Table I. Rates of Exchange and Isotope Effects in the Reaction of 4-(Nitrophenyl)nitromethane with Bases in Toluene Solution at 25 °C

base	k_T, M^{-1} s^{-1} observed	k_T, M^{-1} s^{-1} estimated[a]	k_H/k_T	$(k_H/k_T)^{1/1.442}$	k_H/k_D
tetramethylguanidine	25.0 ± 0.6	4.75 ± 0.34	45.8 ± 1.1	14.2 ± 0.2	45 ± 2[b]
quinuclidine	63.8 ± 1.5	21.8 ± 0.9	17.2 ± 0.4	7.20 ± 0.12	15.6 ± 0.6[c]
triethylamine	2.71 ± 0.04	2.08 ± 0.13	24.3 ± 0.5	9.14 ± 0.13	11.0 ± 0.7[c]
tri-*n*-butylamine	0.675 ± 0.008	0.480 ± 0.032	31.7 ± 0.5	11.0 ± 0.1	14 ± 1[c]
diethyl-*n*-butylamidine	12.6 ± 0.2	9.93 ± 0.81	27.1 ± 1.4	9.84 ± 0.36	11.7 ± 1.0[d]
diethyl-*n*-nonylamidine	34.9 ± 0.1	19.6 ± 1.2	11.4 ± 0.6	5.39 ± 0.19	8.0 ± 0.3[d]
pentamethylguanidine	499 ± 5	518 ± 13	44.1 ± 1.1	13.8 ± 0.2	13.7 ± 0.4[e]

[a] Estimated by using $k_T = k_H/2(k_H/k_D)^{1.442}$ and published[1,10] values of k_H and k_H/k_D. [b] Reference 1b. [c] Reference 1c. [d] Reference 10a. [e] Reference 10b.

It was recently pointed out, however, that these large isotope effects could be experimental artifacts if isotopic exchange, and consequent loss of deuterium from the deuterated substrate, occurred under the ionization-reaction conditions.[3] Detailed kinetic analysis showed that values of k_D would then be erroneously low, and treatment of some data under this assumption reduced very large isotope effects to values of the order of k_H/k_D = 10–15.[4]

This criticism was countered by the argument that the rate of hydrogen exchange in this substrate was not known and that internal return[5] could easily make exchange much slower than ionization;[6] in that eventuality, deuterium would not be lost during the course of kinetic measurements, and the original claim of very large isotope effects would stand. We wish to report that we have now measured rates of hydrogen exchange in this system and find internal return to be absent.

We performed our work using (4-nitrophenyl)nitromethane-*1-t*.[7] This material, in the presence of amine bases in toluene solution, loses essentially all of its tritium smoothly under conditions where at equilibrium only a few percent of the substrate is converted to ion pair; this indicates that the process being followed is in fact isotope exchange and not just ionization.[8] Rates of loss of tritium are accurately first order over their entire course, and first-order rate constants are proportional to amine base concentration.[9] Second-order specific rates of exchange, obtained by least-squares analysis of the relationship between first-order rate constants and base concentration, are listed in column 2 of Table I.

Comparison of these data with specific rates of ionization of the C–T bond (Table I, column 3), estimated by using published values of k_H and k_H/k_D[1,10] and the Swain–Schaad relationship[11] to convert k_H/k_D into k_H/k_T, shows that in no case is exchange slower than ionization; internal return must therefore be absent. In fact, in all cases but one, the measured rate of exchange exceeds the estimated rate of ionization by a substantial amount. This is an implausible situation, but that can be remedied if smaller values of k_H/k_D are used in the ionization rate constant estimates; smaller values are of course also required by the fact that the isotopic integrity of the deuterated substrate is not being maintained by internal return.

When internal return is absent, rates of isotope exchange are equal to rates of ionization. The detritiation rate constants measured here may therefore be combined with published values of k_H to give tritium isotope effects on ionization. These, together with corresponding values of k_H/k_D $(=(k_H/k_T)^{1/1.442})$, are listed in columns 4 and 5 of Table I. It may be seen that these isotope effects are generally lower than the previously published values (column 6); in particular, the very large isotope effect reported for tetramethylguanidine as the proton acceptor, k_H/k_D = 45, is now reduced to k_H/k_D = 14. This is still a rather large isotopic rate ratio, and it could signify some proton tunneling. Support for this idea comes from the fact that rates of detritiation in the presence of this base measured over the temperature interval 5–45 °C gives a difference in activation energies of $E_a{}^T - E_a{}^H = 3.2 \pm 0.2$ kcal mol^{-1} and a ratio of preexponential factors of $A_T/A_H = 6 \pm 2$. These are just outside the limits generally considered to signify no tunneling; they contrast with the values found for detritiation by quinuclidine, $E_a{}^T - E_a{}^H = 1.5 \pm 0.1$ kcal mol^{-1} and $A_T/A_H = 0.7 \pm 0.1$, and triethylamine, $E_a{}^T - E_a{}^H = 1.4 \pm 0.6$ kcal mol^{-1} and $A_T/A_H = 0.5 \pm 0.5$.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council for financial support of this work.

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[2] Bell, R. P. *Chem. Soc. Rev.* **1974**, *3*, 513–544. Lewis, E. S. In "Proton Transfer Reactions"; Caldin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975; pp 317–338.

[3] Rogne, O. *J. Chem. Soc., Chem. Commun.* **1977**, 695–696.

[4] Blanch, J. H.; Rogne, O. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1254–1262. Rogne, O. *Acta Chem. Scand., Ser. A* **1978**, *32*, 559–563.

[5] Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1965.

[6] Caldin, E. F., Second International Symposium on the Mechanisms of Reactions in Solution, Canterbury, England, 1979, Abstract D-2; Caldin, E. F.; Warrick, P.; Mateo, S. *J. Am. Chem. Soc.* **1980**, *102*, following paper in this issue.

[7] This substance was prepared by an adaptation of the method used for making the deuterated substrate.[1]

[8] The isotopic label accumulates in the amine, present in large excess, if the latter has an exchangeable N–H bond, and in adventitious water, which cannot be removed from the system completely. We found that deliberately added water, in concentrations up to its saturation solubility (0.02 M), has no effect on detritiation rates.

[9] This is strictly true only at base concentrations sufficiently low to give little ion-pair formation; at higher concentrations the order in base falls off according to expectation for an accompanying "dead end" reaction giving an ion pair with the isotopic label in a nonexchangeable position: $ArCHTNO_2 + B \rightleftharpoons ArCTNO_2^-HB^+$.

[10] (a) Caldin, E. F.; Rogne, O.; Wilson, C. J. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1796–1803. (b) Heggen, I.; Lindstrom, J.; Rogne, O. *Ibid.* **1978**, *74*, 1263–1276.

[11] Swain, C. G.; Stivers, E. C.; Reuwer, J. F.; Schaad, L. J. *J. Am. Chem. Soc.* **1958**, *80*, 5885–5893. This relationship is known to hold even when there is proton tunneling.[12]

[12] Lewis, E. S.; Robinson, J. K. *J. Am. Chem. Soc.* **1968**, *90*, 4337–4344. Weston, R. E. In "Isotopes and Chemical Principles"; Rock, P. A., Ed.; American Chemical Society: Washington, DC, 1975; pp 44–63. McLennan, D. J. *Aust. J. Chem.* **1979**, *32*, 1883–1896.

Kinetics of the Reaction of (4-Nitrophenyl)nitromethane with Tetramethylguanidine in Toluene

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The proton-transfer reaction of the carbon acid (4-nitrophenyl)nitromethane (4-NPNM; $NO_2C_6H_4CH_2NO_2$; AH_2) with tetramethylguanidine (TMG; $HN{=}C(NMe_2)_2$; BH) and the corresponding deuteron-transfer reaction (eq 1), in various aprotic

$$AH_2 + BH \underset{k_b{}^H}{\overset{k_f{}^H}{\rightleftharpoons}} AH^-HBH^+ \text{ and } AD_2 + BH \underset{k_b{}^D}{\overset{k_f{}^D}{\rightleftharpoons}} AD^-DBH^+ \quad (1)$$

solvents, were studied by Caldin and Mateo.[1] With base in excess (concentration *b*), the kinetics were pseudo first order, and the

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[1] Caldin, E. F.; Mateo, S. *J. Chem. Soc., Faraday Trans. 1* **1975**, *71*, 1876.

rate constants in eq 1 were obtained from plots of the observed first-order rate constant k(obsd) against b (eq 2). The isotopic

$$k^{\mathrm{H}}(\mathrm{obsd}) = k_f^{\mathrm{H}}b + k_b^{\mathrm{H}};\ k^{\mathrm{D}}(\mathrm{obsd}) = k_f^{\mathrm{D}}b + k_b^{\mathrm{D}} \quad (2)$$

rate ratio $k_f^{\mathrm{H}}/k_f^{\mathrm{D}}$ at 25 °C was about 12 in polar solvents such as acetonitrile, but in solvents of low polarity it appeared to be much higher; in toluene it was reported as 45 ± 2 at 25 °C (38 at 30 °C).

This high value in toluene has been questioned by Rogne,[2,3] who pointed out that in a reaction of this type there will be isotopic exchange, converting AD_2 eventually to AH_2:

$$AD_2 + BH \rightleftharpoons AD^-DBH^+ \rightleftharpoons AD^-HBD^+ \rightleftharpoons ADH + BD$$

$$ADH + BH \rightleftharpoons AH^-DBH^+ \rightleftharpoons AH^-HBD^+ \rightleftharpoons AH_2 + BD \quad (3)$$

On the assumption that the rearrangement of the ion pair ($AD^-DBH^+ \rightleftharpoons AD^-HBD^+$) is fast compared to the other steps, Rogne's detailed examination gives a value of only about 11 for the isotopic rate ratio $k_f^{\mathrm{H}}/k_f^{\mathrm{D}}$ in toluene at 30 °C. It also explains some deviations from simple kinetics which he observed and the fact that the value of k_b^{D} derived from the intercept of the plot of k^{D}(obsd) against b (eq 2) is about 5 times smaller than that which corresponds to $k_f^{\mathrm{D}}/k_b^{\mathrm{D}} = K^{\mathrm{D}}$ if K^{D} is assumed equal to K^{H}. Rogne also investigated the D^+ transfer from AD_2 to deuteriated TMG ($AD_2 + BD \rightleftharpoons AD^-DBD^+$), which should not involve isotopic exchange, and reported a value of k_f^{D} higher than Mateo's, in accordance with this lower value of $k_f^{\mathrm{H}}/k_f^{\mathrm{D}}$. These results, although the actual rate of the isotopic exchange is unknown, cast doubt on the original high value for the isotope effect.

The kinetics of the reaction in toluene were therefore reinvestigated by S.M.,[4] with special attention to the role of extraneous water in the solutions. Ordinary TMG contains several percent free water by weight, as is shown by the IR spectra of toluene solutions; purification by recommended methods may leave 2.5% of water, and very careful drying still leaves about 1%. Since TMG is a strong base (pK = 13.6 in water), it will react with water to give OH^-, presumably as an ion pair:

$$H_2O + BH \overset{K_3}{\rightleftharpoons} HO^-BH_2^+ \quad (4)$$

This hydroxide ion pair will react with 4-NPNM, in a reaction concurrent with that of TMG, giving the same ion pair as product and so contributing to the observed rate:

$$AH_2 + HO^-BH_2^+ \underset{k_{-2}^{\mathrm{H}}}{\overset{k_2^{\mathrm{H}}}{\rightleftharpoons}} AH^-BH_2^+ + H_2O;$$

$$AD_2 + HO^-BH_2^+ \underset{k_{-2}^{\mathrm{D}}}{\overset{k_2^{\mathrm{D}}}{\rightleftharpoons}} AD^-BH_2^+ + HOD \quad (5)$$

Mateo has determined the equilibrium constant K_3 directly, using IR absorption to measure the concentration of free water; the result is 1.4 ± 0.3 M^{-1}. To get an estimate of the rates of reaction with $HO^-BH_2^+$ (eq 5), he determined rate constants (k_4, k_{-4}) for the reaction of a related ion pair, $NBu_4^+HO^-$, and found $k_4^{\mathrm{H}} = (1.4 \pm 0.1)10^5$ and $k_4^{\mathrm{D}} = (1.3 \pm 0.1)10^4$ L mol^{-1} s^{-1}. We assume that $k_2^{\mathrm{H}} \sim k_4^{\mathrm{H}}$ and $k_2^{\mathrm{D}} \sim k_4^{\mathrm{D}}$. With these values we can estimate the effect of residual water on the overall rate of reaction. For proton transfer, the rate of the hydroxide reaction (eq 5) is always too small to be of importance compared to the reaction with TMG (1). For deuteron transfer, at low base concentrations, up to ~0.01 M, solutions made from TMG containing 1% water or less should show no appreciable deviation from first-order behavior nor from a linear plot of k^{D}(obsd) against b (eq 2), in accordance with Mateo's original observations,[1] which have now been confirmed (cf. Figure 1) using specially dried TMG; but if the water content of the TMG sample is higher, the rate will be higher, and deviations from the linear plot may occur even at 0.005 M, in the way Rogne[2] observed. At higher base concentrations, moreover, we have found that the plot deviates upward with increasing curvature; up to 0.25 M, it agrees with calculations based on the effects of water, i.e., eq 4 and 5 with the values of K_3 and k_2 given.

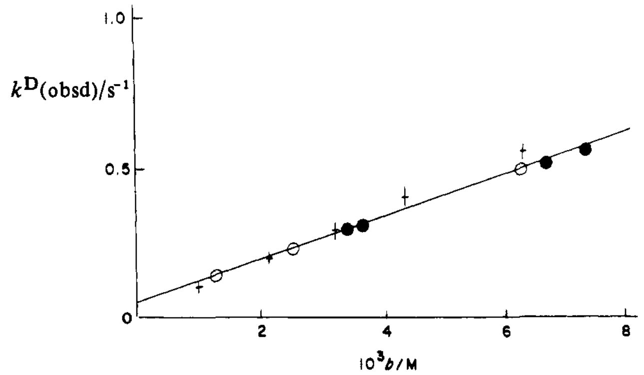

Figure 1. Plot of first-order rate constant k^{D}(obsd) against concentration b of TMG. Comparison of deuterated base (BD) with undeuterated (BH). The values reported for BD in ref 3 lie considerably higher. ●, BH (Mateo[1]); ○, BH (this work); +, BD (this work). Horizontal axis, 10^3b/M; vertical axis: k^{D}(obsd)/s^{-1}.

An indication that isotopic exchange is not kinetically important under these conditions is provided by a comparison of the rates of deuteron transfer (eq 1) to BH and the deuterated base BD. If isotope exchange dominates the situation, the slope of the plot of k^{D}(obsd) against b should be about 4 times larger for BD than for BH. In fact the rates with BD and BH are nearly the same, as is shown in Figure 1. This agreement confirms the low value of k_f^{D} reported earlier and the corresponding high value of $k_f^{\mathrm{H}}/k_f^{\mathrm{D}}$.

A possible reason for this state of affairs is that after the initial deuteron transfer in eq 3, there is a specific deuterium-bonding interaction in the ion pair ($DAD + BH \rightarrow DA^-\cdots DBH^+$), so that it can retain its configuration and revert to DAD + BH, without isomerizing to $DA^-\cdots HBD^+$, thus retarding the sequence of reactions producing ADH and AH_2. This would be a case of "internal return".[5]

An alternative approach is to determine *initial* rates, which would be unaffected by isotopic exchange. P.W. has determined initial rates for the deuteron-transfer reaction with TMG concentrations in the range 10^{-4}–10^{-3} M (lower than those in Figure 1 by 1 order of magnitude). At these concentrations the reaction is slow enough to follow in a spectrophotometer. Although the results exhibit appreciable scatter (possibly due to extraneous water, which despite all precautions was frequently found to be in the region of 10^{-3} M at the end of a run), they yield values of k_f^{D} which are lower by 1 or 2 orders of magnitude than those determined from the complete reaction-time curves at TMG concentrations in the range (1–10) × 10^{-3} M; moreover they increase with base concentration, suggesting a rate proportional to $(AD_2)(BH)^2$. These unexpected results suggest that the reaction that is being studied under these conditions may not be identical with the one that has been studied hitherto.

Another method of determining initial rate is by detritiation of the acid (AHT or AT_2). Since it is the loss of T which is measured, rather than the product concentration, the rate will be independent of isotope exchange. (It will still be dependent on the concentration of $BH_2^+OH^-$ and therefore of water.) Kresge and Powell[6] report the results of such experiments over the concentration range 10^{-5}–10^{-2} M. They find $k^{\mathrm{H}}/k^{\mathrm{T}} = 45.8$ at 25 °C, corresponding to $k^{\mathrm{H}}/k^{\mathrm{D}} = 14$. The rates of detritiation were not affected by addition of water. If the sole reaction under their conditions is indeed the T^+ transfer from AHT to BH, these results are decisively against the original high value for the isotopic ratio;

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[2] Rogne, O. *Acta Chem. Scand., Ser. A* **1978**, *A32*, 559.

[3] Blanch, J. H.; Rogne, O. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1254.

[4] Mateo, S. Unpublished work at the University of Kent, 1978–9.

[5] Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: London, 1965; Chapter 3. Buncel, E. "Carbanions: Mechanistic and Isotopic Aspects"; Elsevier: Amsterdam, 1975; pp 27, 56.

[6] Kresge, A. J.; Powell, M. Accompanying paper.

but they are not easy to reconcile with our observations. Further experiments are desirable.

Isotopic rate ratios much larger than 10 are not impossible where tunneling occurs but will not be observed where the energy barrier is low, as in the reactions of 4-NPNM with other imines.[7] A high value (30 ± 2 at 25 °C) has also been found for the reaction of 4-NPNM with 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene, where the base has no exchangeable proton, in chlorobenzene.[8] Values of 30 to 50 have also been reported for other reactions.[9-12] A full paper is in preparation.

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(7) Rogne, O., et al. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1263, 1796, 2065.

(8) Mateo, C.; Mateo, S. Personal communication; Abstracts of the Second International Conference on Mechanisms of Reactions in Solution, Canterbury, 1979.

(9) Simonyi, M., et al. *Adv. Phys. Org. Chem.* **1970**, *9*, 127. *J. Chem. Soc., Perkin Trans. 2* **1978**, 405.

(10) Brunton, G. D.; Griller, D.; Barclay, L. R. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 6803. *Ibid.* **1978**, *100*, 4197.

(11) Loth, K.; Graf, F.; Gunthard, H. H. *Chem. Phys.* **1976**, *13*, 95.

(12) Bromberg, A., et al. *J. Chem. Soc., Chem. Commun.* **1968**, 1352. *J. Am. Chem. Soc.* **1969**, *91*, 2860. *J. Chem. Soc., Perkin Trans. 2* **1972**, 588.

Circular Dichroism and Absolute Configuration of C_3-Chiral Derivatives of Cyclotriveratrylene

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Recently, we have described several optically active derivatives of cyclotriveratrylene (**1**) (CTV) having C_3 symmetry.[1,2] In this communication, we report that the absolute configurations of these compounds may be correctly established by means of an exciton analysis of their circular dichroism.

The "crown" is the only stable conformation of CTV;[3-5] that derivatives **2** and **3** behave similarly is indicated by the ^{1}H NMR spectra and by their optical activity.[1] The only observable conformational change is a slow interconversion between two identical (**1**) or enantiomeric (**2** and **3**) crown conformers, which leads to racemization when the compounds involved are optically active. We have measured[6] the energy barrier for such ring inversion in **3**. The value found (E_a = 27.0 ± 0.3 kcal·mol^{-1}) is nearly identical with that observed[2] for (C_3)-cyclotriveratrylene-d_9 (26.5 ± 0.5 kcal·mol^{-1}); the rate constants for the (+) → (−) process are close to 10^{-7} s^{-1} at 20 °C in both cases, indicating a mean half-life of the order of 10^6–10^7 s for a given crown at room temperature. In view of these data, it may be assumed that the circular dichroism (CD) spectra discussed here originate from homogeneous populations of such C_3 conformers.

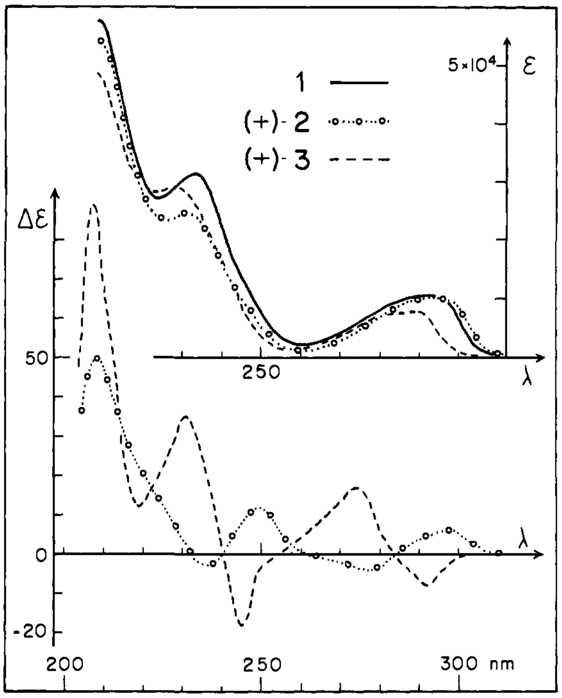
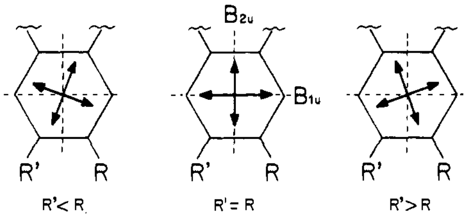
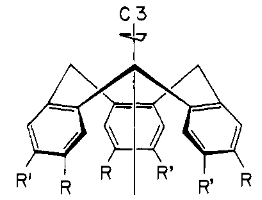


Figure 1. Isotropic absorption spectra and circular dichroism spectra in methanol.[17]

Scheme I





1 R = R' = OCH_3
(+)-2 R = OCH_3 R' = OH
(+)-3 R = OCH_3 R' = $OCOCH_3$

The CD spectra of the triphenol (+)-**2** and of its triacetate (+)-**3** (Figure 1) show two exciton patterns centered at ca. 284 and 240 nm, which are connected to the benzene B_{2u} and B_{1u} transitions, respectively. A striking feature of these spectra is that acetylation of the triphenol *reverses* the signs of these CD couplets.

The intensities of the B_{2u} and B_{1u} transitions of aromatic derivatives are currently interpreted in terms of spectroscopic moments.[7,8] For the CTV derivatives **2** and **3**, the presence of two different substituents R and R′ causes in each of the phenyl rings a rotation of the electric dipole transition moments with respect

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(1) Collet, A.; Jacques, J. *Tetrahedron Lett.* **1978**, 1265–8. Cyclotriveratrylene is also named 10,15-dihydro-2,3,7,8,12,13-hexamethoxy-5*H*-tribenzo[*a*,*d*,*g*]cyclononene.

(2) Collet, A.; Gabard, J. *J. Org. Chem.* **1980**, *45*, 5400. The following Arrhenius and Eyring activation parameters for ring inversion of (C_3)-CTV-d_9 (formula **1**, with R′ = CD_3) have been measured: E_a = 26.5 ± 0.5 kcal·mol^{-1}, A = (0.7 ± 0.5) × 10^{13}, $\Delta G_{25}{}^{*}$ = 26.5 ± 0.1 kcal·mol^{-1}, ΔH^{*} = 25.9 ± 0.5 kcal·mol^{-1}, ΔS^{*} = −1.9 ± 2 eu.

(3) (a) Erdtman, H.; Haglid, F.; Ryhage, R. *Acta Chem. Scand.* **1964**, *18*, 1249–54. (b) Miller, B.; Gesner, B. D. *Tetrahedron Lett.* **1965**, 3351–4. (c) Lindsey, A. S. *J. Chem. Soc.* **1965**, 1685–92. (d) Cookson, R. C.; Halton, B.; Stevens, I. D. R. *J. Chem. Soc. B* **1968**, 767–74. (e) Sato, T.; Uno, K. *J. Chem. Soc., Perkin Trans. 1* **1973**, 895–900. (f) Dale, J. *Top. Stereochem.* **1976**, 9, 199 (see pp 248–50).

(4) Those CTV derivatives substituted at the methylene positions or at the aromatic positions ortho to the nine-membered ring may adopt flexible "saddle" conformations; see, for examples, ref 3d–f. Owing to their conformational mobility, no stable optical activity is expected for these conformers.

(5) Crystal structure of CTV: Cerrini, S.; Giglio, E.; Mazza, F.; Pavel, N. V. *Acta Crystallogr., Sect. B* **1979**, *35*, 2605–9.

(6) The racemization of (+)-**3** was followed polarimetrically at 436 nm in chloroform solution. From the first-order rate constants at 37, 46, and 55.8 °C the following activation parameters were derived: E_a = 27.0 ± 0.3 kcal·mol^{-1}, A = (1.4 ± 0.9) × 10^{13}, $\Delta G_{25}{}^{*}$ 26.5 ± 0.1 kcal·mol^{-1}, ΔH^{*} = 26.4 ± 0.3 kcal·mol^{-1}, ΔS^{*} = −0.5 ± 1 eu.

(7) (a) Platt, J. R. *J. Chem. Phys.* **1951**, *19*, 263. (b) Petruska, J. *Ibid.* **1961**, *34*, 1120.

(8) (a) Sagiv, J. *Tetrahedron* **1977**, *33*, 2303. (b) *Ibid.* **1977**, *33*, 2315.

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