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Transition-State Structure Variation in the Diels-Alder Reaction from Secondary Deuterium Kinetic Isotope Effects: The Reaction of Nearly Symmetrical Dienes and Dienophiles Is Nearly Synchronous

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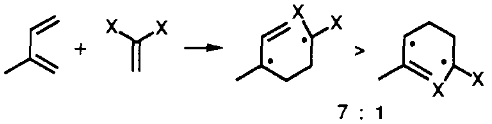
Abstract: Secondary deuterium kinetic isotope effects (KIEs) in the reaction of acrylonitrile, fumaronitrile, vinylidene cyanide, dimethyl fumarate and maleate, and methyl *trans*-β-cyanoacrylate with isoprene were determined by competition with isoprene-d_0 (d_0), 4,4-dideuterioisoprene (*4,4*-d_2), and 1,1,4,4-tetradeuteroisoprene (d_4). The d_4 experiment gives the KIE for 1,1-dideuterioisoprene from the KIEs for *4,4*-d_2. The KIEs for bond making to the β site of acrylonitrile and vinylidene cyanide are much more inverse than those at the α bond making site but are less than the maximum value expected, which indicates an early, unsymmetrical, concerted transition state. The effects with fumaronitrile are the same for both 1,1- and 4,4-dideuterioisoprene, indicating equivalent effects at both sites and not bonding to the preferred C-1 site of isoprene most of the time. The KIEs with methyl *trans*-β-cyanoacrylate are inverse at both bond-making sites to the dienophile and both nearly one-third of the maximum value expected. The results with nearly symmetrical addends are not consistent with a two-step reaction, particularly one with the second step being rate determining, or with a concerted reaction with a highly unsymmetrical transition state, but rather with a concerted pathway that is nearly synchronous. The KIEs with methyl fumarate and maleate suggest an unsymmetrical transition state, but they are within experimental error of a symmetrical transition state.

Diels-Alder reactions are of concern in synthesis and present an important mechanistic question.[1] There is little doubt but that the reaction of unsymmetrical dienophiles proceeds via an unsymmetrical transition state[2] (and is not synchronous[3]); but the question of concert still remains in these cases, and in the case of symmetrical addends, the question of synchrony is paramount. High-level ab initio calculations on the butadiene plus ethylene system by Houk indicate that the lowest energy transition state is symmetrical,[1b] and still higher level calculations by Bernardi[1c] indicate that the symmetrical transition state is marginally lower in energy (2 kcal/mol) than the diradical transition state. However, Dewar calculated that the reaction involves a highly unsymmetrical transition state if not a biradical.[3] Previous work with secondary deuterium kinetic isotope effects (KIEs),[4a-d] the most appropriate probe for these questions, has been criticized for not distinguishing between the alternatives, particularly with symmetrical addends. Optical induction experiments[4e] have been similarily criticized. Since secondary KIEs appear to reveal a large change in the extent of bond making and breaking in 3,3 sigmatropic transition states, which results from reasonably interpreted perturbations by substituents,[5] it seemed reasonable to examine the symmetry of Diels-Alder transition states and perturbations by substituents.

Isoprene is the diene of choice in these experiments because its methyl group might not affect the relative extent of forming of both new σ bonds if the reaction is near synchronous. However, because the methyl strongly affects the adduct regiochemistry with highly unsymmetrical dienophiles—requiring that the methyl strongly perturb the relative energies of the potential biradical pathways—it must be true that the methyl will strongly perturb the biradical path *even with symmetrical dienophiles*. This perturbation appears to give about a 7:1 preference for formation of the "para" over the "meta" adduct with vinylidene cyanide vide infra; interestingly, this same regiopreference is observed with the 4 + 2 adducts from 1,1-dichloro-2,2-difluoroethylene and isoprene.[8] Since the latter reaction accompanies the 2 + 2 reaction, which has been demonstrated to be a two-step process, it appears that a 7-fold larger inverse KIE should be observed at C-1 of isoprene than at C-4 if an unsymmetrical transition state (presumably a biradical-like pathway) were involved even with symmetrical dienophiles like fumaronitrile or dimethyl fumarate and maleate. Since



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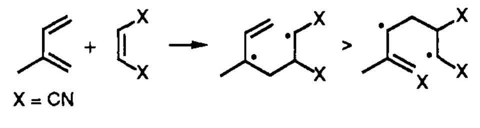

Results

KIEs have been determined with 4,4-dideuterio- and 1,1,4,4-tetradeuterioisoprene, *4,4*-d_2 and d_4, respectively, in their reaction with various dienophiles in benzene solvent (Table I; instead of

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(1) (a) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. (b) Houk, K. N.; Lin, Y.-T.; Brown, F. K. *J. Am. Chem. Soc.* **1986**, *108*, 554. (c) Bernardi, F.; Bottoni, A.; Field, M. J.; Guest, M. F.; Hillier, I. H.; Robb, M. A.; Venturini, A. *Ibid.* **1988**, *110*, 3050. (d) Borden, W. T.; Loncharich, R. J.; Houk, K. N. *Annu. Rev. Phys. Chem.* **1988**, *39*, 213.

(2) Woodward, R. B.; Katz, T. J. *Tetrahedron* **1959**, *5*, 70. Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, England, 1976; Chapter 4.

(3) (a) Dewar, M. J. S.; Olivella, S.; Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 5650. (b) Dewar, M. J. S.; Pierini, A. B. *Ibid.* **1984**, *106*, 203. (c) Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *Ibid.* **1986**, *108*, 5771.

(4) (a) van Sickle, D. E. *Tetrahedron Lett.* **1961**, 687. van Sickle, D. E.; Rodin, J. O. *J. Am. Chem. Soc.* **1964**, *86*, 3091. (b) Seltzer, S. *Ibid.* **1963**, *85*, 1360; *Ibid.* **1965**, *87*, 1534. (c) Brown, P.; Cookson, R. C. *Tetrahedron* **1965**, *21*, 1973. (d) Taagepera, M.; Thornton, E. R. *J. Am. Chem. Soc.* **1972**, *94*, 1168. (e) Tolbert, L. M.; Ali, M. B. *J. Am. Chem. Soc.* **1984**, *106*, 3806.

(5) Gajewski, J. J. In *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, Holland, 1987; Vol. 7, Chapter 3. Note that the equilibrium IEs reported in Appendix B should be inverted.

(6) GC/MS analyses of the excess vinylidene cyanide reactions were irreproducible, so the value of the d_0/d_2 ratio in the standard is that from the excess acrylonitrile runs. Capillary GC analyses required 2-3-h retention times. All four peaks for d_0 and d_2 (and d_0 and d_4) regioisomers from methyl *trans*-β-cyanoacrylate were separated sufficiently (valley 30% above base line in the worse case). Any inaccuracy in the absolute values of the ratios is offset by the cancellation of errors because of identical analytical techniques for the standard.

(7) Calculated from the equation $\log K^{\mathrm{D}_2}/K^{\mathrm{H}} = (291.6/2.303RT) - 0.0818$ ($r = 0.977$): Conrad, N. D. Ph.D. Thesis, Indiana University, 1978. For a discussion of the use of this equation in other pericyclic reactions see ref. 5.

(8) Bartlett, P. D.; Wallbillich, E. H.; Wingrove, A. S.; Swenton, J. S.; Montgomery, L. K.; Kramer, B. D. *J. Am. Chem. Soc.* **1968**, *90*, 2049.

0002-7863/89/1511-9078$01.50/0

Table I. Secondary Deuterium KIEs in Isoprene 4 + 2 Cycloadditions[a]

reactant	T, °C	methylcyclohexene product		maximum[d]
acrylonitrile		5-cyano	4-cyano	
$d_0/4,4\text{-}d_2$	100[b]	1/1.105 (0.007)	1/0.99 (0.002)	1/1.22
$d_0/1,1\text{-}d_2$[f]	100[b]	1/1.020 (0.036)	1/1.13 (0.02)	1/1.22
fumaronitrile		*trans*-4,5-dicyano		
$d_0/4,4\text{-}d_2$	25[c]	1/1.115 (0.03)		1/1.35
$d_0/1,1\text{-}d_2$[f]	25[c]	1/1.13 (0.04)		1/1.35
$d_0/4,4\text{-}d_2$	100[b]	1/1.05 (0.02)		1/1.22
$d_0/4,4\text{-}d_2$	100[c]	1/1.11 (0.046)		1/1.22
$d_0/1,1\text{-}d_2$[f]	100[b]	1/1.05 (0.033)		1/1.22
$d_0/1,1\text{-}d_2$[f]	100[c]	1/1.07 (0.05)		1/1.22
1,1-dicyanoethene		5,5-dicyano	4,4-dicyano	
$d_0/4,4\text{-}d_2$	25[b]	1/1.26 (0.07)	1/0.98 (0.06)	1/1.35
$d_0/1,1\text{-}d_2$[f]	25[c]	1/1.02 (0.11)	1/1.28 (0.07)	1/1.35
methyl *trans*-β-cyanoacrylate		regioisomer 1[e]	regioisomer 2[e]	
$d_0/4,4\text{-}d_2$	25[c]	1/1.14 (0.04)	1/1.125 (0.025)	1/1.35
$d_0/1,1\text{-}d_2$[f]	25[c]	1/1.09 (0.05)	1/1.11 (0.04)	1/1.35
methyl fumarate		*trans*-4,5-dicarbomethoxy		
$d_0/4,4\text{-}d_2$	25[c]	1/1.085 (0.02)		1/1.35
$d_0/1,1\text{-}d_2$[f]	25[c]	1/1.135 (0.03)		1/1.35
$d_0/4,4\text{-}d_2$	100[c]	1/1.08 (0.02)		1/1.22
$d_0/1,1\text{-}d_2$[f]	100[c]	1/1.085 (0.03)		1/1.22
methyl maleate		*cis*-4,5-dicarbomethoxy		
$d_0/4,4\text{-}d_2$	100[c]	1/1.05 (0.02)		1/1.22
$d_0/1,1\text{-}d_2$[f]	100[c]	1/1.09 (0.03)		1/1.22

[a] Standard deviations are given in parentheses; they are determined from multiple analyses of at least duplicate runs. The standard deviations reported for $1,1\text{-}d_2$ are the square root of the sum of the squares of the standard deviations for $4,4\text{-}d_2$ and for $1,1,4,4\text{-}d_4$. [b] Analyses by GC/MS in CI mode; see footnote 5. [c] Analyses by capillary GC; see footnote 6. [d] Calculated for two deuteriums at the reaction temperature; see footnote 7. [e] The regiochemistry could not be assigned due to the inseparability of the diastereomers on a preparative scale; the ratio of regioisomers from methyl *trans*-β-cyanoacrylate is 1:1. ^{1}H NMR of the mixture (360 MHz, $CDCl_3$) δ 5.45 (s, 1 H), 5.36 (s, 1 H), 3.75 (s, 6 H), 3.05 (m, 2 H), 2.85 (m, 2 H), 2.4 (m, 8 H), 1.65 (s, 6 H). [f] Determined from KIE for $1,1,4,4\text{-}d_4$/KIE for $4,4\text{-}d_2$; see Table II.

Table II. Secondary Deuterium KIEs in Isoprene-$1,1,4,4\text{-}d_4$ 4 + 2 Cycloadditions[a]

reactant	T, °C	methylcyclohexene product	
acrylonitrile		5-cyano	4-cyano
d_0/d_4	100[b]	1/1.127 (0.035)	1/1.118 (0.02)
fumaronitrile		*trans*-4,5-dicyano	
d_0/d_4	25[c]	1/1.264 (0.035)	
d_0/d_4	100[b]	1/1.109 (0.025)	
d_0/d_4	100[c]	1/1.184 (0.032)	
1,1-dicyanoethene		5,5-dicyano	4,4-dicyano
d_0/d_4	25[c]	1/1.29 (0.085)	1/1.265 (0.015)
methyl *trans*-β-cyanoacrylate		regioisomer 1[d]	regioisomer 2[d]
d_0/d_4	25[c]	1/1.24 (0.03)	1/1.25 (0.03)
methyl fumarate		*trans*-4,5-dicarbomethoxy	
d_0/d_4	25[c]	1/1.24 (0.02)	
d_0/d_4	100[c]	1/1.18 (0.02)	
methyl maleate		*cis*-4,5-dicarbomethoxy	
d_0/d_4	100[c]	1/1.145 (0.024)	

[a] Standard deviations are given in parentheses; they are determined from multiple analyses of at least duplicate runs. [b] Analyses by GC/MS in CI mode; see footnote 5. [c] Analyses by capillary GC; see footnote 6. [d] The regiochemistry could not be assigned due to the inseparability of the diastereomers on a preparative scale; the ratio of regioisomers from methyl *trans*-β-cyanoacrylate is 1:1.

reporting the d_4 data directly, the KIEs with d_4 (Table II) are divided by those from $4,4\text{-}d_2$ to give the KIEs at C-1 alone for comparison with those at C-4 observed directly from $4,4\text{-}d_2$). The KIEs were determined by competition, reacting the dienophile with excess (>10-fold) of a mixture of d_0 and d_n isoprene and observing the d_0/d_n ratio in each adduct by either GC/MS in CI mode or by capillary GC.[6] The d_0/d_n ratio in starting isoprene was found by using an excess of the dienophile. The standard deviations reported are those for multiple analyses of at least duplicate samples. Also listed in Table I are the maximum kinetic isotope effects expected for two deuteriums, which are derived from the equilibrium constants for fractionation of deuterium between exomethylene carbon and secondary saturated allylic carbon in degenerate thermal 1,3- and 3,3-shifts over nearly a 200 °C range.[7]

Discussion

All reactions in Table I that show an isotope effect proceed faster with deuterium substitution. These inverse isotope effects are expected if the sp^2 carbon site undergoes rehybridization toward sp^3 at the transition state. In addition, in these reactions, the more sp^3 like is the transition state, the larger is the expected inverse KIE.[5]

The reaction of acrylonitrile with isoprene gives a 3:7 mixture of 5-cyano- and 4-cyano-1-methylcyclohexene, respectively, the "meta" and "para" adducts, respectively. The 5-cyano adduct from reaction of $4,4\text{-}d_2$ with acrylonitrile is formed with a moderate inverse KIE that should be related to the extent of bond making at the β site of acrylonitrile; the 4-cyano adduct is formed with but a very small KIE, suggesting little bond making to the α site of acrylonitrile. The difference in the KIEs suggests an unsymmetrical transition state, and the KIEs from $1,1\text{-}d_2$ reveal the same unsymmetrical transition state. It is significant that the inverse KIE observed at the β site of acrylonitrile in both experiments is only half of the maximum value expected, indicating the transition state does not have a fully formed bond, that is, the transition state is not like a biradical. It is true, however, that if the rate-determining step were formation of a biradical intermediate, the KIE at the β site could be less than the maximum value, so this experiment can be interpreted either in terms of concert or a two-step process with the first step being rate determining.

With the more unsymmetrical dienophile, vinylidene cyanide, the ratio of the "meta" to "para" adducts is 1:7. Further, a more unsymmetrical transition state appears to be involved than that with acrylonitrile since the KIE at the bond forming to the β site of the dienophile is half to three-quarters of the maximum value and there is little if any KIE in bond making to the α site.[5,8] This observation is not unlike that by Trahanovsky[9a] and by Holder,[9b] where large inverse KIEs were observed at the initial bond-forming sites in 4 + 4 and 2 + 2 cycloadditions, respectively.

The reaction of fumaronitrile provides only one adduct, but it is significant that the KIEs at C-1 and C-4 of the diene are roughly equal and one-quarter to one-half of the maximum value depending on the temperature. If biradicals were involved, the one with a bond to C-1 of isoprene should dominate by a factor of roughly 7 over the one with a bond to C-4, judging by the regiochemistry with highly unsymmetrical dienophiles.[8] This would require the KIE at C-1 to be near the maximum value and that at C-4 to be very small. Similar conclusions follow from the data with methyl fumarate and maleate although with methyl maleate the data suggest a more unsymmetrical transition state if the error limits are ignored.

Previous kinetic isotope studies of the retro Diels–Alder reaction of the 2-methylfuran–maleic anhydride adduct by Seltzer[4b] can be interpreted similarly. Of the two bonds that can break, the more highly substituted one should do so first, yet the KIE at either carbon α to a carbonyl was the same. This can only be possible if both bonds are breaking simultaneously or are completely broken in the rate-determining transition state of a two-step process. The magnitudes of the KIEs suggest that the bonds are not completely broken, so simultaneous partial and symmetrical cleavage of two bonds is required.

Reaction of *4,4-*d_2 (and *1,1-*d_2) with methyl *trans*-β-cyanoacrylate,[10] with isoprene gives a 1:1 ratio of regioisomeric syn adducts. Both regioisomers show the same inverse KIE (within experimental error) at each site, and it is roughly one-third of the maximum value. If the reaction were stepwise then two biradicals giving each regioisomer should be involved in a ratio of ca. 7:1, assuming that α-cyano-radical stabilization is equivalent to α-carbomethoxy-radical stabilization (since the regiopreference is unity, the assumption must be true). Under this circumstance, the KIE for *4,4-*d_2 should be roughly $^{1}/_{8}$ the maximum value and the KIE for *1,1-*d_2 should be roughly $^{7}/_{8}$'s the maximum value in each regioisomer.

Summary

The secondary deuterium kinetic isotope effects at C-1 and C-4 of isoprene when reacting with unsymmetrical dienophiles suggest unsymmetrical transition states, as might have been expected. However, the KIEs with fumaronitrile and the nearly symmetrical unsymmetrical dienophile, β-cyanoacrylate, are consistent with a nearly synchronous, concerted pathway with an early transition state. The KIEs reported here do not prove that the reaction is synchronous, and there is substantial question as to whether it can ever be experimentally demonstrated to be the case. Indeed, the descriptor synchronous implies a unique point in reaction hyperspace, which cannot be determined with 100% accuracy or precision. The KIEs are more like those expected for a synchronous path—not a highly unsymmetrical one.

Experimental Section

General Procedures. Nuclear magnetic resonance (NMR) spectra were recorded with either a Varian XL-300, EM-390, T-60, HR-220, or a Nicolet-360 spectrometer. Chloroform-d_1, benzene-d_6, acetone-d_6, or carbon tetrachloride was used as the NMR solvent, with tetramethylsilane (TMS) as an internal standard. The chemical shifts are reported in δ values in parts-per-million downfield from the standard. Capillary gas chromatographic data were collected from a Varian Model 3700 gas chromatograph using a Hewlett-Packard 3390A integrator. The columns used for separation were either a 60 M DB-5, a 100 M SPB-5 or a 100 M SPB-5 in series with a 60 M SP-2330. Deuterium incorporations were determined by multiple NMR integrations on either the EM-390 or the T-60 spectrometer. Melting points were determined on a Thomas capillary melting point apparatus and are uncorrected. Gas chromatography/mass spectrometry (GC/MS) spectra were recorded in chemical ionization (CI) mode using a HP 5985 B fitted with a DB-5 30-m capillary column. MS conditions included ion production via ionized methane gas.

1,1,3,3-Tetracyanopropane.[11,12] Freshly distilled malononitrile (5 mL, 0.079 mol) was dissolved in 30 mL of absolute ethanol at 0 °C in a 100-mL round-bottom flask. Formaldehyde solution (37%, 3 mL, 0.039 mol) was added to the flask. Piperidine (five drops) and piperidinium hydrochloride (0.01 g) were then added, and almost immediately a white precipitate formed. The reaction was stirred at 0 °C for 2.5 h and filtered. The crystals were washed with 10% aqueous H_2SO_4 and dried in vacuo. Pure 1,1,3,3-tetracyanopropane (1.1 g, 20% yield) was obtained: mp 136–137 °C (lit.[13] mp 137 °C); NMR (300 MHz, C_3D_6O) δ 4.96 (t, J = 7.5 Hz, 2 H), 3.19 (t, J = 7.4 Hz, 2 H).

1,1-Dicyanoethylene.[14] Vacuum-desiccated 1,1,3,3-tetracyanopropane (20.0 g, 0.14 mol) was placed in a flame-dried 100-mL round-bottom flask fitted with a U-tube directly connected to a liquid nitrogen cooled receiver. A glass wool plug containing 1.5 g of P_2O_5 was placed over the crystals. A small amount of P_2O_5 was also placed in the receiver. After evacuation to 1 Torr pressure, the system was heated to 180 °C for 1 h to give 4 mL of a clear liquid. The collected product was then distilled into a cow flask receiver cooled to 0 °C in an ice–water bath. Fraction 1 (2 mL) was collected at 52 °C (0.5 Torr) while a second fraction (1 mL) was collected at 75 °C. Spectral data indicated that fraction 1 was pure vinylidene cyanide: NMR (90 MHz, $CDCl_3$) δ 6.6 (s).

Methyl α-Chloroacrylate.[15] Concentrated sulfuric acid (93 mL), trichloroethylene (45.6 mL, 0.51 mol), and copper carbonate (1.6 g) were mixed in a 500-mL round-bottom flask fitted with a reflux condenser, dropping funnel, and thermometer. After heating the solution to 60 °C, paraformaldehyde (15.0 g, suspended in 40 mL of methanol) was added to the rapidly stirred solution in small portions over a 1-h period. (*Caution*: exothermic!) The mixture was heated to 100–110 °C for 3.5 h. The solution was cooled and 50 g of ice was added. After steam distillation (using a steam line), the ester was collected in a Dean–Stark trap, separated from the distillate, dried over magnesium sulfate, and distilled in vacuo. Methyl α-chloroacrylate (18.1 g, 30% yield) was collected at 55 °C (55 Torr): NMR (90 MHz, CCl_4) δ 6.47 (m, 1 H), 5.95 (s, 1 H), 3.8 (s, 3 H).

Methyl *trans*-β-Cyanoacrylate.[16,17] Methyl α-chloroacrylate (3.0 g, 0.025 mol) dissolved in 15 mL of 3.5:1 acetone–water solution, was placed in a 25-mL round-bottom flask. Sodium cyanide (1.23 g, 0.025 mol) was added to the rapidly stirred solution. (*Cation*: exothermic!) After stirring at room temperature for 16 h, the two layers were separated; the aqueous layer was extracted with dichloromethane and all organic phases were combined. The solvents were removed by distillation at atmospheric pressure. The residue was distilled at 35 Torr to give 2 mL of a clear liquid: bp 80–83 °C; NMR (360 MHz, $CDCl_3$) δ 6.73 (d, J = 16.3 Hz, 1 H), 6.51 (d, J = 16.5 Hz, 1 H), 3.84 (s, 3 H).

(Methyl-d_3)triphenylphosphonium Iodide.[18] Under an initial atmosphere of dry nitrogen, triphenylphosphine (52.4 g, 0.2 mol) was added to 500 g of dry diethyl ether in a previously flame-dried 1000-mL round-bottom flask. After stirring until all solid was dissolved, iodomethane-d_3 (25.0 g, 0.17 mol) was added and the flask stoppered. The reaction was stirred for 24 h at room temperature. Filtration gave 54.8 g (78% yield) of a white solid: NMR (60 MHz, $CDCl_3$) δ 7.7 (m).

4,4-Dideuterio-2-methyl-1,3-butadiene.[19] Dry dimethyl sulfoxide-d_6 (DMSO-d_6) (4.7 mL, 0.066 mol; distilled and stored over CaH_2) was placed in a 100-mL round-bottom flask under an atmosphere of dry nitrogen. The nitrogen line was equipped with an in-line mercury bubbler. Sodium hydride (2.8 g, 0.066 mol) was added to the room-tem-

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[9] (a) Chou, C.-H.; Trahanovsky, W. S. *J. Am. Chem. Soc.* **1986**, *108*, 4138. (b) Holder, R. W.; Graf, N. A.; Duesler, E.; Moss, J. C. *Ibid.* **1983**, *105*, 2929.

[10] Sauers, C. K.; Cotter, R. J. *J. Org. Chem.* **1961**, *26*, 6.

[11] Diels, O.; Gartner, H.; Kaack, R. *Chem. Ber.* **1922**, *55*, 3439.

[12] Diels, O.; Conn, B. *Chem. Ber.* **1923**, *56*, 2076.

[13] Diels, O.; Gartner, H.; Kaack, R. *Chem. Ber.* **1922**, *55*, 3439.

[14] Ardis, A. E.; Averill, S. J.; Gilbert, H.; Miller, F. F.; Schmidt, R. F.; Stewart, F. D.; Trumbull, H. L. *J. Am. Chem. Soc.* **1950**, *72*, 1305.

[15] Pastushak, N. O.; Dombrovskii, A. V.; Mukhova, A. N. *J. Org. Chem. USSR* (*Engl. Transl.*) **1965**, *1*, 566.

[16] Crawford, J. W. C.; McLeish, N.; Wood, T. K. U.S. Patent 2,293,969, 1942.

[17] Sauers, C. K.; Cotter, R. J. *J. Org. Chem.* **1961**, *26*, 6.

[18] Wittig, G.; Schoellkopf, Y. *Org. Synth.* **1960**, *40*, 66.

[19] Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.

perature reaction, which was then heated to 70 °C with the evolution of gas. Once gas evolution ceased, the reaction was cooled with a room-temperature water bath. A suspension of (methyl-d_3)triphenylphosphonium iodide (27 g, 0.066 mol) in dry DMSO-d_6 was added dropwise with rapid stirring to form the ylide. Freshly distilled methacrolein (5.04 mL, 0.061 mol) was added dropwise to the reaction mixture. After the reaction was stirred at room temperature for 1 h, evacuation of the system to 1 Torr allowed 4.4 mL (70% yield) of the isoprene product to be collected in a previously flame-dried trap cooled with a liquid nitrogen bath. Comparison of the H NMR spectra obtained to that of protioisoprene[20] indicated less than 2% hydrogen at the 4-position: NMR (300 MHz, $CDCl_3$) δ 6.45 (s, 1 H), 4.93 (s, 2 H), 1.85 (s, 3 H).

Preparation of Stock Solutions of d_0/d_2 and d_0/d_4 Isoprene. Stock solutions of isoprene were composed of equivalent amount of protio- and either dideuterio- or tetradeuterioisoprene (>97% *d*).[21] Equivalent amounts (by syringe) of freshly distilled isoprene and either dideuterio- or tetradeuterioisoprene were placed into a flame-dried flask under dry nitrogen. Dry benzene (2 equiv, distilled and stored over Na) was added as solvent. The stock solution was transferred by syringe to flame-dried Pyrex tubes (180 mm × 7 mm, flame sealed at one end) and sealed under vacuum. Each tube held aproximately 450 μL of solution.

General Procedure for the Diels–Alder Reactions. Pyrex tubes (180 mm × 7 mm), which were flame sealed at one end and could be sealed under vacuum, were used as reaction vessels. When a reaction was to be run, a tube of diene stock solution was frozen in liquid nitrogen and opened. Immediately after opening the tube, it was placed under dry N_2 until the solution thawed. Two reactions were set up using the stock solution. The first reaction had a large excess (70–100-fold) of diene. The second reaction had a large excess of dienophile. Once the reactants were combined, the reaction tube was degassed twice and sealed under vacuum. The reactions were run at the temperatures specified in the table. After the reaction was complete, the tube was frozen in liquid nitrogen and opened. The contents were transferred to a 5-mL pear-shaped flask by use of dry benzene. The solvent was then removed in vacuo until the desired concentration was reached. A GC/MS analysis or a capillary GC of the products from these reactions provided the kinetic isotope effects. The reaction product were confirmed by NMR analysis.

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Registry No. Acrylonitrile, 107-13-1; fumaronitrile, 764-42-1; vinylidene cyanide, 922-64-5; dimethyl fumarate, 624-49-7; dimethyl maleate, 624-48-6; methyl *trans*-β-cyanoacrylate, 925-56-4; isoprene, 78-79-5; deuterium, 7782-39-0; 1,1,3,3-tetracyanopropane, 3695-98-5; malononitrile, 109-77-3; formaldehyde, 50-00-0; trichloroethylene, 79-01-6; paraformaldehyde, 30525-89-4; methyl α-chloroacrylate, 80-63-7; (methyl-d_3)triphenylphosphonium iodide, 1560-56-1; 4,4-dideuterio-2-methyl-1,3-butadiene, 64750-98-7; triphenylphosphine, 603-35-0; iodomethane-d_3, 865-50-9; methacrolein, 78-85-3.

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(20) Sadtler Research Laboratories Inc., Nuclear Magnetic Resonance ref no. 3434.

(21) Tanaka, Y.; Takeuchi, Y.; Kobayashi, M.; Tadokoro, H. *J. Pol. Sci. A-2* **1971**, *9*, 43.

Radical Anions of Esters of Carboxylic Acids. Effects of Structure and Solvent on Unimolecular Fragmentations

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Abstract: Pulse radiolysis of alkyl benzoates produces the ester radical anions, which have optical absorptions near 310 nm (~35 000 M^{-1} cm^{-1}) and 450 nm (~9500 M^{-1} cm^{-1}). The radical anions undergo unimolecular fragmentation to form alkyl radicals and carboxylate anions with rates that depend upon the presence of radical stabilizing groups on the alkyl fragment, the nature of the ester group, and the solvent. This cleavage occurs competitively with other processes, such as acyl carbon–oxygen (Bouveault–Blanc) cleavage and electron transfer. The decay rates in ethanol solvent correlate empirically with the bond dissociation energies BDE_{R-H} of the alkyl fragments. Cleavage to form methyl, primary, or secondary alkyl radicals occurs sufficiently slowly that the other mechanisms of decay are found to predominate.

Radical anions are intermediates in many kinds of processes, including dissolving-metal reductions,[1] cathodic reduction,[2,3] excited-state quenching reactions,[4] homogeneous redox reactions,[5] $S_{RN}2$ reactions,[6,7] and nucleophilic substitutions.[8] The radical anions generally form by single-electron transfer from suitable reducing agents (eq 1). Fragmentation of the radical anions to

$$R{-}X + e^- \rightleftarrows R{-}X^{\bullet -} \qquad (1)$$

$$R{-}X^{\bullet -} \rightarrow R^{\bullet} + X^- \qquad (2)$$

produce an anion and a radical (eq 2) is commonly observed.[2-4,6-11] The rate of this fragmentation determines, in part, the efficiencies

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(1) McOmie, J. F. W. *Protective Groups in Organic Chemistry*; Plenum Press: New York, 1973. Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981. Muth, H.; Sauerbier, M. In *Houben-Weyl Methoden der Organische Chemie*; Georg Thieme: Stuttgart, 1980; Part 4/1c, Reduktion, Vol 1.

(2) Andrieux, C. P.; Saveant, J.-M.; Su, K. B. *J. Phys. Chem.* **1986**, *90*, 3815.

(3) Saveant, J. M. *Acc. Chem. Res.* **1980**, *13*, 323.

(4) Julliard, M.; Chanon, M. *Chem. Rev.* **1983**, *83*, 425.

(5) Rorabacher, D. B., Endicott, J. F., Eds. *Mechanistic Aspects of Inorganic Reactions*; ACS Symposium Series 198; American Chemical Society: Washington, DC, 1982.

(6) Wade, P. A.; Morrison, H. A.; Kornblum, N. *J. Org. Chem.* **1987**, *52*, 3102.

(7) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

(8) Bordwell, F. G.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 8112.

(9) (a) Prasad, D. R.; Hoffman, M. Z.; Mulazzani, Q. G.; Rodgers, M. A. J. *J. Am. Chem. Soc.* **1986**, *108*, 5132. (b) Maslak, P.; Guthrie, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 2628. (c) Lan, J. Y.; Schuster, G. B. *Ibid.* **1985**, *107*, 6710.

(10) Neta, P.; Behar, D. *J. Am. Chem. Soc.* **1981**, *103*, 103.

(11) Hamill, W. H. *Radical Ions*; Kaiser, E. T., Kevan, L., Eds.; Interscience: New York, 1968; Chapter 9, pp 408–412. Ward, J. A.; Hamill, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 1853.