Am. Chem. Soc.*, **95**, 5055 (1973).

(25) P. D. Bartlett, C. J. Dempster, L. K. Montgomery, K. E. Schueller, and G. E. H. Wallbillich, *J. Am. Chem. Soc.*, **91**, 405 (1969).
(26) P. D. Bartlett and G. E. H. Wallbillich, *J. Am. Chem. Soc.*, **91**, 409 (1969).
(27) P. D. Bartlett, K. Hummel, S. P. Elliott, and R. A. Minns, *J. Am. Chem. Soc.*, **94**, 2898 (1972).
(28) (a) H. H. Wasserman, A. J. Solodar, and L. S. Keller, *Tetrahedron Lett.*, 5597 (1968); (b) I. Tabushi, R. Oda, and K. Okazaki, *ibid.*, 3743 (1968).
(29) M. Jones and R. H. Levin, *Tetrahedron Lett.*, 5593 (1968).
(30) R. W. Hoffmann, U. Bressel, J. Gehlhaus, and H. Hauser, *Chem. Ber.*, **104**, 873 (1971).

may be ascribed to the Coulombic attraction of the charge centers and suggests a cisoid or gauche conformation of the zwitterion.

Structure–Rate Relationship

The reactivity of an olefin toward TCNE to form a zwitterionic intermediate depends on its nucleophilicity. In considering overall rate constants, we must keep in mind that these are composite figures to which several rate constants contribute. Even on using substrates which do not occur as cis,trans isomers, one obtains an experimental constant k_2 which consists of the formation constant k_I of the zwitterion and a partition coefficient for its cyclization (k_C) and dissociation (k_D).

$$k_2 = k_I k_C / (k_C + k_D) \tag{1}$$

The structure–rate relationship is based on the expectation that k_2 reflects mainly k_I. The rate correlations of this and the next section testify indeed that at least k_I and the partition coefficient in eq 1 vary systematically.

Tetracyanoethylene forms colored charge-transfer (CT) complexes with enol ethers; the equilibria are immediately established when the reactants are mixed. As cycloaddition occurs, the CT color fades. When a large excess of enol ether is used, the extinction of the CT complex is proportional to the TCNE concentration and the cycloaddition rate can be measured photometrically. Division of the pseudo-first-order rate constants by the molar concentration of the enol ether provides k_2 values for the bimolecular reaction. Some of our data are shown in Table II.

The first section of Table II shows that rate diminishes 60 000-fold as the R group of vinyl ethers changes from *tert*-butyl to phenyl.[31] The donor activity of the RO function decreases in the same sequence; indeed, the log k_2 are linearly related to Taft's polar substituent constants σ^*. The second formula line of Table II provides evidence of acceleration by α substituents which stabilize positive charge.

Should not an immonium zwitterion be superior to the oxonium structure? Actually, some enamines produce with TCNE at −40 °C stable 1,4 dipoles which lose HCN at 20 °C, giving tricyanobutadienes.[32] Their inability to cyclize reduces the significance of these 1,4 dipoles for the 2 + 2 cycloaddition problem.

In the formation of the carboxonium zwitterion, the β carbon of the vinyl ether binds the TCNE. The introduction of a β-methyl group (second section of Table II) increases the rate constant independently of trans or cis configuration, but exchange of the β-methyl by ethyl, butyl, or isopropyl diminishes the addition rate. The favorable alkyl effect may be due to the increase of electron density of the double bond. Larger alkyl groups screen the reaction center and decrease the rate.

Cis–trans isomeric enol ethers do not differ greatly in their aptitude to add TCNE. The ratio k_{cis}:k_{trans} varies for alkyl 1-butenyl ethers from 1.31 to 0.49. The contrast to cycloadditions of ketenes, which react with cis enol ethers by several powers of ten faster than with the trans isomers,[17] underlines a fundamental mechanistic disparity.

Table II
Rate Constants of TCNE Cycloadditions to Enol Ethers;[31] $10^3 k_2$ (L mol^{-1} s^{-1}) in Ethyl Acetate at 25 °C

Influence of O- and α-substituents

$H_2C=C$ with H and OR:

R =			
C(CH$_3$)$_3$	255	C$_2$H$_5$	18
c-C$_6$H$_{11}$	112	CH$_2$CH$_2$Cl	0.92
n-C$_4$H$_9$	20	C$_6$H$_5$	0.0043

$H_2C=C$ (H)(OC$_2$H$_5$)	$H_2C=C$ (C$_6$H$_5$)(OCH$_3$)	$H_2C=C$ (CH$_3$)(OC$_2$H$_5$)	$H_2C=C$ (OC$_2$H$_5$)(OC$_2$H$_5$)
18.5	~250	very fast	very fast

Influence of β-substituents

R\C=C/H with H and OC$_2$H$_5$:

R =			
H	18	n-C$_4$H$_9$	15
CH$_3$	53	CH(CH$_3$)$_2$	1.52
C$_2$H$_5$	17	OC$_2$H$_5$	8.8

Cis,trans isomeric enol ethers

	R = CH$_3$	C$_2$H$_5$	CH(CH$_3$)$_3$	C(CH$_3$)$_3$
C$_2$H$_5$\C=C/OR (with H and H)	5.5	15	28	80
C$_2$H$_5$\C=C/H (with H and OR)	4.2	17	57	140

α-Methoxystyrene adds TCNE 100 000 times faster than β-methoxystyrene ($10^3 k_2 = 0.0025$).[31] While 1,2-diethoxyethene is only half as reactive as ethyl vinyl ether (Table II), 1,1-diethoxyethene reacts so rapidly with TCNE that the CT complex does not even become visible. This massive acceleration by α substituents suggests that the transition state of the rate-determining step structurally resembles the zwitterion. One should expect charge separation in the activation process.

Solvent Polarity and Rate

The dependence of TCNE cycloaddition constants on solvent polarity is immense: k(acetonitrile)/k(cyclohexane) amounts to 63 000 for 4-methoxystyrene,[33] 29 000 for anethole, 10 800 for ethyl isobutenyl ether, and 2600 for butyl vinyl ether.[34] Also, k(acetonitrile)/k(CCl$_4$) is 17 000 for 2,3-dihydro-4H-pyran.[34] The log k_2 values, measured in ten solvents, correlate linearly with the E_T values of Dimroth and Reichardt,[35] an empirical parameter of solvent polarity based on the solvatochromism of a pyridinium phenoxide.

Such huge dependencies appear to be unique among cycloadditions. They suggest a substantial increase of the charge separation during the activation process, and this fits one's expectation for the formation of a zwitterion from two neutral molecules. However, it would be wise not to succumb to the suggestive power of the term "1,4 dipole". Let us deal with the question: should one anticipate a hypothetical, synchronous one-step cycloaddition of TCNE to enol ether to show a positive or a negative dependence on solvent polarity?

Comparison of the dipole moments (benzene, 25 °C) of anethole, ethyl isobutenyl ether, and their TCNE cycloadducts shows a considerable increase in polarity

(31) R. Huisgen and G. Steiner, *Tetrahedron Lett.*, 3763 (1973).
(32) R. Gompper and H. J. Müller, quoted by R. Gompper, *Angew. Chem., Int. Ed. Engl.*, 8, 312 (1969).

(33) Dr. D. W. Wiley, E. I. du Pont de Nemours Co., private communication.
(34) G. Steiner and R. Huisgen, *J. Am. Chem. Soc.*, 95, 5056 (1973).
(35) K. Dimroth, C. Reichardt, T. Siepmann, and F. Bohlmann, *Liebigs Ann. Chem.*, 666, 1 (1963); C. Reichardt, "Lösungsmitteleffekte in der organischen Chemie", Verlag Chemie, Weinheim, 1969.

Table III
Calculated Dipole Moments of Transition States and Estimated μ Values of the Zwitterions for
TCNE Cycloadditions to Four Enol Ethers[34]

	Butyl vinyl ether	Ethyl isobutenyl ether	2,3-Dihydro-4H-pyran	Anethole
$R = \Delta \log k_2 / \Delta [(\epsilon - 1)/(2\epsilon + 1)]$	12.2	15.2	15.3	19.6
μ(enol ether), D	1.25	1.28	1.33	1.76
Molar vol (enol ether), cm³	129	129	91.4	150
Molar vol (transition state), cm³	236	236	198	257
$\mu_{\ddagger}$(transition state), D, calcd	10.3	11.0	10.7	14.0
Charge distance zwitterion, A	3.0	3.0	3.5	4.0
Charge moment, D	14	14	16	19
Estd μ cis zwitterion, D	17	17	18	21

Scheme III
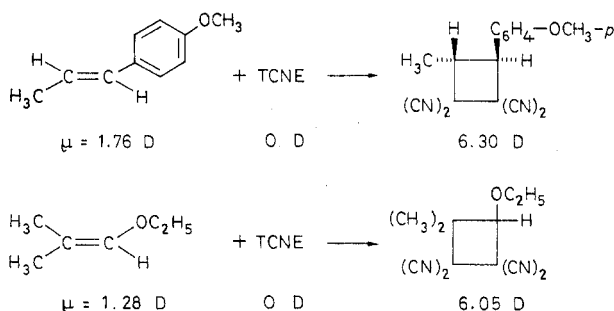
during the overall reaction (Scheme III).[34] Therefore, the activated complex of a synchronous cycloaddition should be more strongly solvated than the reactants. The question arises: is there a *numerical relationship* between the sensitivity of the rate constant to the change of solvent polarity and the *amount of charge separation* during activation?

$$\ln k = \ln k_0 - \frac{1}{k_B T}\left(\frac{\epsilon - 1}{2\epsilon + 1}\right)\left(\frac{\mu_A^2}{r_A^3} + \frac{\mu_B^2}{r_B^3} - \frac{\mu_{\ddagger}^2}{r_{\ddagger}^3}\right)$$
$$+ \frac{\Phi_A + \Phi_B - \Phi_{\ddagger}}{k_B T} \tag{2}$$

Based on a simple electrostatic model of Kirkwood,[36] Laidler and Eyring[37] developed eq 2 which describes the rate constant of the reaction of spherical dipolar molecules A and B (radii r_A and r_B) as a function of solvent polarity; k_0 refers to vacuum and k to a solvent with the dielectric constant ϵ. Besides the dipole moments of the reactants A and B, the dipole moment of the transition state, $\mu_{\ddagger}$, also appears in the equation. Conceivably, $\mu_{\ddagger}$ could be calculated from the known solvent dependence of the rate constant. The non-electrostatic interactions Φ in eq 2 can be neglected under certain conditions.

Equation 2 has been applied to a few binary solvent mixtures with limited success,[38] but failed when used for a greater range of solvents. The function $(\epsilon - 1)/(2\epsilon + 1)$ does not reproduce satisfactorily the dependence of the rate constant on solvent polarity because the
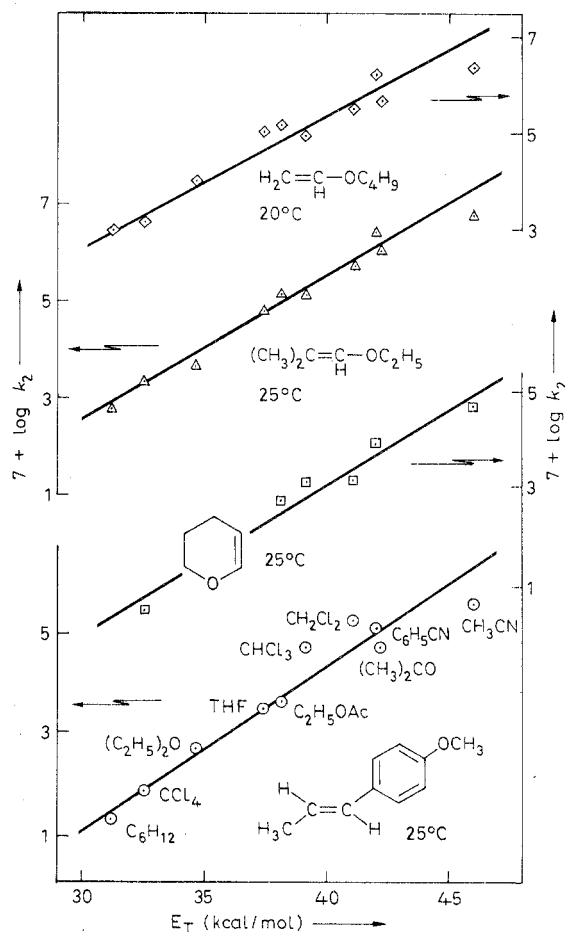
(36) J. G. Kirkwood, *J. Chem. Phys.*, 2, 351 (1934). See also C. J. F. Böttcher, "Theory of Electric Polarization", Elsevier, New York, N.Y., 1952.

(37) K. J. Laidler and H. Eyring, *Ann. N.Y. Acad. Sci.*, 39, 303 (1940); S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes", McGraw-Hill, New York, N.Y., 1944, p 419. See also E. S. Amis, "Solvent Effects on Reaction Rates and Mechanisms", Academic Press, New York, N.Y., 1966, p 59.

(38) See examples quoted in ref 37 and by G. Heublein, *Z. Chem.*, 6, 201 (1966).

Figure 1. Rate constants, $\log k_2$, for TCNE cycloadditions to butyl vinyl ether, ethyl isobutenyl ether, 2,3-dihydro-4H-pyran and anethole as a function of the parameter E_T of solvent polarity.[34]

Kirkwood model[36] neglects specific solvation forces.

The most specific solvation phenomenon is perhaps the hydrogen bond between protic solvents and anionic centers. Protic solvents are not suitable for the kinetic study of TCNE cycloadditions. Perhaps this is the reason the $\log k_2$ values of TCNE cycloadditions to four model enol ethers (Figure 1) fulfill fairly linear relations with $(\epsilon - 1)/(2\epsilon + 1)$.[21,34] The slopes of the straight lines, R, serve as a measure of the sensitivity of the rate constant to the change of solvent polarity.

Utilization of eq 2 required estimation of the radii of the idealized spherical molecules, and they were evaluated from molar volumes. The molar volume of the transition state was set equal to the sum of the reactants minus one double bond increment.[39] Making

appropriate substitutions in eq 2, one obtains eq 3 in which subscript A refers to the enol ether.

$$\mu_{\ddagger}^2 = r_{\ddagger}^3[(\mu_A^2/r_A^3) + 2.303Rk_BT] \tag{3}$$

Dipole moments of 10.3–14.0 D were calculated for the transition states of TCNE cycloadditions to four enol ethers (Table III). These dipole moments are greater than expected for the transition states of synchronous cycloadditions (Scheme III). Are they consistent with zwitterion formation in the rate-determining step?

The steric course of the cycloaddition and, even more so, the stereochemistry of the trapping reaction[40] suggest strongly that the zwitterion is generated in a conformation of low Coulomb potential, i.e., cis or gauche. We have estimated the dipole moment of the cis structure 21, although a gauche 2,3 bond would
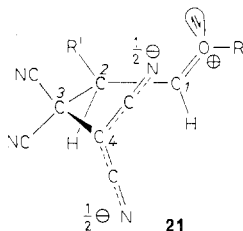
suffer less from conformational strain. The oxonium oxygen would be the positive center of the 1,4-dipole while the negative one is projected into the middle of the line which connects the two nitrogens of the malononitrile anion group. The transfer of an electronic charge over that distance provides the "charge moments" of Table III. After further correction for the partial moments of the nitrile groups at the tetrahedral C-3, one estimates values of 17–21 D for the dipole moments of the zwitterions.[34]

The calculated dipole moments of the transition states amount to roughly two-thirds of the estimated μ values of the fully developed zwitterions. Inasmuch as the complete charge separation of the latter is not yet achieved in the transition state (Figure 2), one finds the figures reasonable. One must bear in mind that derivation of the Kirkwood–Laidler–Eyring expression (eq 2) involved drastic simplifications. That the $\mu_{\ddagger}$ values do not contradict the occurrence of zwitterions is probably a modest statement of the outcome.

In the tentative energy profile of Figure 2 the trough of the intermediate is surrounded by barriers of similar heights, in accordance with a partition ratio of ~1 for dissociation and cyclization (vide supra). The distance between the solid and dashed line corresponds to the energy profit by solvation and diminished Coulomb potential in the polar solvent. The charge separation is greatest for the zwitterion and decreases with dissociation or cyclization.

Whereas TCNE enters with first order into the rate equation of the 2 + 2 cycloaddition, variation of the enol ether concentration (excess) creates discomfiting trends in the k_2 values. The solution of this puzzle is the polarity change of the medium due to increasing shares of the enol ether as testified by a linear relation with E_T.[41]

(39) Molar volumes are an additive property; see W. Biltz, *Justus Liebigs Ann. Chem.*, **453**, 259 (1927); *Z. Phys. Chem., Abt. A*, **151**, 13 (1930).
(40) R. Huisgen, *Acc. Chem. Res.*, submitted for publication.
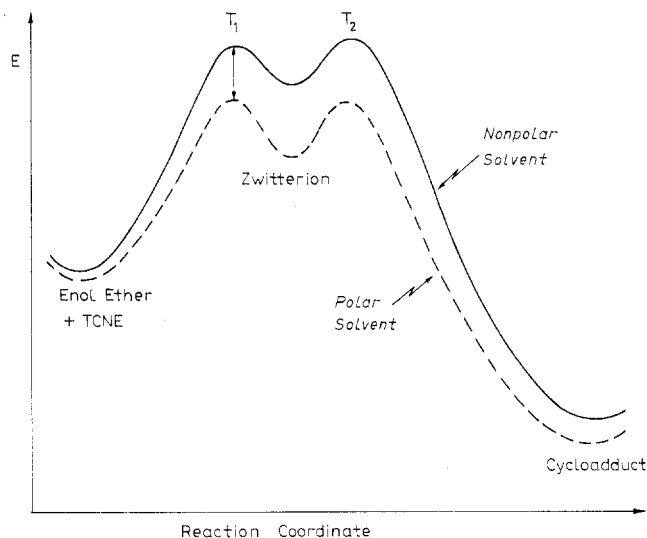

Figure 2. Energy profile for the stepwise cycloaddition of TCNE to an enol ether.

Activation Entropy

The high polarity assigned to the transition state finds further confirmation in the activation parameters, especially the entropy of activation. $\Delta S^{\ddagger}$ ranges from −31 to −58 eu, being somewhat dependent on the solvent.[42] Besides the loss of translational and rotational degrees of freedom in the 2 + 2 cycloaddition, the high order of the transition state and the electrostriction of solvent molecules to the incipient charge centers contribute to the negative $\Delta S^{\ddagger}$ values which exceed even those for Diels–Alder reactions[43] and 1,3-dipolar cycloadditions.[44]

Pressure Dependence of Rate

Rate measurements over a range of pressure provide the activation volume, $\Delta V^{\ddagger}$, which is defined for a reaction A + B as the difference between the molar volume of the transition state and that of the reactants. According to eq 4, the experimental $\Delta V^{\ddagger}$ can be dissected into a fictitious $\Delta V^{\ddagger}_0$ with no interaction between solute and solvent and the portion $\Delta V^{\ddagger}_s$ which is due to solvation.

$$\begin{aligned}
\Delta V^{\ddagger}_{exp} &= V^{\ddagger} - (V_A + V_B) = \Delta V^{\ddagger}_0 + \Delta V^{\ddagger}_s \\
&= V^{\ddagger}_0 - (V^0_A + V^0_B) + V^{\ddagger}_s \\
&\quad - (V^s_A + V^s_B)
\end{aligned} \tag{4}$$

Fleischmann and Kelm[45] measured the rate constants for the cycloaddition of TCNE to butyl vinyl ether giving 22 at various pressures up to 2000 atm and
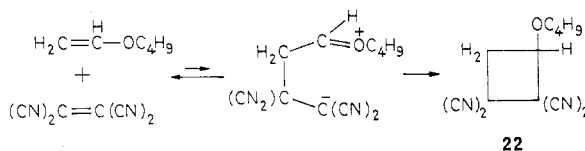
evaluated the activation volume in five aprotic solvents.

(41) R. Huisgen and R. Schug, *J. Chem. Soc., Chem. Commun.*, 59 (1975).
(42) G. Steiner and R. Huisgen, *Tetrahedron Lett.*, 3769 (1973).
(43) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16, 28, 30 (1967).
(44) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 633, 637 (1963).
(45) F. K. Fleischmann and H. Kelm, *Tetrahedron Lett.*, 3773 (1973).

Table IV
Comparison of Rate Constants of 4 + 2 and 2 + 2 Cycloaddition Reactions with Polycyanoethylenes[50]

	Diels–Alder (dioxane, 20 °C)		2 + 2 (benzene, 25 °C) Isobutenyl methyl ether	
	Cyclopentadiene $10^5 k_2$, L mol^{-1} s^{-1}	Dimethylanthracene $10^5 k_2$, L mol^{-1} s^{-1}	$10^5 k_2$, L mol^{-1} s^{-1}	k_{rel}
Acrylonitrile	1.04	0.89	0	
Fumaronitrile	81	139	0	
1,1-Dicyanoethylene	45 500	127 000	31.6	16.0
Tricyanoethylene	480 000	5 900 000	2.39	1.2
Tetracyanoethylene	43 000 000	13 000 000 000	3.97	$\equiv 1.0^a$

^{a} Divided by statistical factor of 2.

Scheme IV

Scheme V
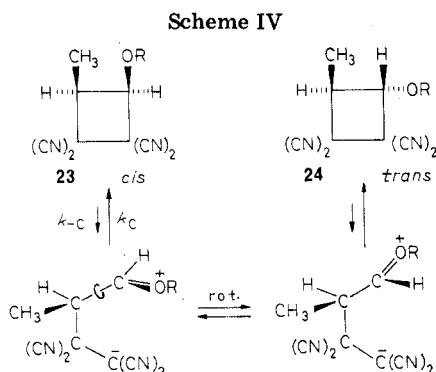
$\Delta V^\ddagger$ varied from -19 cm^3/mol in acetonitrile to -46 cm^3/mol in CCl$_4$. Of the total $\Delta V^\ddagger$, they allocated -14 cm^3/mol to $\Delta V^\ddagger_0$ in every solvent, and the rest to $\Delta V^\ddagger_s$. Characteristically, this portion due to solvation contributes most in nonpolar solvents; here the strongest electrostriction occurs when ionic charges are developed. The $\Delta V^\ddagger_s$ values and their solvent dependence resemble those of the Menschutkin reaction of pyridine and methyl iodide.[46]

Reversibility of TCNE Cycloaddition

The data quoted above on the steric course of the reaction of Scheme I and its trans counterpart refer to conditions of kinetic control. The stereoisomeric adducts **23** and **24** are stable in nonpolar solvents. However, in acetonitrile a slow cis,trans isomerization, **23** $\rightleftharpoons$ **24**, was observed at room temperature. Due to concurrent reactions, it did not fully reach equilibrium. Evaluation of the kinetic plots established equilibria which contained 17% (R = CH$_3$), 18% (R = C$_2$H$_5$), and 19% (R = C$_3$H$_7$) of the cis isomer.[20,21]

The restriction of this reaction to the highly polar solvent suggests the process of Scheme IV: the rotamers of the zwitterion occur as intermediates, i.e., the cyclization of the zwitterion is reversible. One and the same zwitterion is attained quickly from the olefinic reactants and slowly from the cyclobutane. The cycloaddition of TCNE + *cis*-propenyl propyl ether is at 20 °C 400 000 times faster than the subsequent conversion **23** → **24**. Although partition coefficients (see eq 1) complicate the kinetic scheme, the $\Delta G^\ddagger$ values of zwitterion formation from both sides (Figure 2) differ by ca. 8–9 kcal/mol; this $\Delta\Delta G^\ddagger$ might come close to the free energy of the cycloaddition.

Free-energy changes of that magnitude are too large to allow direct measurement of an equilibrium concentration of enol ether + TCNE alongside of the cyclobutane. Nevertheless, in the reaction of TCNE with α-methoxystyrene (Scheme V) cycloadduct **25** is thermodynamically less favored than **26**. On warming a chloroform solution of **25** to 40–60 °C, the red-violet color of the CT complex of the reactants is developed reversibly. An excess of ethyl vinyl ether smoothly traps the TCNE in equilibrium with **25** to give 95% of **26**. For reasons which are not fully understood, cycloadducts of enol ethers with α substituents are thermodynamically less favorable.[21]

The Role of the Charge-Transfer Complex

The question of whether the charge-transfer complex is an intermediate during the cycloaddition may be disregarded because we are not aware of a method which allows a decision. The trick which recently gave a positive answer in the case of the Diels–Alder reaction of TCNE and 9,10-dimethylanthracene[47] is not applicable here. In the reaction of TCNE with para-substituted styrenes, Bartlett and Kramer[22] found no correlation of CT complex stabilities and cycloaddition constants.

Kinetic Comparison with the Diels–Alder Reaction

Sauer[43] has compared the dienophilic activities of polycyanoolefins in Diels–Alder reactions. On going from acrylonitrile to TCNE, one observes a 40 million-fold increase of k_2 with cyclopentadiene and a 15 billion-fold with 9,10-dimethylanthracene (Table IV, Scheme VI).

The concerted Diels–Alder reaction has an *early transition state* which makes the application of MO perturbation theory (PMO) to reactivity sequences successful.[48,49] The formation of **27** and **28** belongs to

(46) H. Hartmann, H. D. Brauer, H. Kelm, and G. Rinck, Z. Phys. Chem. (*Frankfurt am Main*), **61**, 53 (1968).
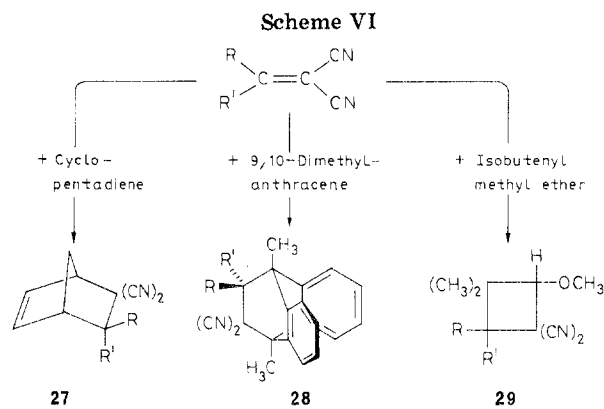
(47) V. D. Kiselev and J. G. Miller, *J. Am. Chem. Soc.*, **97**, 4036 (1975).

(48) (a) O. Eisenstein and N. T. Anh, *Tetrahedron Lett.*, 1191 (1971); (b) R. Sustmann and R. Schubert, *Angew. Chem., Int. Ed. Engl.*, **11**, 840 (1972).

(49) Reviews: (a) R. Sustmann, *Pure Appl. Chem.*, **40**, 569 (1974); (b) K. N. Houk, *Acc. Chem. Res.*, **8**, 361 (1975).

Scheme VI

"normal" Diels–Alder reactions which are HO(diene) – LU(dienophile) controlled. The successive introduction of cyano groups lowers the LU energies of the dienophile. The dwindling frontier orbital separation corresponds to a greater energy gain in the transition state and to steeply increasing k_2 values.

In contrast, the 2 + 2 cycloadditions of 1,1-di-, tri-, and tetracyanoethylenes to give **29** showed a compressed and even slightly inverted rate scale (Table IV).[50] The rate-determining step of the 2 + 2 cycloaddition is the formation of the zwitterion. This endothermic step has a *late transition state* which structurally resembles the zwitterion more than the reactants. The MO energies of the reactants change grossly before the transition state is reached; the validity of PMO which inspects the first infinitesimal part of the reaction becomes questionable.[51]

(50) R. Huisgen and R. Schug, *J. Am. Chem. Soc.*, **98**, 7819 (1976).

The same two cyano groups contribute to the stabilization of the anionic charge of the zwitterions which occur in the formation of **29** from 1,1-di-, tri-, and tetracyanoethylenes. Acrylo- and fumaronitriles are unreactive since the zwitterion would be insufficiently stabilized by only one nitrile group. Cyano functions at the other carbon atom decelerate slightly because of steric screening and loss of ground-state conjugation.

The rate constants of the Diels–Alder reactions in Table IV are by orders of magnitude greater than those of the 2 + 2 cycloadditions. The concerted 4 + 2 addition avoids the energy barrier of the two-step reaction which must be overcome in the 2 + 2 addition due to the "forbiddenness" of the process $[_\pi 2_s + _\pi 2_s]$.[2,3] Thus the enlightening divergence of the reactivity sequences harbors a criterion for presence or absence of concertedness.

Conclusions

All the kinetic and stereochemical evidence supports the zwitterionic intermediate in the model cycloaddition. Further strong confirmation comes from successful trapping experiments.[40] Reaction mechanisms are more or less based on circumstantial evidence. The author regards the network of criteria and findings as very tight in the case under consideration.

(51) K. N. Houk and L. L. Munchausen, *J. Am. Chem. Soc.*, **98**, 937 (1976), calculated by PMO relative reactivities of cyanoalkenes toward "one-bond" and "two-bond" nucleophiles. The "one-bond" reactivity indices which apply, e.g., to the first step of polar cycloadditions show indeed a compressed scale.