

Rates of Enantiomerization of *trans*-1,2-Disubstituted Cyclopropanes correlate with Substituent Radical Stabilization Energies

John E. Baldwin

Department of Chemistry, Syracuse University, Syracuse, New York 13244, U.S.A.

Experimental ΔG^\ddagger (enantiomerization) values for *trans*-1,2-disubstituted cyclopropanes correlate in strict linearity with the sum of substituent radical stabilization energy terms; the two ends of the 1,3-disubstituted trimethylene diradicals implicated in these thermal enantiomerization reactions appear to be thermochemically independent.

Radical stabilizing substituents on a cyclopropane should facilitate reactions proceeding by way of 1,3-diradical transient intermediate or transition state structures.¹ This insight has been generally accepted as a qualitative proposition for years,² yet general quantitative correlations based on this view have not been developed. Uncertainties in radical stabilization energy terms plus a lack of consensus as to which specific reactions might afford a valid basis for quantitative correlations remained unresolved impediments.

However, the enantiomerization reactions shown by *trans*-

1,2-disubstituted cyclopropanes provide a thoroughly suitable test case for attempting a general quantitative correlation, because there are no ΔG° terms which might complicate interpretations of measured ΔG^\ddagger values, no ambiguities from one-centre epimerizations leading to *cis*-isomers (rate constants k_1 or k_2) obtrude, and there are adequate data from different laboratories to afford a meaningful response to the question: does ΔG^\ddagger (enantiomerization) correlate with the sum of radical stabilization energy terms for R¹ and R², thus implicating a diradical in which the two ends are thermochem-

Table 1. ΔG^\ddagger (enantiomerization) for *trans*-1,2-disubstituted cyclopropanes (1) and substituent stabilization energies for 1,3-disubstituted trimethylene diradicals (2).

Cyclopropane (1)		Ref.	$k_{1,2}/$ ($\times 10^{-5} \text{ s}^{-1}$)	$T/^\circ\text{C}$	$\Delta G^\ddagger/$ (kcal/mol)	Trimethylene (2)	ΔG^\ddagger (calc.) ^b (kcal/mol)
R ¹	R ²					SE ^a	
D	D	3	1.48	422.5	57.2	0	57.3
Me	Et	4	3.28	408.0	54.9	3.0	55.2
CN	Me	5	0.88	335.4	50.5	10.1	50.3
Ph	D	6	0.20	309.3	50.0	11.8	49.1
Me	CH ₂ =CH	7	0.82	268.5	44.9	17.4	45.2
Me	<i>trans</i> -MeCH=CH	8	7.25	296.5	44.8	17.4	45.2
CN	Ph	9	0.60	242.1	43.0	20.4	43.2
CN	Ph	10	0.08	217.8	42.9	20.4	43.2
Ph	Ph	11	0.42	220.7	41.5	23.6	41.0
CN	CH ₂ =CMe	12	0.70	217.8	40.8	24.5	40.3
CN	<i>trans</i> -MeCH=CH	13	0.98	207.1	39.6	24.5	40.3
Ph	CH ₂ =CMe	10	0.07	169.5	38.7	27.7	38.1
CH ₂ =CH	CH ₂ =CH	14	2.26	160.0	34.9	31.8	35.3

^a SE(R¹CH₂·) + SE(R²CH₂·), where SE(RCH₂·) for R = D, alkyl, CN, Ph, alkenyl are 0, 1.5, 8.6, 11.8, and 15.9 kcal/mol respectively. ^b From ΔG^\ddagger (calc.) = 57.3 - 0.692 [SE(R¹CH₂·) + SE(R²CH₂·)].

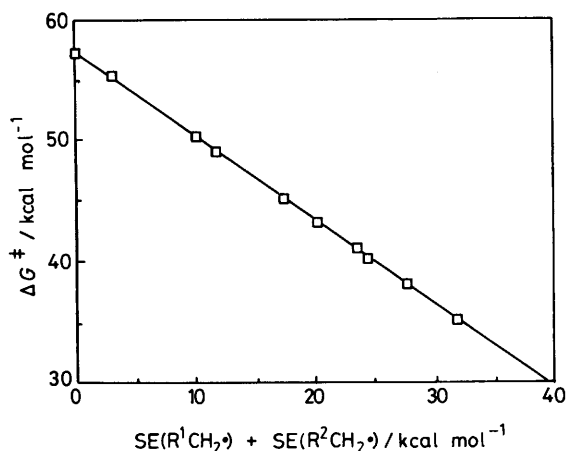
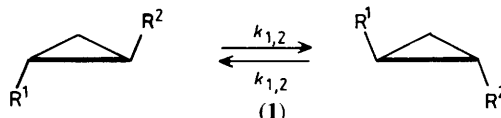
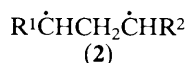


Figure 1. Linear correlation between ΔG^\ddagger (enantiomerization) for *trans*-1,2-disubstituted cyclopropanes (1) and calculated stabilization energies for 1,3-disubstituted trimethylene diradicals (2).



ically independent, or is the free-energy lowering impact of the two substituents ever different from that predicted by a simple arithmetic sum model?

For thirteen instances of this reaction type, kinetic studies³⁻¹⁴ provide values of $k_{1,2}$ at given temperatures, which may be recast as ΔG^\ddagger values (Table 1). A single source¹⁵ provided initial values of stabilization energies (SE's) for the 1,3-disubstituted trimethylene diradicals (2), approximated as $SE(R^1CH_2\cdot) + SE(R^2CH_2\cdot)$.



The correlation of ΔG^\ddagger values with this measure of substituent-induced stabilization in (2) gave a fair straight-line plot, with slope -0.700 and $r = 0.986$ (Figure 1). Departures from the linear correlation were small but consistent: phenyl-substituted systems fell above the line, and alkenyl-substituted cases below. Empirical adjustments of $1 \text{ kcal/mol}^\ddagger$ from Leroy's stabilization energies¹⁵ for $PhCH_2\cdot$ and $CH_2=CH\cdot$ improved the linear correlation ($r = 0.997$) with little change in slope (-0.692). For this correlation, using 1.5, 8.6, 11.8, and 15.9 kcal/mol as stabilization energies for $R^1 =$ alkyl, cyano, phenyl and alkenyl respectively, relative to hydrogen,¹⁶ the average discrepancy between observed and calculated ΔG^\ddagger values was $0 \pm 0.5 \text{ kcal/mol}$, with the maximum deviation being 0.9 kcal/mol (Table 1). Either empirical correlation works extremely well, over a range of experimental ΔG^\ddagger values of 22.3 kcal/mol : there is no break in linearity, thus supporting the view that the two ends of the trimethylene diradical, whatever the substituents R^1 and R^2 , are thermochemically independent.

For all of the substituted cyclopropanes in Table 1, save for the parent hydrocarbon, $(k_1 + k_2) > k_{1,2}$, a generality consistent with these one-centre and two-centre stereomutation reactions proceeding by way of trimethylene diradicals with termini free to rotate independently, as in the tetramethylene diradical.¹⁷ Only 1,2-dideuteriocyclopropane shows the diametrically opposite relationship, $(k_1 + k_2) \ll k_{1,2}$, an experimental finding consistent with synchronous

rotation of the two ends of the trimethylene system without appreciable competitive one-centre epimerization.³ Further work is required before this fascinating change in kinetic and stereochemical behaviour is understood.

For $k_{1,2}$ rate constants of *trans*-1,2-disubstituted cyclopropanes, however, the pattern is already abundantly clear: ΔG^\ddagger correlates linearly with consistent parametric measures of substituent-induced stabilization of the trimethylene diradical, and *trans*-1,2-dideuteriocyclopropane is not *sui generis*.

Partial support for our studies from the National Science Foundation is gratefully acknowledged.

Received, 10th August 1987; Com. 1173

References

- 1 L. B. Rodewald and C. H. Depuy, *Tetrahedron Lett.*, 1964, 2951.
- 2 J. A. Berson, *Annu. Rev. Phys. Chem.*, 1977, **28**, 111; C. F. Wilcox, Jr., and B. K. Carpenter, *J. Am. Chem. Soc.*, 1979, **101**, 3897; J. A. Berson, 'Rearrangements in Ground and Excited States, vol. 1,' ed. P. de Mayo, Academic Press, New York, 1980, p. 311; J. J. Gajewski, 'Hydrocarbon Thermal Isomerizations,' Academic Press, New York, 1981, p. 27; W. von E. Doering, Peter A. Leermakers Symposium Lecture, Wesleyan University, 1981, A.C.S. Science Symposium Series; W. T. Borden, 'Reactive Intermediates,' eds. M. Jones and R. A. Moss, Wiley, New York, 1981, vol. II, p. 176; P. B. Dervan and D. A. Dougherty, in 'Diradicals,' ed. W. T. Borden, Academic Press, New York, 1982, p. 107; E. Schaumann and R. Ketcham, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 225.
- 3 J. A. Berson and L. D. Pedersen, *J. Am. Chem. Soc.*, 1975, **97**, 238; J. A. Berson, L. D. Pedersen, and B. K. Carpenter, *ibid.*, 1976, **98**, 122; rate constant $k_{1,2}$ calculated from reported k_α and k_β values, assuming $k_{1,2} = k_{1,3}$.
- 4 W. L. Carter and R. G. Bergman, *J. Am. Chem. Soc.*, 1968, **90**, 7344; R. G. Bergman and W. L. Carter, *ibid.*, 1969, **91**, 7411; W. von E. Doering and K. Sachdev, *ibid.*, 1974, **96**, 1168.
- 5 J. E. Baldwin and C. G. Carter, *J. Am. Chem. Soc.*, 1982, **104**, 1362.
- 6 J. E. Baldwin, T. W. Patapoff, and T. C. Barden, *J. Am. Chem. Soc.*, 1984, **106**, 1421; J. E. Baldwin and T. C. Barden, *ibid.*, 1984, **106**, 5312, 6364.
- 7 W. R. Roth and T. Schmidt, unpublished results; T. Schmidt, Ph.D. Dissertation, University of the Ruhr, Bochum, 1972; J. Ellis and H. M. Frey, *J. Chem. Soc.*, 1964, 5578.
- 8 G. D. Andrews and J. E. Baldwin, *J. Am. Chem. Soc.*, 1976, **98**, 6705.
- 9 J. E. Baldwin and C. G. Carter, *J. Am. Chem. Soc.*, 1978, **100**, 3942; *J. Org. Chem.*, 1983, **48**, 3912.
- 10 W. von E. Doering and E. A. Barsa, *Tetrahedron Lett.*, 1978, 2495.
- 11 R. J. Crawford and T. R. Lynch, *Can. J. Chem.*, 1968, **46**, 1457.
- 12 W. von E. Doering and K. Sachdev, *J. Am. Chem. Soc.*, 1975, **97**, 5512.
- 13 E. A. Barsa, Ph.D. Dissertation, Harvard University, 1977.
- 14 M. Arai and R. J. Crawford, *Can. J. Chem.*, 1972, **50**, 2158.
- 15 G. Leroy, *Adv. Quantum Chem.*, 1985, **17**, 1.
- 16 These stabilization energy terms are consistent with delocalization energy and resonance energy estimations for the substituents derived and used by others: cf. W. von E. Doering and G. H. Beasley, *Tetrahedron*, 1973, **29**, 2231; R. Wehrli, D. Bellus, H. J. Hansen, and H. Schmid, *Chimia*, 1976, **30**, 416; W. von E. Doering, G. Horowitz, and K. Sachdev, *Tetrahedron*, 1977, **33**, 273; J. J. Gajewski, *J. Am. Chem. Soc.*, 1979, **101**, 4393; R. Merényi, Z. Janousek, and H. G. Viehe, in 'Substituent Effects in Radical Chemistry,' eds. H. G. Viehe, Z. Janousek, and R. Merényi, Reidel, Dordrecht, Holland, 1986, p. 301.
- 17 J. S. Chickos, *J. Org. Chem.*, 1979, **44**, 780; P. B. Dervan and D. S. Santilli, *J. Am. Chem. Soc.*, 1980, **102**, 3863; A. Annamalai, T. A. Keiderling, and J. S. Chickos, *ibid.*, 1984, **106**, 6254; J. S. Chickos, A. Annamalai, and T. A. Keiderling, *ibid.*, 1986, **108**, 4398; M. Cannarsa, Ph.D. Dissertation, Cornell University, 1984; M. J. Goldstein, Lecture, 8th IUPAC Conference on Physical Organic Chemistry, Tokyo, Japan, August 1986.

[†] 1 cal = 4.184 J.