On the Long-standing Question of an ET or Polar Mechanism for the Cycloaddition of Tetracyanoethylene with Electron Rich Alkenes

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An ET mechanism is decisively excluded for the zwitterionic cycloaddition of tetracyanoethylene and bis(4-methoxycinnamyl) ether. A polar mechanism for this and analogous zwitterionic cycloadditions is therefore strongly indicated.

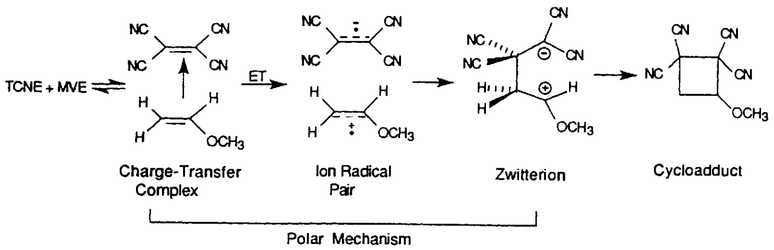
The accelerated development of thermal electron transfer organic chemistry and its emergence as an important sub-area of physical-organic chemistry was brilliantly predicted by Kosower in his 1965 review article, 'Reactions through Charge-Transfer Complexes'.[1] Surprisingly, many of the mechanistic questions raised by the emergence of this new concept have still not been answered with the rigour expected in physical-organic chemistry. A key feature of Kosower's prescient article was the proposal of an ET mechanism for the thermal cycloaddition of tetracyanoethylene (TCNE) to electron rich alkenes and styrenes.[2] The present work was undertaken to provide an appropriately rigorous answer to the very basic question originally posed by Kosower about thirty years ago.

Electron transfer (ET) from ultra-electron rich donors (D), such as 1,4-bis(dimethylamino)benzene, to highly electron deficient acceptors (A), such as tetracyanoethylene (TCNE), is well established and produces intermediate ion radical pairs ($D^{\bullet +}A^{\bullet -}$).[1] The subsequent coupling of such radical ion pairs, affording zwitterions ($D^+{-}A^-$), provides an indirect mechanism for covalent bond formation between a donor and acceptor. This mechanism, usually referred to as the 'ET mechanism' represents a plausible, general alternative to direct, or polar, covalent bond formation. Mechanistic studies of the cycloadditions of electron rich alkenes, such as vinyl ethers, with highly electron deficient alkenes, such as TCNE, have definitively established the involvement of zwitterionic intermediates.[3] The fundamental issue raised by Kosower is whether the initial covalent attachment occurs indirectly *via* an ET mechanism or directly *via* a polar mechanism (Scheme 1).

Results and Discussion

Ethyl vinyl ether (E_p^ox = +1.60 V),[4] phenyl vinyl sulfide (E_p^ox = +1.42 V)[4] and (*E*)-anethole (E_p^ox +1.28 V *vs.* SCE)[5] are typical donor molecules for zwitterionic cycloadditions to TCNE (E_red = +0.15 V).[6,7] Electron transfer from even the best donor of the group [(*E*)-anethole] to TCNE is therefore substantially endergonic ($\Delta G_0 = 1.28 - 0.15 = 1.13$ eV). The corrected free energy change ($\Delta G_0'$) for the formation of a contact ion radical pair, in consideration of the electrostatic attraction between the ions and the loss of solvation energy of the contact ion pair relative to the free ions, should be no less than $\Delta G_0' = 1.0$ eV.[8] Assuming the value for the reorganization energy $\lambda = 0.85$ eV (CH_3CN solvent) found by Gould, Moody and Farid in their classic studies of back electron transfer in contact ion radical pairs,[8] and employing the Marcus equation,† the activation free energy for electron transfer between anethole and TCNE is calculated to be $\Delta G^\ddagger_\mathrm{ET} = 1.01$ eV (23.3 kcal mol^{-1}). For an experimental comparison, the rate constant for the reaction between TCNE and 4-vinylanisole, reported to be 1.5×10^{-1} $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$ (CH_3CN, ambient),[9] corresponds to a value of $\Delta G^\ddagger_\mathrm{exp} = 18.6$ kcal mol^{-1} from the Eyring equation.§ To permit a direct comparison of experimental and calculated $\Delta G^\ddagger$ values, the free energy change for the formation of the CT complex ($\Delta G^\circ_\mathrm{CT}$) must be added to the calculated free energy of activation ($\Delta G^\ddagger_\mathrm{ET}$) for electron transfer within the CT complex. Using the value of $K = 237$ for vinylanisole,[9] $\Delta G^\circ_\mathrm{CT} = -3.3$ kcal mol^{-1}. The calculated activation free energy for the ET mechanism is therefore $\Delta G^\ddagger_\mathrm{calc} = \Delta G^\circ_\mathrm{CT} + \Delta G^\ddagger_\mathrm{ET} = -3.3 + 23.3 = 20.0$ kcal mol^{-1}. This is just 1.4 kcal mol^{-1} greater than the experimental value, $\Delta G^\ddagger_\mathrm{exp} = 18.6$ kcal mol^{-1}. These calculations are, of course, approximate, but they could reasonably be interpreted as suggesting that, energetically, the ET mechanism is not at all implausible and that it does, in fact, warrant serious mechanistic consideration.

The detection of ion radical pair intermediates can be relatively straightforward if the lifetimes are sufficient to permit diffusive separation. In that case, the relatively stable TCNE anion radical might be spectroscopically detectable, and the more reactive donor cation radicals would be decisively revealed by the formation of characteristic cyclodimers through their reaction with a neutral donor molecule.[4] The inability to detect either free cation radicals or anion radicals can be interpreted as indicating either that ion radical pairs are not involved at all or that they are too short-lived to permit diffusive separation to free ions. In acetonitrile solvent, singly charged



Scheme 1 The Kosower ET mechanism for the cycloaddition of TCNE and methyl vinyl ether

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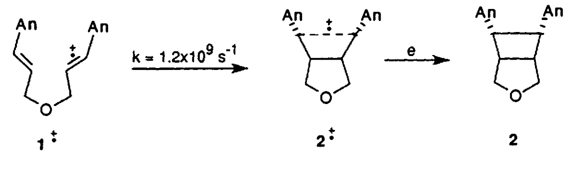
† Using the equation $\Delta G^\ddagger_\mathrm{ET} = \lambda/4(1 + \Delta G'_0/\lambda)^2$, with $\lambda = 0.85$ eV and $\Delta G'_0 = 1.0$ eV.

§ Using $\Delta G_0 = 2.303RT(12.8 - \log k)$ with $T = 300$ K.

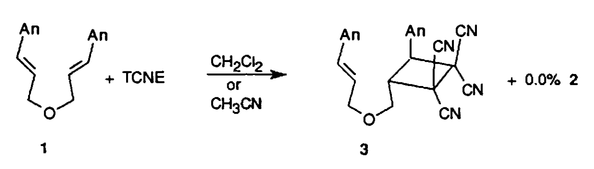
ions typically separate with a rate constant of about 5×10^8 s^{-1}.[10] Assuming that a 5% yield of the cyclodimer could be readily detected, ion radical pairs would escape detection if their lifetimes were less than 10^{-10} s. It is assumed that the lifetimes of caged ion radical pairs are limited, in part, by the proposed rapid coupling reaction. At least equally important, in all probability, is the back electron transfer (BET) reaction which regenerates the original charge transfer complex. Since this reaction is appreciably exergonic, it could easily occur at rates well in excess of 10^{10} s^{-1}. Consequently, the inability to detect free cation or anion radicals in the course of a reaction which involves a caged radical ion pair intermediate is plausible either on the basis of rapid coupling or BET. The latter, incidentally, is also a potentially serious competitor for the coupling reaction.

Intramolecular Cation Radical Probes.—An effective means for the detection of short-lived cation radical intermediates, and particularly for ion radical pairs in which cage escape is negligible, is provided by ion radical probes. A series of cation radical probes has recently been developed in this laboratory and used to investigate the hypothetical ET mechanism for metalloporphyrin-catalysed epoxidation.[11] The probe molecule which appeared to be most appropriate for the present investigation is bis(4-methoxycinnamyl) ether (**1**), which has an electron rich double bond closely analogous to that of (*E*)-anethole. The cyclization of $\mathbf{1}^{\cdot+}$ to the cyclobutane $\mathbf{2}^{\cdot+}$ has been found *via* quenching studies to proceed with a rate constant $k \geqslant 3 \times 10^9\ s^{-1}$ (Scheme 2).[11] Recent picosecond spectroscopic studies have confirmed a very rapid cyclization with rate constant $k = 1.2 \times 10^9\ s^{-1}$.[12] The conversion of $\mathbf{2}^{\cdot+}$ into neutral **2** is typically quite efficient in the presence of donors such as **1**. It was anticipated, and has been confirmed (*vide infra*) that the conversion of $\mathbf{2}^{\cdot+}$ into **2** is indeed efficient in the presence of $TCNE^{\cdot-}$. Since **2** can be detected (GC) at the 0.1% level under appropriate conditions, the probe reaction $\mathbf{1}^{\cdot+} \longrightarrow \mathbf{2}^{\cdot+}$ can be detected in competition with other reactions of $\mathbf{1}^{\cdot+}$ unless these processes have rate constants of at least 10^{12} s^{-1}. No covalent bond-forming reactions even approaching the latter rate are known, but transition-state theory envisions rate constants of up to *ca.* 10^{13} s^{-1}. Even this small window of uncertainty can be (and has been) closed by studying the behaviour of authentic $\mathbf{1}^{\cdot+}/TCNE^{\cdot-}$ ion radical pairs.

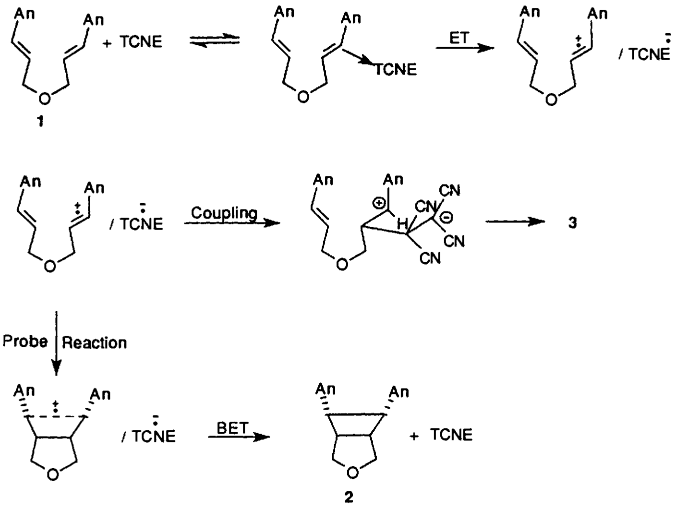


Scheme 2 The cation radical probe reaction

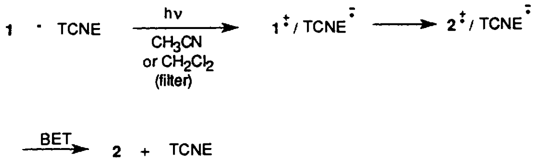
The reaction of TCNE with **1** was therefore studied in both a relatively non-polar solvent (dichloromethane) and a polar solvent (acetonitrile). The reaction, as carried out in dichloromethane, was complete in less than 3 h, giving the adduct **3** in 80% yield (Scheme 3). Control runs established that **2** would have been detectable at the 0.1% level relative to **3**, but no **2** was found. No other products could be detected by GC. Analogous results were obtained when the reaction was carried out in acetonitrile. These results suggest that $\mathbf{1}^{\cdot+}/TCNE^{\cdot-}$ ion radical pairs (Scheme 4) are not likely intermediates in these zwitterionic cycloadditions, but if they are involved they must couple at a rate greater than or equal to 10^{12} s^{-1}. The probability that such highly delocalized and therefore stablized ion radicals might couple this rapidly appears to be quite small, but to eliminate this possibility entirely the authentic ion radical pairs were generated, in both solvents in question, by photochemical means. First, solutions of **1** and TCNE were irradiated through a uranium glass filter *via* a 450 W mercury vapour lamp (Scheme 5). The uranium filter cuts off sharply at 350 nm, so that no appreciable absorption of light by **1** occurs. This assumption was confirmed by establishing the stability of **1** in the absence of TCNE under these photochemical conditions. The excited state of **1**, if formed, would undergo rather efficient *trans–cis* isomerization and also cyclization to **2**, as confirmed by irradiation through a Pyrex filter. When the TCNE–**1** solution is irradiated using the uranium glass filter, **1** is rapidly converted into **2**. After 3 h the conversion is already 16%. Under these conditions, both free ($\lambda_{max} = 400$) and charge transfer complexed ($\lambda_{max} = 574$) TCNE absorb light. Absorption by the CT complex necessarily produces the $\mathbf{1}^{\cdot+}/TCNE^{\cdot-}$ contact ion radical pair directly, while absorption by free TCNE requires subsequent transfer from **1** and this could yield the solvent-separated ion pair, $\mathbf{1}^{\cdot+}/TCNE^{\cdot-}$. In any case, ion pairs must be produced and they result in the efficient formation of **2** as a result of the rapid occurrence of the probe reaction even when its gegenion is $TCNE^{\cdot-}$.



Scheme 3 Reaction of TCNE with **1**



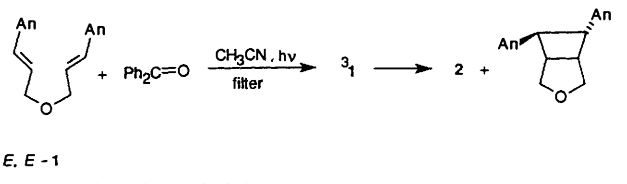
Scheme 4 The hypothetical ET mechanism



Scheme 5 Irradiation of the charge-transfer complex of TCNE and **1**

Similarly, irradiation of solutions of **1** and TCNE selectively at the CT band using either a glass filter (cut off, 450 nm) or a solution filter (window at 520–570 nm) results in the progressive formation of **2**. Consequently, the rate of the probe reaction is confirmed to be at least competitive with all other reactions of the contact ion radical pair, including back electron transfer and coupling. The probe studies using **1** are therefore decisive in excluding the hypothetical ET mechanism for the thermal cycloaddition of **1** and TCNE.

Although it is not crucial to this probe study, it was considered important to exclude the possibility that the **2** formed in the photochemical experiments was derived *via* a cation radical and not a triplet mechanism. In particular, back electron transfer in the ion radical pairs could potentially be exergonic enough to generate the triplet state of **1**, which might then cyclize to **2**. Energetically, this appeared to be highly improbable since the peak oxidation potential of **1** is 1.16 V and the reduction potential of TCNE is 0.15 V, providing a ΔG_0 of only -1.0 eV for back electron transfer. The triplet energy of **1** is undoubtedly well over 2 eV. Nevertheless, experimental confirmation was sought through a study of the triplet-sensitized photochemical reactions of **1**. Using benzophenone as a triplet sensitizer, **1** is indeed partially converted into **2**, but significantly the *trans* isomer of **2** is also formed (Scheme 6).



Scheme 6 Reactions of triplet **1**

This latter product is expected from ^{3}**1**, but is absent in the photochemical studies of the **1**/TCNE system.

Experimental

General.—Proton and carbon-13 NMR spectra were recorded on an AC 250 Hewlett-Packard spectrometer for solutions in $CDCl_3$. UV–VIS spectra were taken on a Hewlett-Packard 8450A spectrometer. Ultraviolet irradiations were carried out with a Hanovia 450 W lamp except where noted. GC analyses were performed on a Perkin-Elmer model 8500 equipped with a DB-1 capillary column (30 m × 0.25 mm × 1 μm). GC yields were calculated using octadecane as an internal standard. GC–MS analyses were done on a Finnigan MAT model 700 equipped with a DB-1 capillary column (15 m). An EG&G Princeton Applied Research model 273 was used to generate cyclic voltammetry data.

All reactions were carried out under a nitrogen atmosphere. Solvents were dried over CaH_2 (CH_3CN) or P_2O_5 (CH_2Cl_2) prior to use. Bis(4-methoxycinnamyl) ether (**1**) was prepared and purified according to the literature method.[11] All other reagents were used as received.

Reaction of Bis(4-*methoxycinnamyl*) *Ether* (**1**) *with Tetracyanoethylene* (*TCNE*) *in Dichloromethane to give the adduct* **3**.—To a solution of **1** (138 mg, 0.45 mmol) in dichloromethane (9 cm^3) cooled to 0 °C were added 115 mg (0.9 mmol) of TCNE. Analysis by GC and TLC revealed completion of the reaction in less than 3 h. No product other than **3** could be detected by GC and, specifically, control runs showed that **2** would have been detected at the 0.1% level (relative to **3**). The reaction mixture was concentrated under vacuum and the product purified by flash column chromatography (hexane–ethyl acetate 2:1) to give 158 mg (80%) of the adduct (**3**): δ_H($CDCl_3$) 7.314 (d, 2 H, J = 8.7 Hz), 7.263 (d, 2 H, J = 8.7 Hz), 6.974 (d, 2 H, J = 8.7 Hz), 6.851 (d, 2 H, J = 8.7 Hz), 6.549 (d, 1 H, J = 15.9 Hz), 6.117 (dt, 1 H, J = 15.9, 6.3 Hz), 4.257–4.205 (m, 3 H), 3.823 (s, 3 H), 3.796 (s, 3 H) and 3.857–3.738 (m, 3 H); δ_C($CDCl_3$) 161.387, 159.641, 133.860, 128.909, 128.781, 127.875, 122.019, 121.760, 115.129, 114.062, 110.178, 109.977, 109.014, 108.781, 72.623, 66.247, 55.413, 55.282, 49.913, 47.681, 42.409 and 37.386 (Found: M$^+$, 438.169 937. Calc. for $C_{26}H_{22}N_4O_3$: *M*, 438.169 191).

Reaction of Bis(4-*methoxycinnamyl*) *ether* (**1**) *with TCNE in Acetonitrile.*—To a solution of **1** (30 mg, 0.09 mmol) in dry acetonitrile (4 cm^3), TCNE (12 mg, 0.09 mmol) was added at 0 °C. After 3 h of stirring at 0 °C, the reaction mixture was analysed by TLC, GC and NMR after evaporation of the solvent. The adduct **3** was isolated (31 mg, 73% yield) by flash chromatography on silica gel, with hexane–ethyl acetate (2:1, v/v) as the eluent. Again, **2** could not be detected in the crude reaction mixture.

UV Studies.—The absorption maxima of **1**, TCNE, and their charge-transfer complex in acetonitrile solution were found to be λ_{max}/nm 240, 400 and 574, respectively. Irradiations of solutions of **1** (25 mg, 0.08 mmol) and TCNE (10 mg, 0.08 mmol) in acetonitrile (4 cm^3) were carried out at 0 °C under several different conditions. (*a*) A uranium filter tube (cut-off 360 nm) was placed around a Pyrex reaction vessel and the solution irradiated with the 450 W medium-pressure lamp for 3 h. Analysis of the products by both GC and ^{1}H NMR spectroscopy revealed the presence of **2** as a major product. GC quantitation using an internal standard revealed the formation of a 16% yield of **2**. In a control run, an acetonitrile solution of **1** irradiated under identical conditions except that TCNE was absent yielded only 1–2% of **2** (*via* a direct photochemical cyclization). (*b*) A reaction mixture containing the standard amounts of **1** and TCNE was placed in one chamber (3 cm) of a Pyrex photochemical reaction cell. The chamber closest to the light source (1 cm path length) contained an aqueous $CuCl_2$–$CaCl_2$ solution, and the middle chamber (5 cm) contained a solution of neodymium nitrate. This solution is known to provide an optical window of 520–570 nm.[13] After 4 h of irradiation with the 450 W lamp, a 4% conversion into **2** had occurred. The conversion into **2** in a control run in which TCNE was omitted was negligible. (*c*) An identical mixture of **1** and TCNE was irradiated with a mercury–xenon lamp (250 W) using a glass filter (500 nm cut-off). After 4 h of irradiation, a 7% conversion into **2** was observed. A control run revealed no conversion into **2**.

Reaction of 1 *with Benzophenone and* 4,4′-*Bis*(*dimethylamino*)*benzophenone.*—(*a*) In a Pyrex test tube, **1** (25 mg, 0.08 mmol) and 4,4′-bis(dimethylamino)benzophenone (22 mg, 0.08 mmol) were dissolved in acetonitrile (4 cm^3). (*b*) In another test tube, **1** (25 mg, 0.08 mmol) and benzophenone (15 mg, 0.08 mmol) were dissolved in acetonitrile (4 cm^3). Both the tubes were then irradiated with UV light using a uranium filter at 0 °C, and **1** was found to convert quantitatively into **2** and its *trans* isomer (*t*-**2**). In reaction (*a*), 4,4′-bis(dimethylamino)benzophenone was removed by washing the ether solution of the solid crude mixture with 20% aqueous H_2SO_4 to yield **2** and *t*-**2** (10:3). In reaction (*b*), the ratio of **2** and *t*-**2** was 10:6. *trans*-**2** was identified by GC–MS, *m*/*z* 310 (M$^+$), 279, 240, 225, 202, 182, 165, 148, 135, 117, 91 and 77, and by ^{13}C NMR spectroscopy, δ_C($CDCl_3$) 158.1, 136.8, 132.6, 128.8, 127.4, 113.8, 73.0, 68.7, 55.1, 46.0, 45.5, 44.2 and 40.3.

Cyclic Voltammetry (*CV*) *of* **1** *and* **2**.—Cyclic voltammetry measurements were performed on **1** and **2** in a four-necked CV cell (10 cm^3) having a three-electrode system, consisting of a platinum disk (working electrode), SCE (reference electrode), and platinum wire (counter electrode). The reference electrode was submerged in a secondary well of supporting electrolytic solution (0.1 mol dm^{-3} tetrabutylammonium perchlorate in CH_3CN) and was separated from the bulk solution by a Vycor frit. All potentials were recorded with respect to SCE under a nitrogen atmosphere. Typically, 7 cm^3 of electrolytic solution were used for a CV experiment. Normally, the CV trace (blank) of the electrolytic solution only was recorded first. Substrate was then added to the cell, dissolved in the electrolyte (4 mmol dm^{-3}), and its CV response recorded.

1 and **2** showed chemically irreversible cyclic voltammetry with oxidation peak potentials of 1.158 V and 1.230 V, respectively.

Acknowledgements

The authors acknowledge the financial support of the National Science Foundation (CHE-9123292) and the Robert A. Welch Foundation (F-149).

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Paper 4/05815A
Received 23rd *September* 1994
Accepted 4th *November* 1994