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ADDITIVITY OF INTERNAL ROTATIONAL PROPENSITY IN THE THERMAL *cis-trans* ISOMERIZATION OF CYCLOPROPANES[1]

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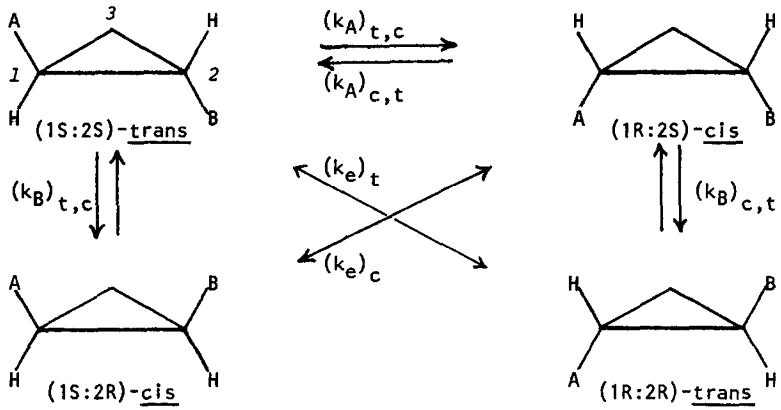
Rotational propensity of substituents has been identified by Doering and Sachdev as a thermodynamically rigorous function for the description of single rotations in reactions of the ring-opening - ring-closing type.[2] The general question follows naturally whether partial rotational propensities might be transferable from one pairing to another. In this paper, the specific question is addressed whether, from the known R_A value of cyano and isopropenyl in cyclopropane[2] and an R_A value for cyano and phenyl, a useful prediction of the R_A value for isopropenyl and phenyl could be expected; that is, if $(R_A)^{CN}_{i-Pr} = k_{CN}/k_{i-Pr}$ and $(R_A)^{CN}_{Ph} = k_{CN}/k_{Ph}$ were known, would their ratio, $[(R_A)^{CN}_{Ph}/(R_A)^{CN}_{i-Pr}]$, be equal to $(R_A)^{i-Pr}_{Ph}$?

For such an approach to be valid, the observed processes must in fact be of the single internally rotational type and not of a double internally rotational type hidden from view by lack of labelling on the methylene group (see, for example, C_3 in the general formulation in the scheme). Since the experimental activation energies for the putatively single rotational processes are satisfactorily predicted by addition of the individual radical-stabilizing capabilities of the substituents on the atoms of the carbon-carbon bond assumed to be involved and are essentially identical to the activation energies of the unambiguously double rotational processes, there is no thermochemically reasonable ground for doubting that the most highly substituted bond is the one actually broken in both processes. Notwithstanding the strength of the thermochemical arguments, Berson and coworkers[3,4] have repeatedly impugned the validity of what they call "the most substituted bond assumption." Since it is an easy matter conceptually, if not experimentally, to test the proposition, Baldwin and Carter[5] and we[6] have provided independent, unambigous confutations. The example of Baldwin and Carter is the better designed as a response specifically to Berson *et al.*, since it offers as the potential partner in a "crypto" double rotation the same deuterium-labelled methylene group which Berson *et al.* had employed so brilliantly. Between the two examples, these doubts are now well buried. Profoundly interesting questions about the origin of the findings of Berson *et al.* remain.

Optically active *trans*-1-cyano-2-phenylcyclopropane (*trans*-II)[4,5] is prepared from racemic *trans*-2-phenylcyclopropane carboxylic acid (Aldrich Chemical Co.) by resolution according to the unpublished procedure of W. Rastetter,[7] and converted to the nitrile[1] (for details, see Barsa).[6] A sample (300 mg) of (1S:2S) (+)-*trans*-II [mp 79-80°; $[\alpha]^{25}_D$ +337.5° (*c* 0.2400, EtOH)] is transformed reversibly without loss of optical activity into (1R:2S) (-)-*cis*-II [mp 59-60°; $[\alpha]^{25}_D$ -21.8° (*c* 0.3584, EtOH)] by treatment with 50 mg $NaOCH_3$ in 2 ml DMSO at 25° for 4 min (separation



$$K_e = [t_e]/[c_e] = (k_A)_{c,t}/(k_A)_{t,c} = (k_B)_{c,t}/(k_B)_{t,c}$$

$$(R_A)^A_B = (k_A)_{t,c}/(k_B)_{t,c} = (k_A)_{c,t}/(k_B)_{c,t}$$

I: A = —CN, B = $\mathrm{CH_3\underset{|}{C}{=}CH_2}$

II: A = —CN, B = $\mathrm{-C_6H_5}$

III: A = $\mathrm{CH_3\underset{|}{C}{=}CH_2}$, B = $\mathrm{-C_6H_5}$

IV: A = —CN, B = $\mathrm{-C{\equiv}C{-}C_6H_5}$

	I[a,b]	II[b]	II[c]	III[d]	IV[e]
$(R_A)^A_B$	2.20	2.47	2.30	1.26	1.76
K_e	2.67	2.79	2.50	10.11	1.66
$(k_A)_{t,c}$	69.5	9.47	76.0	8.00	28.5
$(k_B)_{t,c}$	31.6	3.84	33.0	6.33	16.2
$(k_A)_{c,t}$	185.8	26.4	(190.0)	80.9	47.2
$(k_B)_{c,t}$	84.5	10.7	(82.5)	64.0	26.8
$(k_e)_t$	22.3	8.1	60.0	6.8	21.8
$(k_e)_c$	29.2	7.4	43.0	26.2	29.2

[a] All k in units of 10^{-7} sec^{-1}. [b] At 217.8°C in the gas phase. [c] At 242.1°C. Rate constants in parentheses are the product of K_e and $(k_A)_{t,c}$ and $(k_B)_{t,c}$.[5] [d] At 169.5°C in the gas phase (ampoules of lead-potash glass). [e] In *trans*-decalin solution (2%) at 190.7°C.

and analysis by glc: 5 ft x 3/8 in. 5% Carbowax 20M, Anakrom ABS 50/60; rel. ret. time at 145°: *trans*-II, 1.00; *cis*-II, 1.33).

The kinetics of rearrangement of *cis*- and *trans*-II are studied at 217.8° following the same procedure employed by Sachdev on *cis*- and *trans*-I.[2a] Recovery is greater than 98%. To achieve greater accuracy in measuring the optical purity of *cis*-II, it is isomerized to *trans*-II, which has a specific rotation approximately 15X greater than that of *cis*-II.

Optically active *cis*- and *trans*-1-isopropenyl-2-phenylcyclopropane (*cis*-III and *trans*-III) are prepared simultaneously from an equilibrated mixture of optically active *trans*-II, $[\alpha]_{\mathrm{D}}^{25}$ +331.8° (*c* 0.8565, EtOH), and *cis*-II by treatment with methyllithium. The derived mixture of 1-acetyl-2-phenylcyclopropanes is converted to *trans*-III, $[\alpha]_{365}^{26}$ +1036° (*c* 0.9602, cyclohexane), and *cis*-III, $[\alpha]_{365}^{26}$ -580.1° (*c* 1.0321, cyclohexane), by the Wittig reaction and separation by glc. That there is no loss of optical activity during the entire sequence is established by the oxidation of (+)-*trans*-III, first, with $NaIO_4$ and a trace of $KMnO_4$ to (+)-*trans*-1-acetyl-2-phenylcyclopropane, $[\alpha]_{365}^{26}$ +2717° (*c* 1.0399, cyclohexane) and, second, with NaOBr to (+)-*trans*-2-phenylcyclopropane-1-carboxylic acid, $[\alpha]_{\mathrm{D}}^{25}$ +308.0° (*c* 0.8025, EtOH); reported $[\alpha]_{\mathrm{D}}^{25}$ +314.0°.[7]

The rates of the thermal internal rotations are determined at 169.0°C with the results shown in the scheme. The experimental value of $(R_A)_{Ph}^{i\text{-}Pr}$ (1.26) agrees within 11% with the predicted value, 1.12. How "good" that agreement is thought to be depends on criteria which have not as yet been defined. It may be noted that Baldwin and Carter[5] obtain a value of $(R_A)_{Ph}^{CN}$ = 2.30 at 242.1°C. Were the same trend to a lower value of R_A with increasing temperature be manifested by III, the value of $(R_A)_{Ph}^{i\text{-}Pr}$ expected at 217.8° would be smaller than that found at 169.0°C and agreement would be correspondingly improved.

Like others, we have considered moment of inertia as a plausible factor in determining internally rotational propensities and have therefore compared II with 1-cyano-2-(phenylethynyl)-cyclopropane (*cis*- and *trans*-IV), in which the phenylethynyl group is both heavier and longer by approximately 2.77 Å than the phenyl group in II.

Prepared by the procedure of Yoshimoto, Ishida and Kishida,[8] *trans*-2-(phenylethynyl)cyclopropane carboxylic acid of unknown optical purity is obtained by resolution with ℓ-ephedrine and then converted to the nitrile, (-)-*trans*-1-cyano-2-(phenylethynyl)cyclopropane [(-)-*trans*-IV, $[\alpha]_{365}^{24}$ -1517° (*c* 0.4036, EtOH)], by the usual sequence.[2a] Although base-catalyzed equilibration with *cis*-IV requires care in order to avoid racemization, (-)-*cis*-IV can be shown to have $[\alpha]_{365}^{24}$ -291° (*c* 0.6708, EtOH). From the kinetic results in the scheme, $(R_A)_{PhC_2}^{CN}$ is found to be 1.76 at 190.7°C.[9] This value being lower than $(R_A)_{Ph}^{CN}$, one is discouraged from pursuing moment of inertia as a major factor, and may speculate instead on the importance of steric "width" of the substituent.

Parenthetically, $\Delta\Delta G^{\neq}$ between C_6H_5 and $C_6H_5{-}C{\equiv}C{-}$ is 3.5 kcal/mol in favor of the latter (for *trans*-IV → *cis*-IV at 190.7°, $k = 4.47 \times 10^{-6}$ sec^{-1}; while, for *trans*-II → *cis*-II, at 217.8°, $k = 1.33 \times 10^{-6}$ sec^{-1}). It is also noted that, for *trans*-II → *cis*-II, $\log k = 13.50 - 43{,}500/\theta$ (estimated[10,11] $\Delta H^{\neq} = 63.7 - 13.5 - 8.0 = 42.2$ kcal/mol). This agreement provides another example of the principle of additivity of substituent effects as a quantitative method for estimating the activation energies of not-obviously-concerted thermal rearrangements.

While the internal consistency among rotational propensities revealed by this investigation lends support to the validity of the concept as a fundamental way of describing the rotational components of transition states in reversible reactions, it offers no insight into the origin of rotational propensities or their magnitude. It is particularly impressive that internal consistency is maintained despite the fact that *trans*-III reacts 136X faster at 169.9°C than *trans*-II. This ratio corresponds to $\Delta\Delta G^{\neq} = 4.32$ kcal/mol, a value in good agreement with the difference between the currently best values for the radical-stabilizing capabilities of cyano and vinyl.[12] In terms of the popular "diradical" intermediate, one might have expected the more strongly stabilized "diradical" from III to have exhibited an R_A value closer to 1.00 than that predicted on the basis of two less highly stabilized "diradicals" from I and II, respectively.

References and Notes

(1) The Continuous Diradical as Transition State. III.[2]

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(8) Yoshimoto, M.; Ishida, N.; Kishida, Y. *Chem. Pharm. Bull. (Tokyo)*, 1972, 20, 2593-2602.

(9) Although it had been preferable if IV and II were compared both in the gas-phase, or both in decalin solution, it may be noted that the change from gas-phase to benzene solution exercises no effect on R_A for 1-cyano-2-isopropenylcyclopropane.[2a]

(10) Doering, W. von E.; Horowitz, G.; Sachdev, K. *Tetrahedron*, 1977, 33, 273-283.

(11) We apologize for having failed to cite the contribution of Belluš and Rist on the radical-stabilizing effect of the cyano group: Belluš, D.; Rist, G. *Helv. Chim. Acta*, 1974, 57, 194-196.

(12) Doering, W. von E.; Beasley, G. H. *Tetrahedron*, 1973, 29, 2231-2243.

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