*Crypto*Cope Rearrangement of 1,3-Dicyano-5-phenyl-*4,4-d₂*-hexa-2,5-diene. Chameleonic or Centauric?

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Abstract: The "centauric" model for evaluation of the effect of radical-stabilizing perturbations on the Cope rearrangement conjectures independent action of substituents that make conflicting electronic demands on the two halves of the transition region. The present test of this conjecture compares 1,3-dicyano-[5-protio]-hexa-1,5-diene (**1(H)**) and 2-phenylhexa-1,5-diene, with 1,3-dicyano-5-phenylhexa-1,5-diene (**1(Ph)**). Thermochemical information required for a proper comparison includes new data of the van't Hoff type on conjugative interaction of cyano with the carbon−carbon double bond, reevaluation of the radical-stabilizing potential of the cyano group on secondary and allyl radicals, comparison with the (reevaluated) stabilizing effect of cyano in "nodal" positions of the Cope transition region, and determination of the enthalpy and entropy of activation of the *crypto*Cope rearrangement of otherwise Cope-incompetent, thermodynamically more stable hexa-2,5-dienes related by prototropy to the Cope-competent hexa-1,5-dienes above. The "chameleonic" model is concluded to be unsatisfactory, while the "centauric" is in better, if not complete, accord with experiment.

An exploration is continued here of the proposition that the response of Cope's rearrangement to perturbation by radical-stabilizing substituents is fruitfully thought of as "centauric", in addition to "chameleonic".[1] The latter gives name to a long held conceptual scheme, in which the Cope is viewed as a continuum between a transition region sometime-called "aromatic", and a "biradicaloid", thought closely to resemble the cyclohexa-1,4-diyl diradical.[2−4] Throughout this continuum, retention of a basic C_{2h} symmetry is imagined; that is, the two, three-carbon halves remain essentially identical in their electronic character. At one furthermost extreme, the two halves simulate the character of allyl radicals and are expected to respond to radical-stabilizing substituents in "active", 1-(6-) and 3-(4-) positions, but not in "nodal", 2-(5-) positions. At the other extreme, the diyl, the reverse obtains: the four previously active positions are expected to become inactive while the two nodal, now having acquired the characteristics of an aliphatic secondary radical, become active (Scheme 1).

When substituents are positioned to compete with each other, one in active positions and the other in a nodal position, new questions arise. Is the transition region obligated to retain its basic, chameleonic C_{2h} symmetry and thus accommodate the opposing demands in the two halves by satisfying the full stabilizing potential of either one or the other, but not both? Or may it move in a new, symmetry-lowering dimension along a centauric continuum, in which one-half responds to the allylic demand, and the other to the secondary radical-like demand?
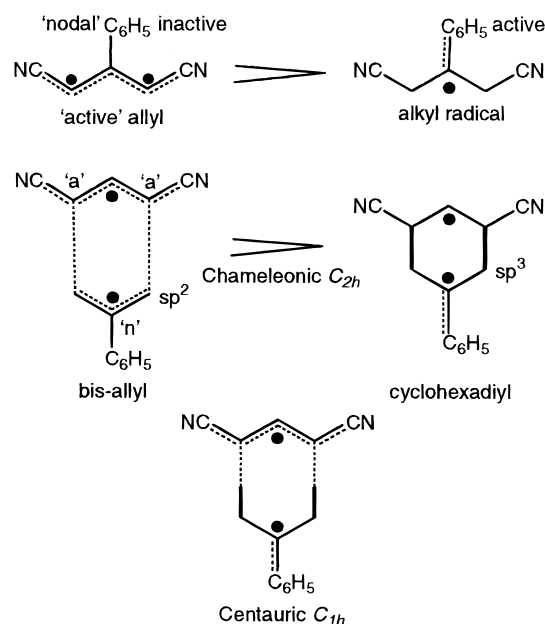
(1) Doering, W. v. E.; Wang, Y.-h. *J. Am. Chem. Soc.* **1999**, *121*, 10112−10118.

(2) (a) Dewar, M. J. S.; Wade, L. E., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 290 ("...**1** (hexa-1,5-diene) itself may be more or less poised between the biradical and pericyclic mechanisms and that the balance can be displaced in either way by appropriate substitution.").

(3) Wehrli, R.; Schmid, H.; Bellus, D.; Hansen, H.-J. *Helv. Chim. Acta* **1977**, *60*, 1325−1356.

(4) (a) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1978**, *100*, 6269−6270. (b) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 6693−6704.

Scheme 1

The thinking is caricatured in Scheme 1, in which the specific illustration is the subject of the present paper.

Distinction between the two propositions is quantitative. Given that the radical-stabilizing abilities of a perturbing substituent have been established in each of the two extremes of the chameleonic continuum, are two groups in positions of opposing demands no more effective than the stronger of the two, or does each contribute its full potential? In a previous paper, in which phenyl has been employed as the perturbing substituent, the centauric model appears to have been the more successful.[1] Phenyl as the perturbing group, however, has inescapable drawbacks. One is the sensitivity to steric factors of both its conjugative interaction with double bonds and its

ability to stabilize radicals. Another is its unsuitability, at the moment at least, for calculation at the highest level of theory required to deal with the Cope rearrangement. The importance of cooperative interaction between experiment and theory, here and in general, is self-evident. By contrast, the cyano group is amenable to theoretical calculation,[5] has a small, probably negligible, steric factor as will be supported below,[6] but suffers from its own disadvantages, as we shall see.
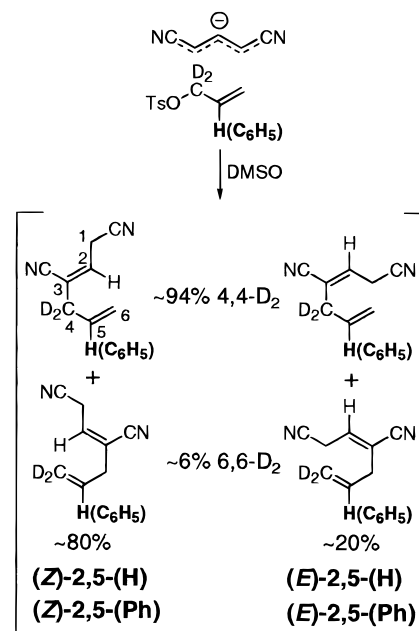
1,3,5-Tricyanohexa-1,5-diene might have seemed the centaur of choice, but, owing to the high acidity of its 1,3-dicyanopropene system, was deemed likely to destruction by facile intramolecular Michael cyclization under the conditions of Cope rearrangement,[7] and therefore unsuitable. That 2-cyanohexa-1,5-diene, a second compound needed to construct the centauric model, was unknown constituted a further dissuasion. Choice finally settled on a comparison of 1,3-dicyanohexa-1,5-diene (**1**) and 1,3-dicyano-5-phenylhexa-1,5-diene (**2**), both labeled with deuterium in the 4,4-positions to break the degeneracy of their Cope rearrangements.[8] Substitution of cyano by phenyl in the 5-position had the further advantage that both 2-phenylhexa-1,5-diene and 2,5-diphenylhexa-1,5-diene had already been studied by Dewar and Wade,[9] however much the absolute values of the activation parameters of the former might beg for refinement. As a further attraction, three examples of the replacement of allyl by a 2-phenylallyl group in Cope rearrangements already existed in the literature for comparison.
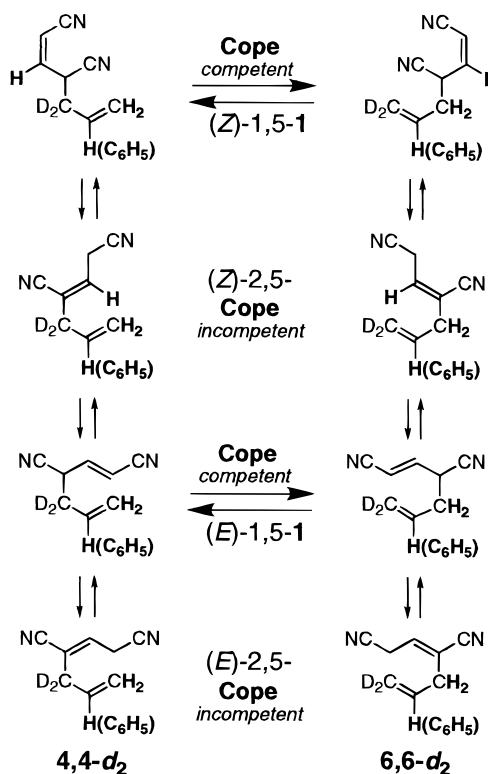
*Crypto*Cope Rearrangement

Syntheses of the two dicyano compounds, **1(H)-d_2** and **1-(Ph)-d_2**, take advantage of a high acidity of 1,3-dicyanopropene (Scheme 2) that would allow generation of a carbanion for allylation by reaction with 3,3-dideuterio-3-tosylyoxypropene and 3,3-dideuterio-2-phenyl-3-tosylyoxypropene, respectively. These displacements in fact proceeded well, if only in dimethyl sulfoxide as solvent,[10] with a regioselectivity of ~94%. Disastrously at first sight, the products were not the Cope-*competent* 1,5-dienes, but, by rapid prototropy, the thermodynamically more stable, Cope-*incompetent* 2,5-isomers.

There seeming to be no obvious way of isolating and studying the 1,5-dienes directly (barely visible in NMR), the project was near abandonment until it was recognized that the thermal rearrangement of the small quantities of Cope-competent 1,5-diene in equilibrium might be followed by observing the rate of increase in hydrons at the 4,4-position of the Cope-incompetent 2,5-dienes (a *crypto*Cope rearrangement!) under rapidly equilibrating conditions. The unusually complicated situation is depicted in Scheme 3. To be trustworthy, this approach demands sufficiently fast maintenance of preequilibrium to bring the system into the Curtin–Hammett domain;[11] that is, equilibration within each of the columns of Scheme 3

(5) (a) Hrovat, D. A.; Borden, W. T.; Vance, R. L.; Rondan, N. G.; Houk, K. N.; Morokuma, K. *J. Am. Chem. Soc.* **1990**, *112*, 2018−2019. (b) Beno, B. R.; Hrovat, D. A.; Lange, H.; Yoo, H.-y.; Houk, K. N.; Borden, W. T. *J. Am. Chem. Soc.* **1999**, *121*, in press.

(6) Vögtle, F.; Neumann, P.; Zuber, M. *Chem. Ber.* **1972**, *105*, 2955−2962.

(7) For the same reason at least, we shall not examine 1,3,4,6-tetracyanohexa-1,5-diene for its bearing on the theoretically uncovered prediction of a synergistic effect,[5b] but see Figure 2 (**I**). Neither do we intend to pursue 2- or 3-cyanohexa-1,5-diene, or 1,4-, 3,4-, or 2,5-dicyanohexa-1,5-diene.

(8) Sunko, D. E.; Humski, K.; Malojcic, R.; Borcic, S. *J. Am. Chem. Soc.* **1970**, *92*, 6534−6538.

(9) Dewar, M. J. S.; Wade, L. E., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 4417−4424.

(10) Zaugg, H. E. *J. Am. Chem. Soc.* **1961**, *83*, 837−840.

(11) Klumpp, G. L. *Reactivity in Organic Chemistry*; Wiley: New York, 1982; pp 231−249.

Scheme 2

Scheme 3

must be much faster than the Cope rearrangements linking the two columns. The resulting experimental enthalpy and entropy of activation would then consist of the sum of those of the Cope rearrangement (on the necessary assumption that deuterium interchange originates in that reaction alone) and the difference in enthalpies and entropies of formation of the more stable, kinetically incompetent 2,5-isomers and the less stable, kinetically competent 1,5-isomers. Consequently, knowledge of these differences in conjugative interaction must be in hand if the concealed Cope activation parameters are to be separated from the experimentally observed parameters. Note that there is no obvious way of resolving the relative contribution of (Z) and (E) isomers to the rearrangement. Despite the several complica-

Table 1. Specific Rate Constants and Derived Activation Parameters for the Reversible Interconversion of *4,4-* and *6,6-D2*-1,3-dicyanohexa-2,5-diene (H) and *4,4-* and *6,6-D2*-1,3-dicyano-5-phenylhexa-2,5-diene (C_6H_5) in Isopropyl Alcohol-*d8*

H		C_6H_5	
T, °C	$(k_1 + k_{-1})^{a,b}$	*T*, °C	$(k_1 + k_{-1})^{a,b}$
165.2 ± 0.3	2.88 ± 0.10	164.9 ± 0.2	8.84 ± 0.27
176.9 ± 0.1	7.92 ± 0.26	176.7 ± 0.2	23.24 ± 0.30
185.4 ± 0.1	14.84 ± 0.11	185.2 ± 0.2	41.80 ± 1.6
194.1 ± 0.1	28.24 ± 0.60	194.4 ± 0.3	81.07 ± 2.8
Arrhenius Parameters			
$E_a = 32.36 \pm 0.63$ kcal mol^{-1}		$E_a = 30.36 \pm 0.59$ kcal mol^{-1}	
log $A = 10.45 \pm 0.27$		log $A = 10.10 \pm 0.28$	
Eyring Parameters^c			
$\Delta H^{\ddagger} = 31.5$ kcal mol^{-1}		$\Delta H^{\ddagger} = 29.5$ kcal mol^{-1}	
$\Delta S^{\ddagger} = -13.5 \pm 1.2$ cal mol^{-1} K^{-1}		$\Delta S^{\ddagger} = -15.1 \pm 1.3$ cal mol^{-1} K^{-1}	

^{a} In units of 10^{-6} s^{-1}. ^{b} Calculated by linear regression of the standard expression for reversible first-order reactions: $(k_1 + k_{-1}) = \ln[(x_e - x_o)/(x_e - x_t)]/t$, where $x_e = 47.21\%$ of *6,6-d2*-isomers. ^{c} Calculated at 179.7 °C.
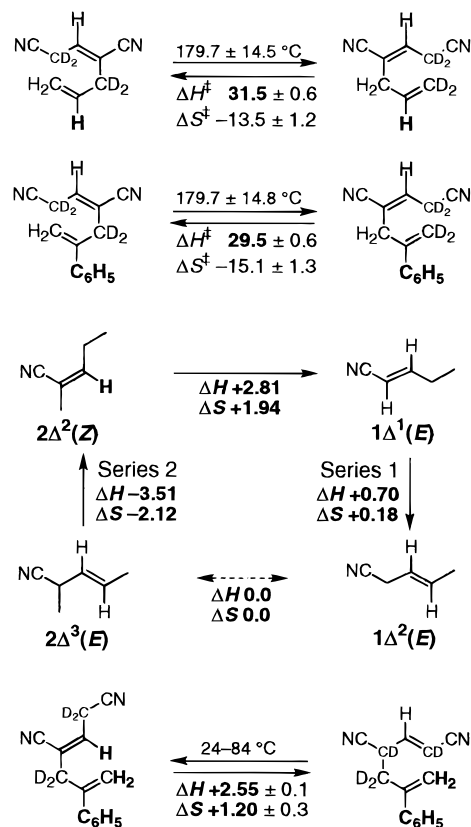
tions, the main conclusion will not be compromised because comparison is between pairs of systems that are subject to the same, presumably small differences in steric and electronic influence of the allyl and 2-phenylallyl moieties on the ground states.

The kinetic acidity of the 1,3-dicyanopropene system in 1,3-dicyanohexa-2,5-diene is in fact so high that fast deuterium exchange as an indication of rapid establishment of preequilibrium is easily realized in methanol-*d4* as solvent, even without a basic catalyst. Were it not for the high proclivity of the system to undergo Michael addition and consequently induce intolerably low recoveries at the higher temperatures needed to follow the *crypto*Cope rearrangement, this solvent would be fine. In the event, a tolerable compromise is found in perdeuterioisopropyl alcohol.

In 1,3-dicyano-5-phenylhexa-2,5-diene, deuterium exchange is slower, but can be sufficiently accelerated by 10% pyridine, an addition which incidentally improves the quality of the NMR spectrum for analytical purposes. At the higher temperatures required for the *crypto*Cope rearrangement to transfer deuterium to C-6 from its initially predominant position at C-4, recovery has dropped to 80% by the time the reaction has proceeded 90% toward equilibrium. Perhaps more seriously, the sum of the concentrations of educt and product, which can be measured independently in this instance relative to hydrons at C-2, also suffers erosion, its value gradually falling to ~90% by the time equilibrium is reached at the highest temperature (Table S2 of Supporting Information). If it be assumed in the absence of any other explanation that hydrons at C-6 are slowly lost by exchange with deuterium (perhaps by reversible homodienyl rearrangement), the relative concentrations of educt and product may be normalized to a sum of 100% for the purpose of calculating $(k_1 + k_{-1})$. No such adjustment can be made with 1,3-dicyano-4,4-dideuteriohexa-2,5-diene, if indeed it is needed, because the product of rearrangement alone, but not the educt, can be analyzed quantitatively by NMR spectroscopy.

The results of the kinetic studies in Table 1 are based on experimental data recorded in Tables S1 and S2 of the Supporting Information. Specific rate constants are calculated point by point by the usual equations for reversible first-order reactions, and extrapolated to zero time by linear regression to afford the specific rate constants reported in the tables. In these calculations, the concentration of product at equilibrium is taken as the square root of the equilibrium isotope effect reported by

Scheme 4

Sunko et al.[8] and Gajewski[4b] for tetradeuteriohexa-1,5-diene. Activation parameters for reversible exchange in the Cope-incompetent isomers are calculated in the usual manner (Table 1, repeated in the upper part of Scheme 4).

The difference in enthalpy of activation of the 5-protio and 5-phenyl compounds is 2.0 ± 1.2 kcal mol^{-1}. In an effort to improve the precision and accuracy of this quantity, the relatively small, ~3-fold ratio of their specific rate constants is turned to good use by effecting rearrangement of both compounds together in the same flask under identical conditions of solvent, temperature, etc. The window offered is not large. From the data in Table 2, a seemingly improved value of 1.6 ± 0.6 kcal mol^{-1} for the difference in enthalpies of activation is obtained. A weighted average of 1.7 kcal mol^{-1} is recommended.

Conjugative Interaction

Understanding how perturbations in general affect rates of reaction requires not only analysis of their effect on the transition region relative to an unperturbed reference, but equally an understanding of their effect on the educt. As obvious as this assertion may be, it has not been applied by previous workers in the field. For the present purpose, as well as for an analysis of 2,5-dicyano-3-methylhexa-1,5-diene,[3] conjugative interactions of the cyano group with a double bond in β- and α,β-alkyl-substituted olefins are missing.

Conjugation by cyano has a long history without having been brought to a satisfactory conclusion. Early determinations at single temperatures by Bruylants, and by Linstead, have revealed a greater effectiveness of cyano vis-à-vis methyl of ~1 kcal mol^{-1} in $\Delta\Delta G$,[12] while a more recent result gives a value of ~0.4 kcal mol^{-1}.[13] New data bearing on three cyano olefins

(12) For succinct reviews, see: Bennett, G. M. *Ann. Rep.* **1929**, *26*, 116−120. Kon, G. A. R. *Ann. Rep.* **1932**, *29*, 136−144.

Table 2. Specific Rate Constants and Derived Differences in Activation Parameters for the Reversible Interconversions among *4,4-* and *6,6-D₂*-1,3-dicyanohexa-2,5-diene (**H**) and *4,4-* and *6,6-D₂*-1,3-dicyano-5-phenylhexa-2,5-diene (**C₆H₅**) in Isopropyl Alcohol-*d₈* (90%) and Pyridine-*d₅* (10%) Together in the Same Reaction Vessel

t, s⁻¹	$(C_6H_5)^{a,b}$	$(H)^{a,b}$	$(k_1 + k_{-1})$ $(C_6H_5)^c$	$(k_1 + k_{-1})$ $(H)^c$	$(C_6H_5)/(H)^d$
		164.8 °C; 438.0 ± 0.2 K			
0	5.52	6.23			
50940	22.16	12.70	10.000	3.373	2.964
104700	32.65	18.33	10.048	3.342	3.006
172980	38.46	23.58	9.025	3.183	2.836
		193.8 °C; 467.0 ± 0.2 K			
0	4.52	5.93			
7020	23.49	14.28	83.71	32.19	2.600
15120	34.19	20.82	78.54	29.59	2.654
19860	38.61	24.72	80.66	30.58	2.638

a Concentration of 6,6-dideuterio isomers relative to sum in %. *b* In units of 10⁻⁶ s⁻¹. *c* Calculated by linear regression of the standard expression for reversible first-order reactions: $(k_1 + k_{-1}) = \ln[(x_e - x_o)/(x_e - x_t)]/t$, where $x_e = 47.21\%$ 6,6-dideuterio isomers. *d* Average values of the ratio are used to calculate $\Delta\Delta_f H = 1.6 \pm 0.6$ kcal mol⁻¹: 2.937 ± 0.089 (438.0 K) and 2.630 ± 0.027 (467.0 K).

have now been acquired by the van't Hoff method from the temperature dependence of equilibrium constants, and are reported in Tables S4, S5, and S6 of the Supporting Information. Calculation therefrom of thermochemical quantities proceeds in two stages. First, the natural logarithm of the equilibrium concentrations in percent and the reciprocal of temperatures (K) are subjected to linear regression. Second, the resulting intercepts and slopes, being related to entropy and enthalpy, respectively, are multiplied by the gas constant, R. Relative to an unconjugated isomer taken as reference and set to 0.00, these are then reported as $\Delta\Delta_f S$ (cal mol⁻¹ K⁻¹) and $\Delta\Delta_f H$ (kcal mol⁻¹), respectively, along with the *sum* of the standard errors pertaining to the isomeric and reference compounds. Included in Scheme 5 are differences in free energies at room temperature (by extrapolation), enthalpies and entropies of conjugation relative to one of the unconjugated isomers (0.00),[14,15] and heats of formation and hydrogenation relative to the reference, unconjugated isomers, for which values are estimated in relatively direct and uncomplicated fashion.[16,17]

The system of pentenenitriles in Series 1 has been studied in benzene-*d₆* over the temperature range 61–154 °C, using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBN) (∼5 mol %) as the basic catalyst. The system behaves relatively well, particularly with

(13) Procházka, M.; Zelinka, J.; Vilim, A.; Černy, J. V. *Collect. Czech. Chem. Commun.* **1970**, *35*, 1224–1234.

(14) The unconjugated isomers provide an internal check on accuracy when compared with "generic" values collected in Figure 1 of ref 15. In Series 1, the difference between **1Δ²(E)** and **1Δ²(Z)** is +1.13 kcal mol⁻¹ compared with the "generic" value of +1.04 kcal mol⁻¹; in Series 3, the difference between **3Δ³(E)** and **3Δ⁴** is +1.43 kcal mol⁻¹ compared to the "generic" value of +1.52 kcal mol⁻¹.

(15) Doering, W. v. E.; Benkhoff, J.; Carleton, P. S.; Pagnotta, M. *J. Am. Chem. Soc.* **1997**, *119*, 10947–10955.

(16) The change in enthalpy of formation on replacing 1° hydron by cyano is +32.69 ± 0.24 kcal mol⁻¹ from six heats of formation of 1° nitriles and corresponding saturated hydrocarbons.[17] [A similar value is obtained from two allylcyanides, 3-cyanopropene and (E)-cyanobut-2-ene: +32.84 ± 0.1 kcal mol⁻¹.] Application of this increment to *n*-butane affords 1-cyanobutane, $\Delta_f H = +2.67$ kcal mol⁻¹. From 2-cyanopropane and cyanocyclohexane, the only 2° nitriles in Pedley et al.,[17] a hydron-cyano replacement value of +30.62 kcal mol⁻¹ is derived. Application of this value to pentane and 2-methylpentane generates 2-cyanopentane, $\Delta_f H = -4.49$ kcal mol⁻¹, and 2-cyano-4-methylpentane, $\Delta_f H = -11.16$ kcal mol⁻¹, respectively. The corresponding heats of hydrogenation are calculated using the "generic" values, −27.25 (Series 1 and 2) and −26.38 (Series 3).[15]

(17) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds*, 2nd ed.; Chapman and Hall: London, 1986.

Scheme 5

Series 1	$1\Delta^1(E)$	$1\Delta^2(E)$	$1\Delta^1(Z)$	$1\Delta^2(Z)$
$\Delta\Delta G$ (298 °C)	−0.67	0.00	−0.48	+1.08
$\Delta\Delta_f H$ (kcal mol⁻¹)	−0.70±0.08	0.00±0.00	−0.54±0.08	+1.09±0.16
$\Delta\Delta_f S$ (cal mol⁻¹ K⁻¹)	−0.18±0.20	0.00±0.00	−0.10±0.22	+0.01±0.43
$\Delta_f H$ (kcal mol⁻¹)	+29.3	+30.0	+29.5	+31.1
$\Delta\Delta H$ H₂ (kcal mol⁻¹)	−26.6	−27.3	−26.7	−28.3

Series 2	$2\Delta^2(E)$	$2\Delta^3(E)$	$2\Delta^2(Z)$	$2\Delta^3(Z)$	$2\Delta^1$
$\Delta\Delta G$ (298 °C)	−2.00	0.00	−2.88		−0.34
$\Delta\Delta_f H$ (kcal mol⁻¹)	−2.35±0.13	0.00±0.00	−3.51±0.10		+0.04±0.16
$\Delta\Delta_f S$ (cal mol⁻¹ K⁻¹)	−1.17±0.31	0.00±0.00	−2.12±0.24		−0.99±0.38
$\Delta_f H$ (kcal mol⁻¹)	+20.6	+23.0	+19.5		+23.0
$\Delta\Delta H$ H₂ (kcal mol⁻¹)	−24.9	−27.3	−23.8		−27.3

Series 3	$3\Delta^2(E)$	$3\Delta^3(E)$	$3\Delta^2(Z)$	$3\Delta^4$	$3\Delta^1$
$\Delta\Delta G$ (298 °C)	−0.34	0.00	−1.10	1.71	
$\Delta\Delta_f H$ (kcal mol⁻¹)	−0.93±0.04	0.00±0.00	−1.52±0.03	+1.43±0.39	
$\Delta\Delta_f S$ (cal mol⁻¹ K⁻¹)	−1.98±0.11	0.00±0.00	−1.42±0.09	−0.93±1.06	
$\Delta_f H$ (kcal mol⁻¹)	+14.3	+15.2	+13.7	+16.7	
$\Delta\Delta H$ H₂ (kcal mol⁻¹)	−25.5	−26.4	−24.9	−27.8	

respect to recoveries and freedom from side reactions. Of interest is the small difference (−0.16 ± 0.16 kcal mol⁻¹) in $\Delta_f H$ favoring (E)-β-ethylacrylonitrile, **1Δ¹(E)**, over its (Z) isomer, **1Δ¹(Z)**. The contrast with phenyl, where the comparable favoring is −2.5 kcal mol⁻¹, points to a very much smaller steric factor operating in the nitriles. The discrepancy between these results and those reported for two simple pairs determined by combustion warrants note. From that work, the (Z) isomers appear more *stable* than the (E) by ∼1.3 ± 0.3 kcal mol⁻¹ (in the gas phase).[18] Although some work slightly favors (Z) over (E) isomers, while other work slightly favors the reverse, all previous investigations based on equilibration agree that the difference, whether in $\Delta\Delta G$ or $\Delta\Delta H$, in the gas phase[19] or solution,[20] is very small. We advise caution in accepting the combustion data,[18] which have been incorporated into a revision of Benson group additivity parameters of nitriles.[21]

The system of 2-methylpentenenitriles comprising Series 2 included compounds **2Δ²(E)** and **2Δ²(Z)**, they being of a type needed to evaluate conjugative interaction in the two cyano compounds under study here, and also **2Δ¹**, the system present in 2,5-dicyanohexa-1,5-diene (vide infra).[3] As catalyst, DBN was not as effective as it had been in Series 1, while stronger bases led to severe decomposition. The ruthenium catalyst of Osborn and Wilkinson for isomerizing olefins proved effective and allowed measurements in benzene-*d₆* solution (101–191 °C).[22] A disadvantage inherent in Series 2 lay in the low concentrations of **2Δ¹** and **2Δ³(E)**, the reference unconjugated isomer, at equilibrium.

In Series 3, neither DBN nor the ruthenium catalyst were effective in establishing the equilibria. A much stronger base, potassium *tert*-butoxide in benzene-*d₆*, was employed success-

(18) Koniček, J.; Procházka, M.; Křestanová, V.; Smišek, M. *Collect. Czech. Chem. Commun.* **1969**, *34*, 2249–2257.

(19) Butler, J. N.; McAlpine, R. D. *Can. J. Chem.* **1963**, *41*, 2487–2491.

(20) Crump, J. *J. Org. Chem.* **1962**, *28*, 953–956.

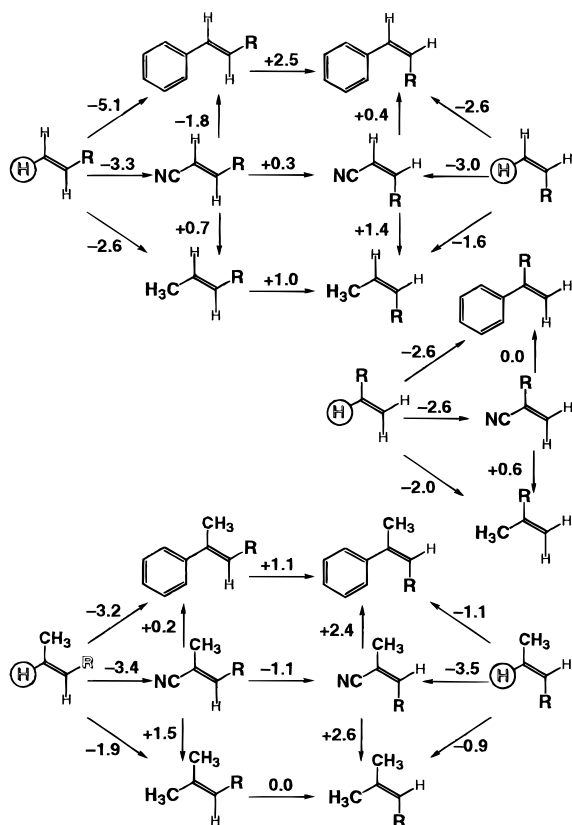(21) Chu, J. Y.; Nguyen, T. T.; King, K. D. *J. Phys. Chem.* **1982**, *86*, 443–447.

1,3-Dicyano-5-phenyl-4,4-d₂-hexa-2,5-diene

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Figure 1. Enthalpies of conjugation (kcal mol⁻¹) are shown relative to the replacement of circled hydrogen atoms by phenyl, cyano, and methyl. These and the other values shown also correspond to differences in enthalpies of hydrogenation of the double bond.

fully (98−160 °C), but formation of byproducts and the failure of perhaps the most vulnerable of the isomers, **3Δ¹**, to appear for analysis were disturbing. With some hesitation, the results are included in Scheme 5, but are not incorporated in the construction of Figure 1.

Conjugative interactions are defined as discrepancies in $\Delta\Delta_f H$ between the substituted olefinic compound and either the corresponding unsubstituted olefin (conjugative interaction (CI) relative to hydron (CI$_{X/H}$) or the corresponding alkyl-substituted congener (CI$_{X/R}$). Translation from values of $\Delta\Delta_f H$ in Scheme 5 to values of CI$_{X/H}$ in Figure 1 may involve the conjugative interactions of methyl vis-à-vis hydrogen. For example, that the difference of −0.70 kcal mol⁻¹ between **1Δ¹(E)** and **1Δ²(E)** equals CI$_{X/R}$ is based directly on the assumption that NCCH₂− is the equivalent of an alkyl group. To generate a value for CI$_{X/H}$, 2.67 kcal mol⁻¹, the generic value for replacement of H by (*E*)-R, is added. The resulting conjugative interaction is 3.4 kcal mol⁻¹.

Attention is directed in Figure 1 to the failure of a *single* quantity to represent the enthalpy of conjugative interaction of either phenyl or methyl, the values being sensitively dependent on α- and β-alkyl substitution. By contrast, the differences among (*E*)- and (*Z*)-α,β-unsaturated nitriles are negligible within experimental uncertainty (with one exception), and reflect a far smaller susceptibility of nitrile to steric factors. At present levels of accuracy, −3.3 ± 0.2 kcal mol⁻¹ seems an acceptable value for the conjugative interaction of cyano in β- or α,β-substituted acrylonitriles. The single observation on 2-cyanopent-1-ene (**2Δ¹**) in Series 2 constitutes the sole basis for an analysis of

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Table 3. Temperature Dependence of Equilibrium between 1,3-Dicyano-5-phenylhexa-2,5-dienes and 1,3-Dicyano-5-phenylhexa-1,5-dienes in Isopropyl Alcohol-d_8 (80%) and Pyridine-d_5 (20%)

T, °C	2,5-hexadienes[a]	1,5-hexadienes[a]	ln K[b]
24	97.58	2.42	−3.697
44	96.96	3.04	−3.462
64	96.07	3.93	−3.196
84	95.16	4.84	−2.979

[a] Concentration in % at equilibrium. [b] Linear regression of ln$K$ versus $1/T$(K) affords $-\Delta H/R + \Delta S/R$: $\Delta\Delta H = +2.55 \pm 0.1$ kcal mol⁻¹; $\Delta\Delta S = +1.2 \pm 0.3$ cal mol⁻¹ K⁻¹.

2,5-dicyanohexa-1,5-diene (vide infra). That its conjugative interaction of 2.6 kcal mol⁻¹ is 0.7 kcal mol⁻¹ lower should perhaps be accepted with some skepticism. Would not a similarly low value for the conjugative interaction have been expected of the two nitriles of the type **2Δ²(E)** and **2Δ²(Z)** (bottom level of Figure 1)? With recovery being less than 100% in Series 2, compound **2Δ¹** may have been the most likely to have suffered. A case can be made to agree, −3.3 ± 0.2 kcal mol⁻¹, for all types of nitriles.

The critically important difference in enthalpy of conjugation between Cope-incompetent and Cope-competent isomers (e.g., (*Z*)-**2,5-** and (*E*)-**1,5-** of Scheme 3) can be estimated from these data to be $\Delta\Delta H = 2.81$ kcal mol⁻¹ by the thermodynamic cycle shown in the middle of Scheme 4. [Note: 0.0 kcal mol⁻¹ is assumed as a reasonable difference between **2Δ³(E)** and **1Δ²-(E)**.] By good fortune, it has been possible to measure the temperature dependence directly by NMR (Table 3), despite the low concentration of the Cope-competent isomers present at equilibrium (2−4%). The resulting value, $\Delta\Delta H = 2.55 \pm 0.1$ kcal mol⁻¹, is in gratifyingly good agreement. Both values accord with the generic value of 2.67 kcal mol⁻¹ for the difference in enthalpies of conjugation of α-substituted olefins and (*E*)-α,β-disubstituted olefins (Figure 1), and thus once again point to a negligible steric effect of cyano, quite comparable to that of hydron.

Cyano-Stabilized Radicals

The other information required about the cyano group concerns the magnitude of its interactions with simple aliphatic free radicals, and with the active position of an allyl radical. An extensive literature on the stabilization energy of the cyanomethyl radical goes back almost two-thirds of a century, and still may be without definitive (±1 kcal mol⁻¹) resolution. Values range from ca. −5 kcal mol⁻¹ vis-à-vis methyl to ca. −14 kcal mol⁻¹ vis-à-vis hydron.[23,24] Confusion has surrounded the heat of formation even of acetonitrile. Its value of 15.4 kcal mol⁻¹, accepted by Pedley et al.,[17] has been revised drastically to 17.8 kcal mol⁻¹ by An and Månsson,[25] and Barnes and Pilcher in 1983,[26] although this change had already been forewarned in 1975 by King and Goddard,[27a] and recognized without discussion by Lias et al.[28] Significant revisions to the basic enthalpies of formation of 2° and 3° aliphatic radicals have also appeared, largely owing to the efforts of the late David Gutmann and co-workers.[29]

Reevaluation of the stabilization energy afforded by cyano vis-à-vis hydron to a secondary alkyl radical is based without reservation on the bond dissociation energy, DH°[(CH₃)₂C-

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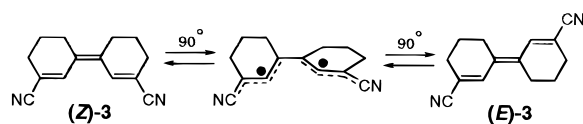(24) Mayer, P. M.; Glukhovtsev, M. N.; Gauld, J. W.; Radom, L. *J. Am. Chem. Soc.* **1997**, *119*, 12889−12895 and references therein.
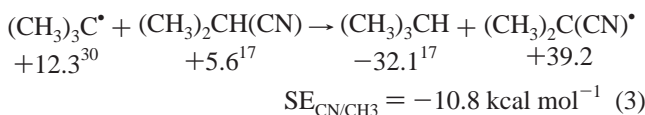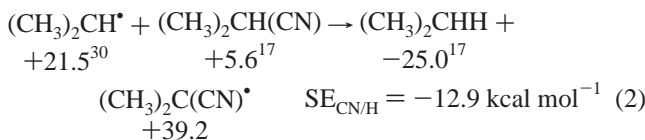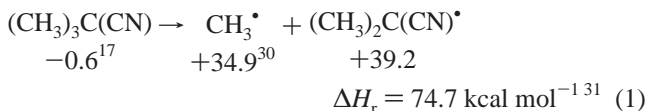(25) An, X.-W.; Månsson, M. *J. Chem. Thermodyn.* **1983**, *15*, 287−293.
(26) Barnes, D. S.; Pilcher, G. as an Appendix to An and Månsson.[25]

Scheme 6

(CN)−CH$_3$] = 74.7 ± 1.6 kcal mol^{-1}, so elegantly determined by King and Goddard in pyrolyses of alkyl nitriles at very low pressures. Recast in eq 1 using currently accepted values of

$$(CH_3)_3C(CN) \rightarrow \quad CH_3^{\bullet} \quad + (CH_3)_2C(CN)^{\bullet}$$
$$-0.6^{17} \qquad +34.9^{30} \qquad +39.2$$
$$\Delta H_r = 74.7 \text{ kcal mol}^{-1\,31} \quad (1)$$

$$(CH_3)_2CH^{\bullet} + (CH_3)_2CH(CN) \rightarrow (CH_3)_2CHH +$$
$$+21.5^{30} \qquad +5.6^{17} \qquad -25.0^{17}$$
$$(CH_3)_2C(CN)^{\bullet} \qquad SE_{CN/H} = -12.9 \text{ kcal mol}^{-1} \quad (2)$$
$$+39.2$$

$$(CH_3)_3C^{\bullet} + (CH_3)_2CH(CN) \rightarrow (CH_3)_3CH + (CH_3)_2C(CN)^{\bullet}$$
$$+12.3^{30} \qquad +5.6^{17} \qquad -32.1^{17} \qquad +39.2$$
$$SE_{CN/CH3} = -10.8 \text{ kcal mol}^{-1} \quad (3)$$

enthalpies of formation of *tert*-butylnitrile and methyl radical lead to an enthalpy of formation of the dimethylcyano radical of +39.2 kcal mol^{-1}.[31] A corresponding stabilization energy (SE) is defined by the replacement of *hydron* by cyano and evaluated by the isodesmic manipulation of eq 2: (SE$_{CN/H}$) = −12.9 kcal mol^{-1}.[32,33] The stabilization energy resulting from replacement of a *methyl* group by cyano is derived by eq 3: SE$_{CN/CH3}$ = −10.8 kcal mol^{-1}. Both are based on the same enthalpy of formation of the dimethylcyano radical.

The enthalpy of stabilization afforded to allyl by two cyano groups in the 1,3-dicyanoallyl radical has not been determined. The effect of a single cyano, however, has now been established. Using the device of thermal cis−trans isomerization about a double bond, the kinetics of the thermal approach to equilibrium of (E)- and (Z)-bi-3-cyanocyclohex-2-enylidenes has been pursued (Scheme 6). An unexceptional preparation leads to a mixture of (Z) and (E) isomers, the structures of which have been assigned by X-ray crystallography.[34] The ^{1}H NMR spectra of (**E**)-3 and (**Z**)-3, although almost identical in benzene-d_6, differ sufficiently in a mixture of benzene-d_6 and pyridine-d_5 (10:1) to allow distinction between the two isomers on the basis of the chemical shifts of their 2-vinyl hydrons (6.67 and 6.77 ppm), respectively. Both isomers have essentially coplanar triene

(27) (a) King, K. D.; Goddard, R. D. *Int. J. Chem. Kinet.* **1975**, *7*, 837−855. (b) King, K. D.; Goddard, R. D. *J. Phys. Chem.* **1978**, *82*, 1675−1679.

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(31) King, K. D.; Goddard, R. D. *J. Phys. Chem.* **1976**, *80*, 546−552.

(32) Similar recalculations of the heats of formation of H$_2$C(CN)$^{\bullet}$ [+55.6 kcal mol^{-1},[31] +57.8 kcal mol^{-1}][33] and CH$_3$CH(CN)$^{\bullet}$ [+49.5 kcal mol^{-1}][31] lead to stabilization energies of −15.0 and −12.7, and −11.8 kcal mol^{-1}, respectively. A value calculated for H$_2$C(CN)$^{\bullet}$ at the G2 level of theory is SE$_{CN/H}$ = −6.9 kcal mol^{-1}.[24]

(33) Trenwith, A. B. *J. Chem. Soc., Faraday Trans. 1* **1983**, *79*. 2755−2764.

(34) Wang, Y.-h.; Doering, W. v. E.; Staples, R. J. *J. Chem. Crystallogr.* **1999**, *29*, submitted.

Table 4. Specific Rate Constants and Derived Activation Parameters for the Reversible Rearrangement of (E)- and (Z)-3-Cyanocyclohex-2-enylidene, (**E**)-3 and (**Z**)-3, in Benzene-d_6

T, °C	$10^6 k_1$, s$^{-1\,a}$
154.0 ± 0.2^b	1.31 ± 0.01
154.0 ± 0.2^c	1.25 ± 0.03
165.2 ± 0.1^b	4.02 ± 0.08
165.2 ± 0.1^c	3.82 ± 0.06
186.1 ± 0.1^b	28.5 ± 0.4
186.1 ± 0.1^c	27.7 ± 0.5
193.9 ± 0.1^b	55.9 ± 0.9
193.9 ± 0.1^c	56.0 ± 0.3

Arrhenius Parameters
E_a = 37.57 ± 0.19 kcal mol^{-1}
log A = 13.33 ± 0.09

Eyring Parameters^d
$\Delta H^{\ddagger}$ = 36.7 ± 0.2 kcal mol^{-1}
$\Delta S^{\ddagger}$ = −0.4 ± 0.4 cal mol^{-1} K^{-1}

^{a} Calculated by linear regression of the standard expression for reversible first-order reactions: $(k_1 + k_{-1}) = \ln[(x_e - x_o)/(x_e - x_t)]/t$. ^{b} Starting with pure (**E**)-3. ^{c} Starting with pure (**Z**)-3. ^{d} Calculated at 174.0 °C.

systems and no apparent hydron−hydron separations within the sum of their van der Waals radii.

The results of the kinetic experiments are recorded in Table 4, the original experimental data being available in Table S3 of the Supporting Information. The enthalpy of activation, $\Delta H^{\ddagger}$ = 36.7 ± 0.2 kcal mol^{-1}, may be compared with values for three closely related trienes: cyclohex-2-enylidene, gas phase, 40.9 kcal mol^{-1};[35] solution, 38.9 kcal mol^{-1};[36] and a more extended example, 40.0 kcal mol^{-1}.[37] If a mean of 39.9 kcal mol^{-1} is taken as the unperturbed value, the two cyano groups have lowered the enthalpy of activation by −3.2 kcal mol^{-1}, or −1.6 kcal mol^{-1} per cyano group. By comparison, two phenyl groups (the cinnamyl radical) lower the enthalpy of activation by −5.0 kcal mol^{-1}, or −2.5 kcal mol^{-1} per phenyl group,[38,39] while two additional conjugated double bonds (the pentadienyl radical)[36,37,40] lower the enthalpy by −7.8 kcal mol^{-1}, or −3.9 kcal mol^{-1} per double bond. By rights, differences in conjugative interactions of a double bond with the groups, cyanovinyl, styryl, and butadienyl, should be taken into account, but at present that is not possible.

Cyano in a Chameleonic Cope Rearrangement

The chameleonic Cope has been defined in terms of a transition region having C_{2h} symmetry, that is, having two identical halves.[1] Although the effect of two cyano groups in active positions, as in 1,4-dicyanohexa-1,5-diene, has not been examined, the effect of two in the nodal position has been determined by Wehrli, Schmid, Belluš, and Hansen.[3] Their example, 2,5-dicyano-3-methylhexa-1,5-diene, is somewhat flawed by the use of methyl as the degeneracy-breaking element. They reported the activation parameters $\Delta H^{\ddagger}$ = 23.2 kcal mol^{-1} and $\Delta S^{\ddagger}$ = −14.2 cal mol^{-1} K^{-1}. The lowering in enthalpy of

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(40) Doering, W. v. E.; Birladeanu, L.; Cheng, X-h.; Kitagawa, T.; Sarma, K. *J. Am. Chem. Soc.* **1991**, *113*, 4558−4563.

activation vis-à-vis the archetype, hexa-1,5-diene ($\Delta H^\ddagger = 33.5$ kcal mol^{-1}; $\Delta S^\ddagger = -13.8$ cal mol^{-1} K^{-1}),[41] is impressively large. It has been reproduced almost exactly in very recent theoretical calculations by Beno, Hrovat, Lange, Yoo, Houk, and Borden ($\Delta H^\ddagger = 23.9$ kcal mol^{-1}).[5b] Are these experimental results consistent with the conjecture that the transition region has behaved *as if* it were approximated by a cyclohexa-1,4-diyl diradical?

The necessary correction for conjugative interaction in the educt can now be made on the basis of the van't Hoff studies reported above. If conjugation operating in an α-substituted acrylonitrile is taken to be -2.6 kcal mol^{-1}, the model for the educt is the archetype corrected by twice this amount: $33.5 + (2 \times 2.6) = 38.7$ kcal mol^{-1}. Recall, however, the reservation that -3.3 kcal mol^{-1} might be the preferred value for cyano regardless of the degree of alkyl substitution (40.1 kcal mol^{-1}). In neglect of an energetic disturbance by the methyl group, stabilization of the transition region thus amounts to -15.5 kcal mol^{-1}, or -7.8 kcal mol^{-1} per cyano group, a value only slightly less than the -8.7 kcal mol^{-1} per phenyl group deduced in similar manner from the rearrangement of 2,5-diphenylhexa-1,5-diene.[9,42]

Since the transition region seems to have been moved toward the cyclohexa-1,4-diyl extreme by the demands of the two perturbations in "nodal" positions, a more appropriate model for the unstabilized transition region might be the *diradical*, corrected similarly for conjugative interaction in the educt. Two estimates of the enthalpy of formation of a thermochemical model for the cyclohexa-1,5-diyl diradical have been made: one based on the nonconcerted cleavage of cyclobutane to two molecules of ethylene, the other by calculation of the cost of removing two hydrons from cyclohexane. Both agree on a value close to 43.3 kcal mol^{-1} above that of hexa-1,5-diene.[43,44] Vis-à-vis this model, corrected by 2×-2.6 kcal mol^{-1}, the estimated stabilization in the transition region is -25.3 kcal mol^{-1}, or -12.7 kcal mol^{-1} per cyano group. This value compares well with that of -12.9 kcal mol^{-1} estimated above as the stabilization enthalpy afforded a secondary alkyl radical by the replacement of hydron with cyano.

Centauric Cope Rearrangement

Thermochemical analysis of the effect of replacing the 5-hydron in 1,3-dicyanohexa-1,5-diene [**1(H)**] by a phenyl group at the C-5 nodal position [**1(Ph)**] proceeds stepwise. The empirical activation parameters for the transposition of deuterium in the Cope-incompetent hexa-2,5-dienes are given in Table 1 and Scheme 4. These are converted into activation parameters of the Cope-competent hexa-1,5-dienes by subtraction of the difference in enthalpies and entropies of formation of the two types. For both, the same mean correction is taken, $\Delta\Delta H^\circ = +2.7$ kcal mol^{-1} and $\Delta\Delta S^\circ = +1.6$ eu, as summarized above and in Scheme 4. The resulting parameters for the Cope rearrangements of **1(H)** (**J**) and **1(Ph)** (**K**) are given in Figure 2.

The enthalpy of activation, $\Delta H^\ddagger$, of **J** is lower than that of archetype **A** by -4.7 kcal mol^{-1}. This value is not far from
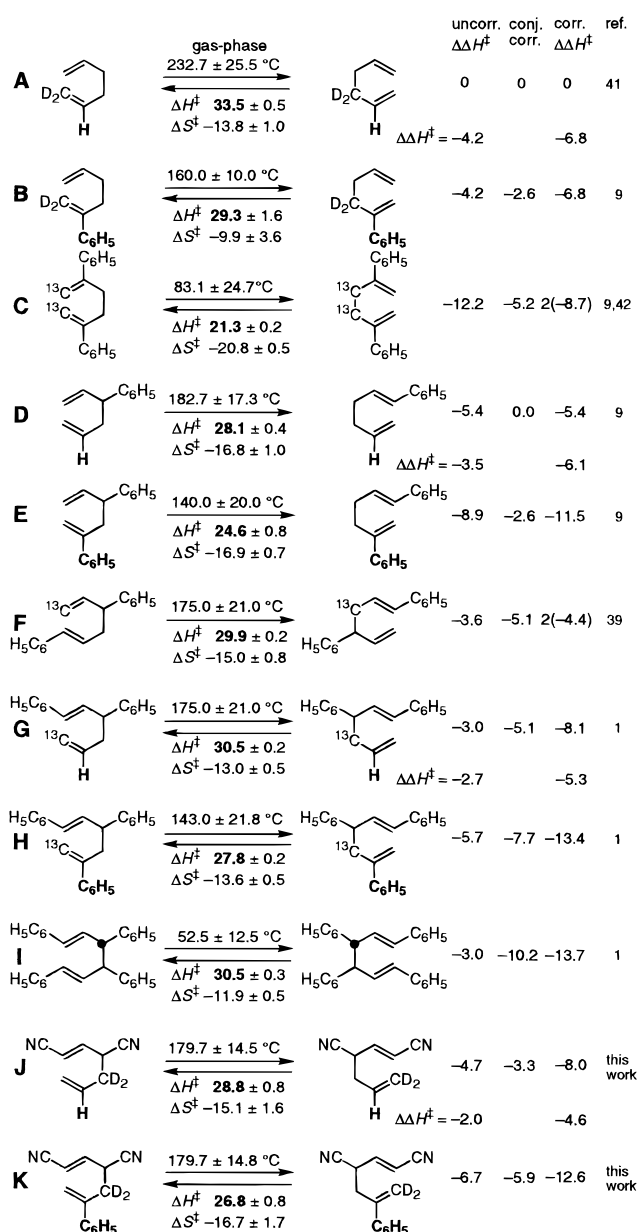
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(42) Roth, W. R.; Lennartz, H.-W.; Doering, W. v. E.; Birladeanu, L.; Guyton, C. A.; Kitagawa, T. *J. Am. Chem. Soc.* **1990**, *112*, 1722−1732.

(43) This value emerges from consideration of the ethene−cyclobutane system,[44] and application of the 1992 value for the heat of formation of the isopropyl radical.[30]

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Figure 2. Activation parameters for several Cope rearrangements: $\Delta H^\ddagger$ in kcal mol^{-1} and $\Delta S^\ddagger$ in cal mol^{-1} K^{-1}. Differences in enthalpies of activation relative to the archetype **A** are collected in column, "uncorr. $\Delta\Delta H^\ddagger$". Corrections for conjugative interaction in the educt are listed in "conj. corr", and applied to produce effective enthalpies of stabilization in the transition region as "corr. $\Delta\Delta H^\ddagger$". Four differences between pairs of allyl and 2-phenyl allyl types are interpolated.

that of -3.5 kcal mol^{-1} calculated by Beno et al.[5b] The comparable lowering in 1,3-diphenylhexa-1,5-diene, **G**, is -3.0 kcal mol^{-1}. Recall that the stabilization in an allyl radical provided by a *single* active cyano group is -1.6 kcal mol^{-1}, while that provided by a single phenyl is -2.5 kcal mol^{-1}.

The results of theoretical calculations are generally reported directly as $\Delta\Delta H^\ddagger$, the differences in calculated enthalpies of activation compared to that calculated for an unperturbed archetype, and are to be compared to the experimental values, "uncorr. $\Delta\Delta H^\ddagger$" of Figure 2, without correction for conjugative interaction. In the classical type of analysis undertaken here, the question is addressed directly, What effect have the perturbations had on the transition region? For this purpose, obligatory corrections are made for conjugative interaction in the educts. These are listed in the column "conj. corr." of Figure 2, and are added to "uncorr. $\Delta\Delta H^\ddagger$" to generate "corr. $\Delta\Delta H^\ddagger$",

which are the "experimental" enthalpies of stabilization produced in the transition region by the perturbation, relative to archetype **A** as model. For example, the corrections made for conjugative interactions in **1(Ph)** (**K**) are −3.3 and −2.6 kcal mol⁻¹ for cyano and phenyl, respectively, taken from Figure 1. The result, 39.4 kcal mol⁻¹, is the enthalpy of activation expected if the perturbations were to have affected only the educt. The difference between that value and the experimental value (26.8 kcal mol⁻¹) measures the stabilization afforded to the transition region (−12.6 kcal mol⁻¹). Note the obvious that stabilization enthalpies of **J** and **G** are substantially larger than they appear to be before correction for conjugative interaction in the educts.

A point of interest concerns the magnitude of the stabilization afforded by the replacement of allyl by 2-phenylallyl in the pairs, **A** and **B**, **D** and **E**, **G** and **H**, and **J** and **K**. These are shown in Figure 2 as interpolated values of $\Delta\Delta H^{\ddagger}$ in columns uncorr. $\Delta\Delta H^{\ddagger}$ and corr. $\Delta\Delta H^{\ddagger}$. Whether a trend is discernible as the demand for allylic character increases in the arranged order or whether one should be satisfied to accept the mean of the corrected values (−5.7 ± 1.0 kcal mol⁻¹) is moot. The nodal phenyl group in **K** has lowered the uncorrected enthalpy of activation, $\Delta H^{\ddagger}$, by −2.0 kcal mol⁻¹ vis-à-vis **J**. Although phenyl may contain too many carbon atoms to allow reasonably accurate calculations at the present time, the calculated lowering by a C-5 cyano group, as in 1,3,5-tricyanohexa-1,5-diene vis-à-vis 1,3-dicyanohexa-1,5-diene, is −0.6 kcal mol⁻¹.[5b] The lacuna is partly filled by calculations on vinylhexa-1,5-dienes, reasonable surrogates for the phenyl analogues. The calculated difference between 1,3,5-trivinyl- and 1,3-divinylhexa-1,5-diene[5b] is +0.5 kcal mol⁻¹. [Agreement between experiment and calculation is much improved by correcting for an estimated enthalpy of conjugation in the educt of −5.2 kcal mol⁻¹.]

In terms of the chameleonic model as defined, *either* the actively positioned 1,3-dicyano group *or* the nodally positioned phenyl group could be accommodated, but not both. The expected lowering would be either −8.0 kcal mol⁻¹ (**J**) or −6.8 kcal mol⁻¹ (**B**) [−8.7 kcal mol⁻¹ (**C**)], substantially less than the experimental value of −12.6 kcal mol⁻¹. Here, as in the all-phenyl case,[1] the chameleonic model leads to a serious underestimation.

In the centauric model, the 1,3-dicyanoallyl group (**J**), optimally served by C-1 and C-3 being sp² planar (−8.0 kcal mol⁻¹), and the phenyl group (**B**), optimally served by C-5 being sp² planar and C-4 and C-6 sp³ tetrahedral (−6.8 kcal mol⁻¹), might contribute a maximum stabilization energy of −14.8 kcal mol⁻¹ [−16.7 kcal mol⁻¹ (**C**)]. The experimental value of −12.6 kcal mol⁻¹ falls between but closer to the centauric model. Although the full stabilizing potential of each group operating independently seems not to have been expressed, the centauric is the preferred model, as it is in the example of 1,3,5-triphenylhexa-1,5-diene.[1]

Theory may provide a "calculational" answer to the possibly nonoperational, geometrical question whether the transition region retains a basic C_{2h} symmetry in the six-atom cycle of the chameleon type, but still allows sufficient, if partial, stabilization by conflicting substituents so that the sum exceeds that of either extreme working alone. One accepts that such questions based on current and past mechanistic concepts may become redundant in the coming world of calculational omnipotence. Meanwhile, the task of predicting the effects of perturbation by radical-stabilizing groups in Cope's rearrangement, and some other thermal rearrangements as well, may be served by a conceptual scheme combining conjugative interac-

tions in the educt, independently evaluated radical-stabilizing abilities of the individual perturbations, and an *incompletely* realized, centauric model of the transition region.

Experimental Section

General Procedures. ¹H NMR and ¹³C NMR (125.8 MHz) spectra are obtained in the noted solvents on a Bruker AM-500 instrument (500 MHz). Spin−lattice relaxation times (T_1) are determined by the inversion−recovery method with use of vacuum-sealed solutions in benzene-d_6. Chemical shifts are reported in ppm (δ) with respect to C_6D_5H; coupling constants, J, are reported in Hz. Analytical GC are effected on a Hewlett-Packard 5890A Gas Chromatograph with J & W Scientific column DB 225, 30 m × 0.5 m. Preparative GC is effected on a Varian Aerograph Model 90-P: column CW 20M with 20 psi He, flow-rate 6 L/h, detector 200 °C, injector 175 °C. High-resolution mass spectra (HR-MS) are measured on a JEOL AX 505 spectrometer equipped with a data-recovery system and reported as m/z (density as % of major peak). In both the kinetic and equilibrating experiments, the procedure is the same: to an NMR tube that has been oven- and vacuum-dried, evacuated for 10 min, and filled with argon, there are added the reactants. After three freeze−thaw cycles, the tube is sealed under vacuum and placed in the vapors of compounds of appropriate boiling point, boiling under reflux. Temperature is monitored periodically by a thermocouple, as is barometric pressure. The compounds employed are redistilled before use: 2-(2-methoxyethoxy)ethanol (194 °C), 4-*tert*-butyltoluene (191 °C), diethyl oxalate (185 °C), 4-methylanisole (176 °C), mesitylene (165 °C), cyclohexanol (160 °C), anisole (154 °C), cumene (152 °C), nonane (151 °C), *o*-xylene (144 °C), ethylbenzene (136 °C), 1,1,2,2-tetrachloroethane (121 °C), toluene (111 °C), dioxan (101 °C), propanol-1 (97 °C), 3-methylhexane (92 °C), benzene (80 °C), chloroform (61 °C), and methylene chloride (40 °C). The tubes are periodically withdrawn from the bath for analysis, immediately cooled in a dry ice/isopropyl alcohol bath, centrifuged, analyzed, and returned for heating until no further change in relative concentrations of isomeric nitriles is noted. Where analysis is by NMR, normal parameters are used with recovery and relaxation delay times as noted. Each signal is integrated three times. Details of unexceptional preparative procedures are reported in the Supporting Information.

1,3-Dicyanohexa-2,5-diene (1). In a 100-mL, round-bottomed flask, 0.36 g (0.012 mol) of sodium hydride (80% oil dispersion) was washed twice with pentane. Freshly distilled DMSO (30 mL) was added with stirring. The resulting suspension was stirred at room temperature for 10 min, then at 70 °C for 1 h, cooled, and treated dropwise with 1.13 g (0.012 mol) of 1,3-dicyanopropene[45] in 3 mL of DMSO. After 30 min, this solution was added dropwise to 1.04 mL (0.012 mol) of allyl bromide and 5 mL of DMSO in a 100-mL, round-bottomed flask. After 1 h, the reaction mixture was quenched by saturated aqueous NH_4Cl. Standard workup followed by preparative column chromatography (CHCl₃ as eluting solvent) gave 0.35 g (22%) of (**Z**)- and (**E**)-**1** (ratio 4:1). (**Z**)-**1**: ¹H NMR 6.16 (t, $J = 7.2$, 1H), 5.76 (m, 1H), 5.24 (dd, $J = 18.2, 17.0, 10.2$, 2H), 3.45 (d, $J = 7.2$, 2H), 3.03 (d, $J = 6.5$, 2H). (**E**)-**1**: ¹H NMR 6.37 (t, $J = 7.2$, 1H), 5.76 (m, 1H), 5.24 (dd, $J = 18.2, 17.0, 10.2$, 2H), 3.27 (d, $J = 7.1$, 2H), 3.03 (d, $J = 6.5$, 2H). MS (CI) 282 (2M + NH_4^+, 53), 150 (M + NH_4^+, 100).

1,3-Dicyano-*4,4-d₂*-hexa-2,5-diene (2,5(H)*d₂*). *1,1-D₂*-Allyl alcohol, prepared regiospecifically from acryloyl chloride by reduction with $LiAlD_4$,[46] was converted to *3,3-d₂*-3-tosyloxypropene according to the procedure for 3-tosyloxypropene:[47] ¹H NMR 7.8 (d, $J = 8.3$, 2H), 7.34 (d, $J = 8.3$, 2H), 5.81 (dd, $J = 17.2, 10.2$, 1H), 5.28 (dd, $J = 32.8, 17.2, 10.2$, 2H), 2.44 (s, 3H). Following the procedure above, 1,3-dicyanopropene and *3,3-d₂*-3-tosyloxypropene were converted in 33% yield of theory to a mixture consisting of (**Z**)-**2,5(H)*d₂*** and (**E**)-**2,5(H)*d₂*** (~94%, ratio 4:1) and 1,3-dicyano-*6,6-d₂*-hexa-2,5-diene (~6%). (**Z**)-1,3-Dicyano-*4,4-d₂*-hexa-2,5-diene: ¹H NMR 6.16 (t, $J = 7.2$, 1H), 5.76 (dd, $J = 17.0, 10.2$, 1H), 5.24 (dd, $J = 18.2, 17.0, 10.2$,

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2H), 3.45 (d, J = 7.2, 2H). (*E*)-1,3-Dicyano-*4,4-d₂*-hexa-2,5-diene: ¹H NMR 6.37 (t, J = 7.2, 1H), 5.76 (dd, J = 17.0, 10.2, 1H), 5.24 (dd, J = 18.2, 17.0, 10.2, 2H), 3.27 (d, J = 7.1, 2H).

1,3-Dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene (2,5(Ph)*d₂*). Following the procedure for the preparation of *1,1-d₂*-2-methylallyl alcohol, ethyl α-phenylacrylate,[48] prepared in two steps from ethyl phenylacetate, is reduced to *1,1-d₂*-2-phenylallyl alcohol: ¹H NMR 7.26 (d, J = 7.6, 2H), 7.17 (t, J = 7.4, 2H), 7.12 (t, J = 7.6, 1H), 5.23 (d, J = 63.6, 2H), 1.60 (s, 1H). Following the procedure above for *3,3-d₂*-3-tosyloxypropene, the corresponding tosylate, 2-phenyl-*3,3-d₂*-3-tosyl-oxypropene, was prepared: ¹H NMR 7.73 (d, J = 8.3, 2H), 7.28 (d, J = 8.1, 2H), 7.25 (m, 5H), 5.43 (d, J = 95.9, 2H), 2.42 (s, 3H). Reaction with 1,3-dicyanopropene in the procedure developed above for 1,3-dicyano-*4,4-d₂*-hexa-2,5-diene afforded, in 36% of theory, a mixture consisting of ~95% of (**Z**)- and (**E**)-**2,5(Ph)*d₂*** (ratio 4:1) and ~5% of 1,3-dicyano-*6,6-d₂*-5-phenylhexa-2,5-diene. (*Z*)-1,3-Dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene: ¹H NMR 7.38−7.30 (m, 5H), 6.14 (t, J = 7.1, 1H), 5.41 (d, J = 170.2, 2H), 3.39 (d, J = 7.1, 2H). (*E*)-1,3-Dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene: ¹H NMR 7.38−7.30 (m, 5H), 6.14 (t, J = 7.2, 1H), 5.37 (d, J = 140.4, 2H), 3.20 (d, J = 7.2, 2H).

Kinetics of Rearrangement of 1,3-Dicyano-*4,4-d₂*-hexa-2,5-diene (2,5(H)*d₂*) and 1,3-Dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene (2,5-(Ph)*d₂*). A solution of **2,5(H)*d₂*** (0.09 M) in 0.5 mL of degassed isopropyl alcohol-*d₈* in a vacuum-sealed NMR tube with 18-crown-6 ether as an internal standard was heated (165−194 °C). Quantitative analysis by ¹H NMR (500 Hz) measured relative concentrations of methylene hydrons of product at C-4 and vinyl hydrons of both starting material and product at C-2. Recovery was monitored by comparing the amount of vinyl hydron at C-2 with that of the hydron of 18-crown-6 ether. Each datum was generated from at least three integrations of the NMR signals accumulated over eight scans. An acquisition time of 2.77 s and relaxation delay time of 150 s were employed. The data and details of calculation for rate constants and kinetic parameters are given in Table S1 of the Supporting Information. Results are summarized in Table 1.

Kinetic experiments with 1,3-dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene paralleled those above with 1,3-dicyano-*4,4-d₂*-hexa-2,5-diene, but for the use of isopropyl alcohol-*d₈* containing 10% of pyridine-*d₅* as solvent. Quantitative analysis was based on methylene hydrons of product at C-4, vinyl-hydrons of starting material at C-6, and the vinyl hydron of both starting material and product at C-2. An acquisition time of 2.77 s and a relaxation delay time of 83 s were employed. Eight scans were accumulated for each measurement. Data and details of calculation are given in Table S2 of the Supporting Information. Results are collected in Table 2.

The kinetics of rearrangement of a mixture of equal amounts of 1,3-dicyano-*4,4-d₂*-hexa-2,5-diene and 1,3-dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene were determined in isopropyl alcohol-*d₈* containing 10% of pyridine-*d₅* at 165 and 194 °C. The results are summarized in Table 3.

Thermal Equilibrations of (*E*)- and (*Z*)-3,3′-Dicyanocyclohex-2-enylidene, (*E*)-3 and (*Z*)-3. Studies of the kinetics were effected in degassed solutions of benzene-*d₆*/pyridine-*d₅* (10:1) in vacuum-sealed NMR tubes with samples of either pure (*E*)-3 or (*Z*)-3 as starting material in a concentration of 0.076 M. The course of thermal equilibration was followed by ¹H NMR at four temperatures, 154.0 (anisole), 165.2 (mesitylene), 186.1 (diethyl oxalate), and 193.9 °C (2-(2-methoxyethoxy)ethanol), using the ratio of integrated areas of the 2-vinyl hydrons of (*E*)-3 at 6.67 ppm and (*Z*)-3 at 6.77 ppm. Acquisition times of 2.77 s and relaxation delay times of 8 s were employed. A total of 32 scans was accumulated for each measurement. Each datum was generated from at least three integrations of the NMR signals. The data from the eight runs are given in Table S3 of the Supporting Information. Specific rate constants, derived according to the general expression for a reversible, first-order reaction, and Arrhenius, and Eyring activation parameters are reported in Table 3.

Equilibration among Pentenenitriles (Series 1, Scheme 5). Following the preliminary procedure developed by Benkhoff,[49] (*Z*)-pent-2-enenitrile [**1Δ²(Z)**] or (*E*)-pent-2-enenitrile [**1Δ²(E)**] (DuPont de

Nemours & Co.) was equilibrated using 3 µL (0.024 mmol) of diazobicyclononene (DBN) as catalyst. A relaxation delay time of 175 s was employed in analysis. The data from three sets of experiments are collected in Table S4 of the Supporting Information, and combined for calculation.

2-Methylpentenenitriles (Series 2, Scheme 5). To 5−10 mg of hydridonitrosyl tris(triphenylphosphine) ruthenium (preparation in the Supporting Information) in an NMR tube was added a solution of 0.6 mmol of benzene-*d₆* and 5−8% percent of 2-methylpentenenitrile(s) with a syringe. The reaction was monitored by ¹H NMR until there was no further change with time. The contents of the tube were then transferred by trap-to-trap distillation under vacuum to give a clear distillate, which was analyzed directly by GC. To ensure the establishment of true equilibrium, the distillate was returned to another NMR tube, fresh catalyst was added, and the procedure above was repeated. Generally, one refreshment of catalyst sufficed to establish equilibrium. At a given temperature, usually two independent runs on different samples were made. All but two of the six isomers of 2-methylpentenenitrile can be resolved quantitatively by analytical GC. Retention times (min) of all six isomers at 70 °C follow: **2Δ¹**, 4.6; **2Δ²(Z)**, 5.1; **2Δ³(E)**, 7.2; **2Δ³(Z)**, 7.4; **2Δ⁴**, 7.4; **2Δ²(E)**, 9.5. Since the amounts of **2Δ³(Z)** and **2Δ⁴** at equilibrium are very small (<1%), and could not be resolved satisfactorily, only **2Δ²(Z)**, **2Δ²(E)**, **2Δ³(E)**, and **2Δ¹** were analyzed quantitatively. The response factors of these four isomers are very nearly identical, so the relative percent of each isomer among all four isomers is calculated without correction. Generally, measurements of each sample were repeated five times, the average value being used in the calculations. The experimental data are found in Table S5.

2,4-Dimethylpentenenitriles (Series 3, Scheme 5). A sample of *t*-BuOK, freshly sublimed in a vacuum and stored in a desiccator, was transferred under nitrogen in an air box to a preweighed, flame-dried flask flushed with argon. In proportion to the amount of *t*-BuOK transferred, a volume of freshly distilled benzene-*d₆* was added via syringe calculated to make a 0.16 M solution. Further dilution of 0.5 mL of this solution by 2.5 mL of freshly distilled benzene-*d₆* afforded a 0.0032 M solution of *t*-BuOK, 0.6 mL of which was then transferred into a vacuum-dried, argon-flushed NMR tube. Following addition of 10 µL of **3Δ²(Z)** (7.3 mg, 0.66 mmol) (or **3Δ²(E)**, or a mixture of the two) and 20 µL (0.095 M, 0.0019 mmol) of 18-crown-6 ether, the initially colorless solution slowly became brown. For details of the analysis by NMR and experimental data, see Table S6 of the Supporting Information.

Equilibration of 1,3-Dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene and 1,3-Dicyano-*4,4-d₂*-5-phenylhexa-1,5-diene. Temperature dependence of equilibria among 1,3-dicyano-*4,4-d₂*-5-phenylhexa-2,5-dienes and -hexa-1,5-dienes was determined directly in the NMR spectrometer in 0.5 mL of 10% pyridine-*d₅* in isopropyl alcohol-*d₈* at four temperatures: 24, 44, 64, and 84 ± 1 °C. The ratio of vinyl hydron at C-2 in 1,3-dicyano-*4,4-d₂*-5-phenylhexa-2,5-diene and 1,3-dicyano-*4,4-d₂*-5-phenyl-1,5-hexadiene was measured, the results being summarized in Table 3.

Supporting Information Available: Two sets of three tables each giving details of the kinetic data and the experimental data of the van't Hoff equilibrations and a second Experimental Section providing detailed descriptions of the preparation of materials (PDF). This material is available free of charge via the Internet at http://www.pubs.acs.org.

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