sodium hydride (drybox, under nitrogen). Bubbles appeared, and after stirring for 35 min, the mixture was shaken with ice-water and ether. The ether layer was washed with water, dried, and evaporated, and the mixture was submitted to glc. The ratio of the weights of the peak with (*E*)-**1** retention time to that with (*Z*)-**1** in one determination was 9.4, and in a second was 11.2. In a larger run, the (*E*)-**1** produced from **8** was isolated by preparative glc and shown to possess an nmr spectrum identical with that of authentic material.

Kinetics of Epimerizations of (*Z*)-1 to (*E*)-1 Catalyzed by Lithium Halides in DMF (Runs 16–26). Runs 16 and 22 carried out in nmr tubes resembled run 13 except 42.0 mg of (*Z*)-**1** was weighed in a 3-ml volumetric flask that was filled to the mark with 0.100 *M* LiBr or LiCl in dry DMF at 41° in a drybox (time 0). The solution was immediately syringed into an nmr tube at 41°; the tube was capped with Teflon tape and transferred from the drybox to the probe of an A60D nmr machine. The signals of the methyl protons of (*Z*)-**1** and (*E*)-**1** were integrated at time intervals and compared to the internal standard impurities in the DMF. No other methyl signals were observed. In run 16, the sum of the integrals at the end of the run (75% conversion) was equal to that at the beginning. In run 22, the sum at the end (80% conversion) was 0.94 that at the beginning. Table I records the results.

In runs 17, 19–21, and 23–26, 42.0 mg of (*Z*)-**1** was weighed into a 3-ml volumetric flask, and in run 18, 21.0 mg was used. Solutions of LiBr, LiCl, or LiI in dry DMF freshly prepared under nitrogen in the drybox were added to the mark, the flasks were shaken, and a clean, dry syringe was filled with solution. The syringe was quickly removed from the drybox, and the content was delivered into clean dry ampoules attached to a sealing apparatus under dry argon. The solutions were immediately frozen (liquid nitrogen). Manipulations from mixing to freezing took 20–30 sec. The solutions were degassed with three freeze–thaw cycles and the ampoules sealed at <0.01 mm. The ampoules were first warmed to 0° to melt the liquid, and then placed in a constant-temperature bath. The first tube (time 0) was withdrawn after 5 min and immediately frozen, and additional tubes were removed at appropriate intervals covering about 2 half-lives. The tubes were opened and added to a water–ether mixture (10 ml of each containing a weighed amount of octadecane or tridecane as an internal standard). The ether layer was washed with water and dried with a small amount of sodium sulfate, and the volume of ether was reduced through a distillation column to about 3 ml. This solution was subjected to glc analysis. Less than 3% loss of (*E*)-**1** and (*Z*)-**1** as measured against the internal standards was observed. Most data points fell between 20 and 80% conversion of (*Z*)-**1** to (*E*)-**1**. The pseudo-first-order rate constants were calculated by a least-squares computer program, and errors are reported with two standard deviations. Table I reports these results.

Studies in Stereochemistry. XLV. Zwitterionic Transition States in Epimerization Reactions of Substituted Cyclopropanes[1,2]

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Abstract: An operational criterion was developed to differentiate between zwitterionic and singlet diradical transition states in thermal, geometric isomerization reactions of substituted cyclopropanes in solution. Changes in rates and products with changes in solvent polarity served as criteria for differentiating between zwitterion and diradical paths at the orthogonal point (transition state of highest energy) on the reaction coordinate. Epimerization rates (first order) were measured for each chiral center of optically active (+)-methyl 1-(*R*)-cyano-2-(*R*)-phenylcyclopropanecarboxylate ((+)-(*Z*)-**1**) in dimethylformamide (DMF) and in benzene at two temperatures. The product of epimerization at the cyanoacetate center (k_a) was (+)-methyl 1-(*S*)-cyano-2-(*R*)-phenylcyclopropanecarboxylate ((+)-(*E*)-**1**). Epimerization at the benzyl center (k_b) gave (−)-methyl 1-(*R*)-cyano-2-(*S*)-phenylcyclopropanecarboxylate ((−)-(*E*)-**1**). Racemization rates of (+)-(*Z*)-**1** were also estimated in DMF and measured in benzene at two temperatures. These rates were much slower in DMF than the epimerization rates, and comparable in benzene. The values of the equilibrium constant, *K*, for (*Z*)-**1** $\rightleftarrows$ (*E*)-**1** were measured at 175° ($K = 8.1$) and at 200° ($K = 7.3$) in benzene, and were already known in DMF at 25° ($K = 20$). Interpolation of these values to 126° gave $K = 10$, and to 100° gave $K = 12$. From the rate and equilibrium data, the following rate ratios were calculated: $(k_a^{\mathrm{DMF}}/k_a^{\mathrm{C_6H_6}})_{126°} \sim 4 \times 10^4$; $(k_b^{\mathrm{DMF}}/k_b^{\mathrm{C_6H_6}})_{126°} \sim 7 \times 10^3$; $(k_a^{\mathrm{DMF}}/k_b^{\mathrm{DMF}})_{100°} \sim 86$; $(k_a^{\mathrm{DMF}}/k_b^{\mathrm{DMF}})_{126°} \sim 27$; $(k_a^{\mathrm{C_6H_6}}/k_b^{\mathrm{C_6H_6}})_{175°} \sim 5$; $(k_a^{\mathrm{C_6H_6}}/k_b^{\mathrm{C_6H_6}})_{197°} \sim 5$. Each kind of epimerization passes through a different face-to-edge structure at some point on the reaction path, in which the original bonding orbitals of the starting material become orthogonal to one another. The $\sim 10^4$ greater rate of epimerization at each chiral center in the more polar DMF as compared to benzene as solvent indicates the transition states are close to being orthogonal, and are zwitterionic rather than singlet diradical. In both media, the cyanoacetate group rotates faster than the benzyl, the opposite of what is expected sterically (hydrogen of edge turned inward toward cyanoacetate face of the edge-to-face structure). Charge separation is less in the zwitterionic, orthogonal state in which the carboxymethoxyl group carrying most of the negative charge is turned inward in the edge of the face-to-edge structure. This zwitterionic transition state explains the thermal results. In an acetone-sensitized, photolytic stereoisomerization reaction, (+)-(*Z*)-**1** gave racemic (*E*)-**1** and largely racemized (*Z*)-**1**; (+)-(*E*)-**1** gave racemic (*Z*)-**1** and largely racemized (*E*)-**1**. The photochemical results are interpreted as involving triplet state, open-chain trimethylene derivatives of long enough life to undergo multiple rotations at both chiral centers before collapsing to the covalent ground state.

Conceivably, reaction coordinates for geometric or optical isomerization reactions of 1,2-substituted cyclopropanes might involve singlet structures A–D or a number of triplet structures summarized by E. Structure A is a face-to-face singlet whose orbital geometry and proximity allow different blends of diradical and zwitterionic character. Structure B is a face-to-edge singlet diradical whose orbitals do not overlap since

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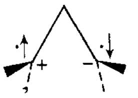
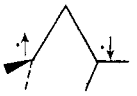
[1] Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

[2] A preliminary account of part of this work has appeared: E. W. Yankee and D. J. Cram, *J. Amer. Chem. Soc.*, 92, 6331 (1970).

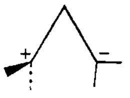
they are orthogonal, and which therefore cannot blend diradical and zwitterionic character. Structure C is a face-to-edge zwitterion whose orthogonal orbital arrangement prevents it from having diradical character. Structure D is an edge-to-edge, π cyclopropane,[3] where again, a blend of singlet diradical and zwitterionic character is compatible with orbital disposition.


A

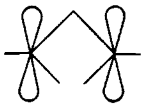
face-to-face
(blend)


B

face-to-edge
singlet diradical


C

face-to-edge
zwitterion


D.

edge-to-edge
π-cyclopropane


E

triplet diradical

Salem, *et al.*,[4a] concluded from *ab initio* SCF calculations that the face-to-face singlet geometry of trimethylene formed from cyclopropane is stabilized 6.2 kcal/mol by mixing strong zwitterionic character into the diradical wave function. The terminal carbons are somewhat pyramidal, with their hydrogens folded toward each other. The transition state for geometric isomerization of cyclopropane has been calculated[4b] as approaching a face-to-edge structure, with no energy minima on the reaction coordinate between starting, labeled cyclopropanes and their geometrically or optically rearranged products. The calculations apply to gas model structures, where solvation energies can be disregarded.

Several authors have used configurational changes at the chiral centers of 1,2-disubstituted cyclopropanes to follow their thermal stereoisomerization reactions in the gas phase.[5] In most of these studies, diradical intermediates were invoked, a hypothesis consistent with thermochemical calculations.[6]

This and the following paper[7] report the results of a study designed to differentiate between structures A–E as lying on the reaction paths for stereoisomerization reactions of substituted cyclopropanes in solution. The reactions described here involve the epimerizations and racemizations of the stereoisomers of methyl 1-cyano-2-phenylcyclopropanecarboxylate (**1**).[2] This system was designed to favor a zwitterion-like reaction path by locating negative-charge-distributing substituents (cyano and carbomethoxy) on one chiral center, and positive-charge-distributing substituents (phenyl) on a second. The system of the next paper,[7] methyl 1,2-diphenylcyclopropanecarboxylate (**2**), possesses substituents that provide less electronic bias for a zwitterion-like reaction path. The preparation and determination of the absolute configurations and maximum rotations of the four stereoisomers of **1** are reported in the previous paper, coupled with a description of the stereochemical course of the methanolysis[8] and nucleophile-catalyzed isomerization reactions of these isomers.[8a]

Changes in rates and products with changes in solvent polarity served as criteria for differentiating between zwitterion-like and radical-like mechanisms. The reactions studied are outlined in Chart I. First-order rate constants for the processes are defined by placing them beside the arrows. Rate constant k_α^Z measures inversion at both chiral centers of (+)-(*Z*)-**1** ((+)-(*Z*)-**1** → (−)-(*Z*)-**1**) and k_α^E at both chiral centers of (+)-(*E*)-**1** ((+)-(*E*)-**1** → (−)-(*E*)-**1**). Epimerization of either (+)- or (−)-(*Z*)-**1** at the cyanoacetate center only is identified with the rate constant k_a, and at the benzyl center only with k_b. Geometric isomerization (*e.g.*, (*Z*)-**1** → (*E*)-**1**) occurs with a rate constant k_i, and by definition, $k_i = k_a + k_b$. If only racemizations and not epimerizations were observed, no face-to-edge structures would be required for the reaction coordinate, and the whole singlet reaction path might be a blend of zwitterionic and diradical character (structures A and D). If geometric isomerization does occur, face-to-edge structures (B or C) are required for the singlet reaction path. In these geometries, the molecule must be either zwitterionic or diradical. The transition state of highest energy for the singlet reaction coordinate for geometric isomerization probably resembles the orthogonal, face-to-edge structure. If this structure is zwitterionic, polar media should increase the values of k_a and k_b drastically relative to nonpolar media. If this structure is singlet diradical, polar and nonpolar media should provide similar k_a and k_b values.

Chart I

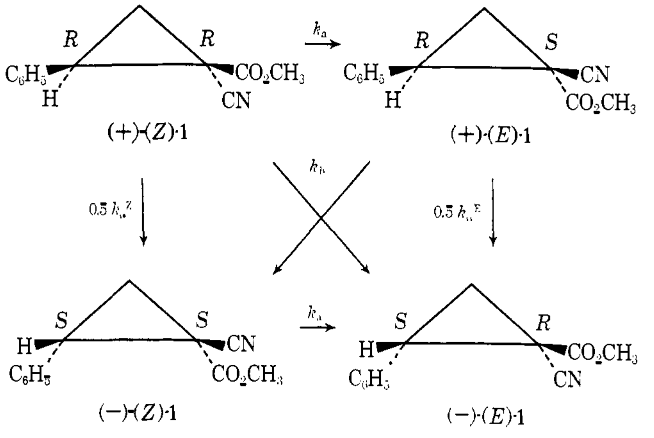


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Table I. First-Order Rate Constants for Stereoisomerizations of Methyl 1-Cyano-2-phenylcyclopropanecarboxylate (1) Stereoisomers

Run no.	Temp, °C	Solvent	Starting material		First-order rate constants[a] (sec^{-1}) × 10^6				
			Nature	Concn, *M*	k_i	k_a	k_b	$k_\alpha{}^Z$	$k_\alpha{}^E$
1	197.3	C_6H_6	(+)-(*Z*)-**1**	0.0133	7.22 ± 0.28	6.01 ± 0.34	1.21 ± 0.30	3.73 ± 0.43	2.13 ± 0.12[b]
2	174.7	C_6H_6	(+)-(*Z*)-**1**	0.0152	0.848 ± 0.033	0.708 ± 0.042	0.140 ± 0.032	0.276 ± 0.037	0.433 ± 0.046[b]
3	205.2	C_6H_6	(+)-(*E*)-**1**	0.0142					4.43
4	184.4	C_6H_6	(+)-(*E*)-**1**	0.0142					0.623
5	126	C_6H_6	(+)-(*Z*)-**1**	0.010	0.0037 ± 0.0011	0.00316 ± 0.0011	0.0006 ± 0.0004		
6	126	DMF	(+)-(*Z*)-**1**	0.010	~117	~113	~4.2	≳1.3	
7	100	DMF	(+)-(*Z*)-**1**	0.010	~20.9	~20.7	~0.24	≳0.08	
8	126	DMF	(−)-(*E*)-**1**	0.016					~0.88 ± 0.11
9	125.8	DMF	(+)-(*Z*)-**1**	0.00614	103 ± 5				
10	99.4	DMF	(+)-(*Z*)-**1**	0.00614	18.7 ± 0.9				

[a] Runs 1–5, least-squares rate constants, errors listed with 95% confidence intervals. Runs 6 and 7, one-point rate constants. Runs 8–10, averaged one-point integrated rate constants (4 of them), ± mean deviation. [b] Values obtained by extrapolating $k_\alpha{}^E$ values from runs 3 and 4 to the temperatures of runs 1 and 2.

Results

For the thermal reactions, benzene and dimethylformamide (DMF) were selected as solvents because of their widely differing polarity. Preliminary experiments established that (*Z*)-**1** isomerized to (*E*)-**1** in these media at accessible temperatures, and that the mixture of diastereomers produced could be analyzed (±0.5%) and separated by glc. The first section describes diastereomeric equilibration experiments. The second section outlines the kinetic analysis. The third section gives the results of photochemically sensitized geometric isomerization, racemization, and equilibration experiments, designed to differentiate between triplet and singlet reaction paths.

Thermal Equilibration of *Z* and *E* Isomers of Methyl 1-Cyano-2-phenylcyclopropanecarboxylate ((*Z*)-1 $\rightleftarrows$ (*E*)-1). At 200° in benzene (sealed ampoules) for 15 days, (*Z*)-**1** and (*E*)-**1** each gave K = [(*E*)-**1**]/[(*Z*)-**1**] = 7.3. In benzene first for 7 days at 200° and then for 21 days at 175°, each isomer gave 8.1. At 126°, the higher of the two temperatures used for the kinetic experiments in DMF, the extended period of time required for equilibration led to enough decomposition of (*Z*)-**1** and (*E*)-**1** to indieate only that the equilibrium constant was 10 or greater. The lithium bromide catalyzed equilibration of the two diastereomers in DMF at 25° gave $K = 20 \pm 2$.[8a] A plot of log K against $1/T$ (absolute) for the three points was surprisingly linear. From this plot, K was estimated to be 10 at 126° and 12 at 100°.

Kinetics of Isomerizations and Racemizations of the Stereoisomers of Methyl 1-Cyano-2-phenylcyclopropanecarboxylate (1). Ampoules of (+)-(*Z*)-**1**[8a] in benzene were placed in constant-temperature baths at 197.3° (run 1) and 174.7° (run 2). The tubes were periodically removed and thermally quenched, and a small portion of each sample was submitted to analysis by glc for the relative amounts of (*Z*)-**1** and (*E*)-**1**. Use of octadecane as an internal standard established in a control run that >94% starting material could be accounted for as either (*Z*)-**1** or (*E*)-**1** at 197.3° after 48.76 hr. The isomerization was followed with five to six data points covering from 76 to 62% conversion of (*Z*)-**1** to (*E*)-**1**. The remainder of each ampoule's contents was submitted to preparative glc (base line) separation, and the rotations of the isolated samples of (*Z*)-**1** and of (*E*)-**1** were taken.

The geometric isomerization reaction leading to the equilibrium mixture of the diastereomers followed good first-order kinetics at the two temperatures. In runs 1 and 2, values for k_i, the first-order rate constant for (*Z*)-**1** → (*E*)-**1**, were calculated from the equilibrium constants and the observed rate constants for approach of (*Z*)-**1** to equilibrium. Table I lists the least-squares k_i values. The racemization of (+)-(*Z*)-**1** also followed good first-order kinetics, and Table I lists least-squares values for $k_\alpha{}^Z$. The runs also provided data for plots of the optical purity of (+)-(*E*)-**1** produced from (+)-(*Z*)-**1** as a function of time.

In runs 3 and 4, ampoules of (+)-(*E*)-**1** were thermostated at 205.2 and 184.4°. Periodically tubes were removed and submitted to preparative glc, and the rotations of the isolated (*E*)-**1** samples were taken. The racemizations were followed with four data points in run 3 (60% reaction), and five in run 4 (36% reaction). The racemization of (+)-(*E*)-**1** followed good first-order kinetics. From the least-squares $k_\alpha{}^{\mathrm{E}}$ values at the two temperatures, E_{A} was calculated, and $k_\alpha{}^{\mathrm{E}}$ values at 197.3 and 174.7° were obtained by extrapolation (Table I). Thus k_{i}, $k_\alpha{}^{\mathrm{Z}}$, and $k_\alpha{}^{\mathrm{E}}$ values at two temperatures in benzene became available, as well as five-point plots at the two temperatures of the optical purity of the (+)-(*E*)-**1** produced from (+)-(*Z*)-**1** as a function of time.

From these data at the two temperatures were calculated values of k_{a} and k_{b}. Equations 1 and 2 were obtained by integrating two simultaneous differential equations.[9] These equations represent concentrations [(+)-(*E*)-**1**] and [(−)-(*E*)-**1**] as a function of time and the values of k_{a}, k_{b}, $k_\alpha{}^{\mathrm{Z}}$ and $k_\alpha{}^{\mathrm{E}}$ (Chart I). At time zero, these concentrations are zero, and [(+)-(*Z*)-**1**] equals infinity. In this derivation it was assumed that little, if any, (*E*)-**1** once formed returned to (*Z*)-**1**. Justification for this assumption lies in the fact that the equilibrium constants are fairly high valued (7.3–8.1), the isomerization reactions were only followed about 50% of the way to equilibrium, and the racemization of (+)-(*Z*)-**1** followed good first-order kinetics.

$$[(+)\text{-}(E)\text{-}\mathbf{1}] = 0.5[1 - e^{-(k_{\mathrm{a}}+k_{\mathrm{b}})t}] - \frac{k_{\mathrm{a}} - k_{\mathrm{b}}}{2(k_{\mathrm{a}} + k_{\mathrm{b}} + k_\alpha{}^{\mathrm{Z}} + k_\alpha{}^{\mathrm{E}})}[e^{-(k_{\mathrm{a}}+k_{\mathrm{b}}+k_\alpha{}^{\mathrm{Z}})t} - e^{-k_\alpha{}^{\mathrm{E}}t}] \quad (1)$$

$$[(-)\text{-}(E)\text{-}\mathbf{1}] = 0.5[1 - e^{-(k_{\mathrm{a}}+k_{\mathrm{b}})t}] - \frac{k_{\mathrm{a}} - k_{\mathrm{b}}}{2(k_{\mathrm{a}} + k_{\mathrm{b}} + k_\alpha{}^{\mathrm{Z}} + k_\alpha{}^{\mathrm{E}})}[e^{-k_\alpha{}^{\mathrm{E}}t} - e^{-(k_{\mathrm{a}}+k_{\mathrm{b}}+k_\alpha{}^{\mathrm{Z}})t}] \quad (2)$$

$$k_{\mathrm{a}} - k_{\mathrm{b}} = \frac{[[(+)\text{-}(E)\text{-}\mathbf{1}] - [(-)\text{-}(E)\text{-}\mathbf{1}]][k_{\mathrm{i}} + k_\alpha{}^{\mathrm{E}} + k_\alpha{}^{\mathrm{Z}}]}{e^{-k_\alpha{}^{\mathrm{E}}t} - e^{-(k_{\mathrm{i}}+k_\alpha{}^{\mathrm{Z}})t}} \quad (3)$$

$$k_{\mathrm{i}} = k_{\mathrm{a}} + k_{\mathrm{b}} \quad (4)$$

From eq 1 and 2 was derived 3, which expresses $k_{\mathrm{a}} - k_{\mathrm{b}}$ in terms of experimentally available data. Values of [(+)-(*E*)-**1**] − [(−)-(*E*)-**1**] at times *t* were calculated from the optical purities of (+)-(*E*)-**1** formed from (+)-(*Z*)-**1**, and the fraction of (*Z*)-**1** converted to (*E*)-**1** at times *t*. Equations 5, 6, and 7 indicate the relationships. Solution of two equations (3 and 4) in

$$\text{optical purity of } (+)\text{-}(E)\text{-}\mathbf{1} = \frac{[(+)\text{-}(E)\text{-}\mathbf{1}] - [(-)\text{-}(E)\text{-}\mathbf{1}]}{[(+)\text{-}(E)\text{-}\mathbf{1}] + [(-)\text{-}(E)\text{-}\mathbf{1}]} \quad (5)$$

$$\text{fraction that is } (E)\text{-}\mathbf{1} = \frac{[(+)\text{-}(E)\text{-}\mathbf{1}] + [(-)\text{-}(E)\text{-}\mathbf{1}]}{[(E)\text{-}\mathbf{1}] + [(Z)\text{-}\mathbf{1}]} = [(+)\text{-}(E)\text{-}\mathbf{1}] + [(-)\text{-}(E)\text{-}\mathbf{1}] \quad (6)$$

$$[(+)\text{-}(E)\text{-}\mathbf{1}] - [(-)\text{-}(E)\text{-}\mathbf{1}] = [\text{optical purity of } (+)\text{-}(E)\text{-}\mathbf{1}] \times [\text{fraction that is } (E)\text{-}\mathbf{1}] \quad (7)$$

two unknowns coupled with the fact that [(*E*)-**1**] + [(*Z*)-**1**] = 1 provided values of k_{a} and k_{b} for runs 1 and 2 (Table I). From these values, E_{A}'s associated with k_{i}, k_{a}, and k_{b} were calculated and used to extrapolate k_{i}, k_{a}, and k_{b} to 126°. Table I lists the estimates of these rate constants at this temperature under run 5.

A preliminary experiment was made with (*Z*)-**1** in DMF at 126° for 1.00 hr. The products were analyzed by analytical glc with octadecane as an internal standard, and >95% of the starting material was accounted for in terms of (*Z*)-**1** and (*E*)-**1**. No extraneous peaks were detected. Similarly, runs 6 and 7 were made with optically pure (+)-(*Z*)-**1** at 126 and 100°, respectively. In run 6 after 1 hr, analytical glc (±1%) indicated the presence of 63% (*Z*)-**1**, 37% (*E*)-**1**, and no other peaks. Preparative glc (base line) separation of the products gave (+)-(*Z*)-**1** of 100% and (+)-(*E*)-**1** of 92.8 ± 0.4% optical purity. In run 7 after 17 hr, 25% of (+)-(*Z*)-**1** of 100% optical purity and 75% of (+)-(*E*)-**1** of 97.7 ± 0.3% optical purity were obtained. Estimates of one-point, first-order constants for k_{i} were made (Table I) from the per cent conversions and the equilibrium constants. Higher limits were placed on the values of $k_\alpha{}^{\mathrm{Z}}$ (Table I) from the rotations of (+)-(*Z*)-**1** samples recovered in runs 6 and 7. In control runs that paralleled 6 and 7, samples of (−)-(*E*)-**1** gave ~1% (*Z*)-**1**, and the recovered (−)-(*E*)-**1** was of the same rotation as the starting material. In run 8, racemization of (−)-(*E*)-**1** in DMF at 126° (ampoules) was followed polarimetrically with four points through 3% reaction (12 hr). Control experiments demonstrated that at 126° with longer times decomposition occurred. A rough, first-order rate constant, $k_\alpha{}^{\mathrm{E}}$, was estimated (Table I). In runs 9 and 10, kinetics (ampoules) of optically pure (+)-(*Z*)-**1** → [(+)-(*Z*)-**1** ⇄ (+)-(*E*)-**1**] equilibrating were followed polarimetrically in DMF at 125.8 and 99.4°, respectively. The rotations at $t = \infty$ (equilibrium) were calculated from the rotations of optically pure (+)-(*Z*)-**1** and (+)-(*E*)-**1** in DMF and the equilibrium constants at 126° ($k = 10$) and 100° ($k = 12$). In run 9, the reaction was followed with four points 36%, and in run 10, with four points 45% of the way to equilibrium. Values of k_{i} were calculated (Table I) from these data and from the equilibrium constants. The value of k_{i} obtained by glc analysis in run 6 (117×10^{-6} sec^{-1}) is satisfactorily similar to that obtained by polarimetric analysis in run 8 ($103 \pm 5 \times 10^{-6}$ sec^{-1}). The value from glc analysis in run 7 (20.9×10^{-6} sec^{-1}) is correspondingly close to that from polarimetric analysis in run 10 corrected from 99.4 to 100° ($19.5 \pm 0.9 \times 10^{-6}$ sec^{-1}).

These results in DMF indicate that $k_{\mathrm{i}}/k_\alpha{}^{\mathrm{Z}} \gtrsim 10^2$ (runs 6 and 7), and that $k_{\mathrm{i}}/k_\alpha{}^{\mathrm{E}} \gtrsim 10^2$ (runs 6 and 8). Particularly for low conversions, (+)-(*E*)-**1** and (−)-(*E*)-**1** in effect are produced only from (+)-(*Z*)-**1**, and not from (−)-(*Z*)-**1** or from each other. Accordingly, eq 8 and 9 apply, which in turn provide eq 10. Equations 4 and 10 provide two equations in two unknowns, solution of which for runs 6 and 7 provides the estimated values of k_{a} and k_{b} in DMF listed in Table I.

$$\mathrm{d}[(+)\text{-}(E)\text{-}\mathbf{1}]/\mathrm{d}t = k_{\mathrm{a}}[(+)\text{-}(Z)\text{-}\mathbf{1}] \quad (8)$$

$$\mathrm{d}[(-)\text{-}(E)\text{-}\mathbf{1}]/\mathrm{d}t = k_{\mathrm{b}}[(+)\text{-}(Z)\text{-}\mathbf{1}] \quad (9)$$

$$[(+)\text{-}(E)\text{-}\mathbf{1}]/[(-)\text{-}(E)\text{-}\mathbf{1}] = k_{\mathrm{a}}/k_{\mathrm{b}} \quad (10)$$

Photochemical Stereoisomerization Reactions of the Stereoisomers of Methyl 1-Cyano-2-phenylcyclopropanecarboxylate (1). Solutions (0.0124 *M*) of (*Z*)-**1** and of (*E*)-**1** in acetone were brought to a photochemical steady state in runs 11 and 12. The solutions were irradiated with ultraviolet light >267 nm for 6 hr. Glc analysis

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[9] The authors thank Dr. John Almy (Ph.D. Thesis, UCLA, 1969, pp 96–129), for deriving general equations (steady-state assumption) for describing the first-order kinetics of interconversions of eight systems. Two of these equations in abbreviated form are eq 1 and 2.

of the final solution in each run gave [(*E*)-**1**]/[(*Z*)-**1**] = 1.5. The ultraviolet spectrum of (*E*)-**1** in absolute ethanol gave λ_{max} at 220 nm (log ϵ 4.08) and 260 (2.95). An identical experiment with (*E*)-**1** in cyclohexane gave [(*E*)-**1**]/[(*Z*)-**1**] = 19. Thus, the photochemical steady states observed in runs 11 and 12 appear photosensitized by the acetone solvent.

In run 13, (+)-(*Z*)-**1** (69% optically pure) in acetone (0.00075 *M*) was irradiated under conditions of runs 11 and 12 for 3 hr. Analytical glc indicated 25% conversion of (*Z*)-**1** to (*E*)-**1**. Preparatory glc of the reaction mixture gave racemic (*E*)-**1** and (+)-(*Z*)-**1** of 29% optical purity. In run 14, optically pure (−)-(*E*)-**1** in acetone (0.00381 *M*) under the same conditions for 4 hr gave (preparative glc) racemic (*Z*)-**1** and (−)-(*E*)-**1** of 8% optical purity. Thus, these photolytic geometric isomerizations went with complete loss of optical activity.

Discussion

Effects of Solvent Polarity on Epimerization Rates. The rate constants for geometric isomerization (k_i) and for epimerization (k_a and k_b) show a large solvent polarity dependence. The rate ratios calculated from runs 5 and 6 show that k_i, k_a, and k_b are all close to 10^4 faster than in the dipolar solvent, dimethylformamide (DMF), than in nonpolar solvent benzene. This large a solvent dependence on rate is incompatible with reaction coordinates whose transition states of highest energy are either singlet or triplet diradical in character. Rather, the transition states must be zwitterionic, at least in the polar solvent. This conclusion applies to the transition states for the epimerizations *at both the cyanoacetate* (k_a) *and the benzyl centers* (k_b).

$$(k_i^{DMF}/k_i^{C_6H_6})_{126°} \sim 3.2 \times 10^4 \qquad \text{(runs 5 \& 6)}$$

$$(k_a^{DMF}/k_a^{C_6H_6})_{126°} \sim 3.6 \times 10^4 \qquad \text{(runs 5 \& 6)}$$

$$(k_b^{DMF}/k_b^{C_6H_6})_{126°} \sim 7 \times 10^3 \qquad \text{(runs 5 \& 6)}$$

In both the polar and nonpolar solvents, the cyanoacetate center rotated faster than the benzyl, as is seen by the rate ratios for k_a/k_b that are listed. This effect is more marked in DMF at 100 to 126° than in benzene at 175 to 197°. Possibly the large temperature difference is responsible. Extrapolations to 126° of $(k_a^{C_6H_6}/k_b^{C_6H_6})_{197-175°}$, or of $(k_a^{DMF}/k_b^{DMF})_{100-126°}$ to 175°, to make distinctions of a factor of 6 or less, are well beyond the accuracy of the data. That epimerization occurred at all demonstrates the reaction path includes a face-to-edge structure, in which the electrons of the cyclopropane bond that cleaved are in orbitals orthogonal to one another. This structure is either zwitterionic or diradical, but not a blend. Very likely, the transition state of highest energy possesses a face-to-edge structure. In system 1, the face-to-edge structures appear to be more stable as zwitterions rather than as singlet or triplet diradicals. From runs 1 and 2

$$(k_a^{C_6H_6}/k_b^{C_6H_6})_{197°} \sim 5$$

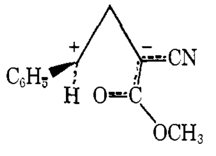
$$(k_a^{C_6H_6}/k_b^{C_6H_6})_{175°} \sim 5$$

and from runs 6 and 7

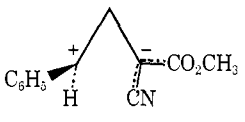
$$(k_a^{DMF}/k_b^{DMF})_{126°} \sim 27$$

$$(k_a^{DMF}/k_b^{DMF})_{100°} \sim 86$$

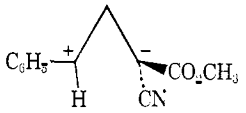
Should steric effects control the relative rates of rotation of the cyanoacetate and benzyl centers, k_a/k_b should be <1. Of the four face-to-edge structures derivable from **1**, H is the least sterically hindered. Yet the k_a/k_b ratios indicate that either F or G must be more stable than H or J. Thus, electronic rather than steric effects appear to dominate the ratio. Since rotation at both centers occurs, and both show the large rate dependence on solvent, both types of competing face-to-edge structures are zwitterionic. Of the two structures that provide for cyanoacetate rotation, F seems the more probable, since less charge separation is involved than in G.[10] For benzyl rotation, H and J provide about the same charge separation, but H is much less hindered, and therefore is the more probable.



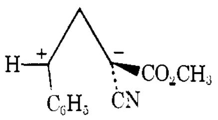
F



G



H



J

Comparisons between Thermal and Photochemical Reactions. This mechanistic interpretation is greatly strengthened through comparisons. The acetone-sensitized photochemical reactions of (+)-(*Z*)-**1** and (−)-(*E*)-**1** of runs 13 and 14 gave completely racemic, geometrically isomerized products under conditions that gave recovered, partially optically active starting material. In other words, in the conversion of (*Z*)-**1** to (*E*)-**1** k_a/k_b = 1, and the same number of molecules underwent inversion at the cyanoacetate as at the benzyl center. The same is true for (*E*)-**1** → (*Z*)-**1**. Acetone-sensitized, photochemically induced geometrical isomerizations of olefins go through triplet states,[11] and the same appears true of these photochemical geometric isomerizations. The triplet intermediates (E) are probably of long enough life to undergo enough rotations of the edge-to-face variety at both chiral centers to provide both racemized starting material and racemic epimeric product. The power of ten difference at ~25° between the photochemical steady-state constant in acetone ($K_{h\nu}$ = [(*E*)-**1**]/[(*Z*)-**1**] = 1.5) and the thermal equilibrium constant in DMF (K_Δ = [(*E*)-**1**]/[(*Z*)-**1**] = 20][8a] provides a further interesting point of contrast between the two processes.

Comparison between Thermal Epimerizations in Different Systems. More striking are the differences between the behavior of systems **1** and **2**. The following paper[7] reports the results obtained when the stereoisomers of **2** were subjected to the same types of experiments as those of **1** reported here. The thermal, geo-

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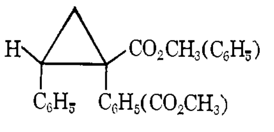
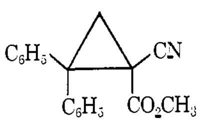
(10) Inclusion of structure F on the reaction coordinate provides a path for a *conducted tour of* C^+ *of benzyl from* C^- *to* O^-*, to inverted* C^-, and resembles ionic conducted tour mechanisms observed in other reactions; see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, p 102; T. D. Hoffman and D. J. Cram, *J. Amer. Chem. Soc.*, **91**, 1009 (1969).

(11) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Amer. Chem. Soc.*, **86**, 3197 (1964).



2



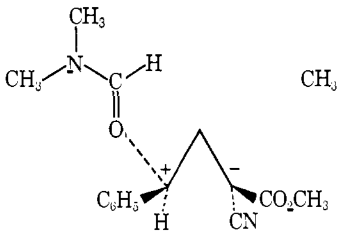
3

metric isomerization reactions of **2** occurred at almost the same rates in methanol and in benzene. The rate of geometric isomerization by rotation at the benzyl center exceeded that at the phenylacetate center by over a power of ten in both solvents. This result corresponds to that expected on steric grounds. *Thus the reaction coordinates for the geometric isomerization reactions of* **2** *involve face-to-edge transition states of singlet diradical character* (B), *in contrast to the zwitterionic character* (C) *observed for those of* **1**. *In* **1**, *cyanoacetate rotation occurred faster than benzyl in both benzene and DMF, in opposition to steric effects. Steric effects dominated in* **2**. We conclude that in benzene as well as DMF, the reaction coordinate for epimerizations of (*Z*)-**1** passes through a face-to-edge zwitterionic, rate-limiting transition state.

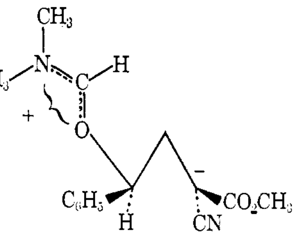
Possible Reaction Intermediates in the Thermal Epimerizations. The question arises as to whether reaction intermediates intervene during the geometric isomerizations of **1**. Strong evidence for face-to-face intermediates (A) capturable by bromide ion was observed in the racemization of the related system **3** in DMF at 126°.[12] System **1** undergoes methanolysis reactions[8] similar to those of ordinary benzyl systems, and ordinary benzyl systems undergo solvolysis reactions through carbonium ion intermediates. If, as analogic reasoning suggests, **1** stereoisomerizes through face-to-face intermediates, the classical question arises as to how intimately involved the solvent is with a benzyl carbonium ion. In benzene, involvement must be minimal. In DMF, involvement is undoubtedly more important. Zwitterionic structure K contains a DMF solvated carbonium ion stabilized by positive charge delocalized into phenyl on the one hand, and by pole–dipole interaction with the solvent on the other. Zwitterionic structure L contains a cation whose positive charge cannot delocalize into phenyl, but which is distributed between oxygen and nitrogen of a covalently bound DMF molecule. Structure K would inhibit, but not prevent, the observed epimerization reaction at the benzyl carbon, k_b. Structure L would prevent this reaction, and allow only epimerization at the cyanoacetate carbon (k_a). Since both reactions are observed in, and helped by the polarity of DMF, structure K as a reaction intermediate is compatible, and L incompatible with the epimerization reaction at benzyl. To invoke L as an intermediate for the cyanoacetate epimerization in DMF, and K for the benzyl epimerization in DMF, and neither of these types for the two epimerizations in benzene violates the principle of minimum explanation.

Intermediates such as K in DMF are probable. They offer a specific explanation for the greater rates of epimerization at both centers in DMF than in benzene, and for the smaller rate of benzyl as compared to cyanoacetate epimerization in DMF.

Other structures as part of the reaction coordinate



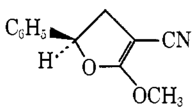
K



L

require consideration. To arrive at π-cyclopropane structure (D), benzyl and cyanoacetate centers must rotate simultaneously. Such a process gives racemization, and not geometric isomerization. This structure is ruled out for the epimerization, and is improbable for the racemization reactions on steric grounds.

The possibility exists that ketene acetal M is a reaction intermediate. Attempts to prepare M failed. Analogies exist for the mechanism, (+)-(*Z*)-**1** → M → (+)-(*E*)-**1**, in which each arrow represents a single transition state.[13] This mechanism is incompatible with the dramatic and roughly similar response of k_a and k_b to solvent polarity change, and is extremely unlikely. This mechanism is impossible for the reaction, (+)-(*Z*)-**1** → (−)-(*E*)-**1**, where benzyl rotates, and would have to be a minor reaction in the stereoisomerizations of **2**.



M

A mechanism is formulated for the epimerization at the cyanoacetate center of (+)-(*Z*)-**1** that involves M and face-to-face zwitterionic intermediates. This mechanism is consistent with the solvent effects only if the transition state of highest energy is zwitterionic, and where $k_2 \gg k_1$. Otherwise M would accumulate. This mechanism cannot be ruled out, but it provides no explanation whatsoever for the companion reaction of epimerization at the benzyl carbon.

$$(+)\text{-}(Z)\text{-}\mathbf{1} \longrightarrow \left\{\begin{array}{c}\text{face-to-face}\\ \text{intermediate}\\ \text{zwitterion}\end{array}\right\} \xrightarrow{k_1} \mathrm{M} \xrightarrow{k_2} \left\{\begin{array}{c}\text{face-to-face}\\ \text{epimeric}\\ \text{intermediate}\\ \text{zwitterion}\end{array}\right\} \longrightarrow (+)\text{-}(E)\text{-}\mathbf{1}$$

Of the various possibilities, the facts concerning the thermal epimerization reactions at each chiral center of (*Z*)-**1** strongly support the following mechanism

$$(Z)\text{-}\mathbf{1} \rightleftarrows \left\{\begin{array}{c}\text{face-to-face}\\ \text{singlet}\\ \text{intermediate}\end{array}\right\} \rightleftarrows \left\{\begin{array}{c}\text{face-to-edge}\\ \text{zwitterionic}\\ \text{transition state}\\ \text{of highest energy}\end{array}\right\} \rightleftarrows \left\{\begin{array}{c}\text{face-to-face}\\ \text{epimeric}\\ \text{singlet}\\ \text{intermediate}\end{array}\right\} \rightleftarrows (E)\text{-}\mathbf{1}$$

Hard evidence has been presented that the transition states of highest energy on the reaction coordinate for both thermal epimerizations are zwitterionic. The face-to-face singlet structures that intervene on the reaction

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[12] (a) E. W. Yankee and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 6328 (1970); (b) E. W. Yankee, F. D. Badea, N. E. Howe, and D. J. Cram, *ibid.*, **95**, 4210 (1973).

[13] (a) C. L. Wilson, *ibid.*, **69**, 3002 (1947); (b) D. W. Boykin and R. E. Lutz, *ibid.*, **86**, 5046 (1964); (c) E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **2**, 1 (1963).

path are blends of diradical and zwitterionic character, and are probably energy minima, at least in DMF. Hard evidence on this point is lacking.

Experimental Section

General. Melting points are uncorrected. Nmr spectra were taken with a Varian A-60 on 10–20% solutions in $CDCl_3$ with TMS as internal standard (1%). Rotations were taken with a Perkin-Elmer 141 polarimeter in a 1-dm thermostated cell, and at less than α_{obsd} of 1° were ±0.002°. Uv spectra were taken in absolute ethanol with a Cary 14 spectrometer. Thermometers for constant-temperature baths were Natural Bureau of Standards calibrated.

Thermal Equilibration of Diastereomers of Methyl 1-Cyano-2-phenylcyclopropanecarboxylates, (*Z*)- and (*E*)-1. Four solutions, two of 10 mg of (*Z*)-**1**[8a] and the other two of 10 mg of (*E*)-**1**[8a] in 1.00 ml of benzene (distilled from 4H sieves), were syringed into heavy-walled, clean and dry Pyrex tubes of about 3-ml capacity. The samples were degassed by freezing in liquid nitrogen, evacuating to 50 μ, and then bleeding in pure nitrogen. The freeze–thaw cycle was repeated twice more, and the tubes were sealed under vacuum and carefully annealed. Two ampoules, one containing each isomer, were held in a constant-temperature Lauda bath at 200.0 ± 0.2° for 15 days. The other two tubes were heated at 200° in the same bath for 7 days at 200° and then for 21 days in a constant-temperature Lauda bath at 175.0 ± 0.2°. The ampoules were cooled and opened, the contents were concentrated, and the product was submitted to glc analysis. An Aerograph 200 machine with a flame ionization detector was employed. The column was 1% Epon 1001 on Anakrom SD, 10 ft × $^1/_8$ in., the carrier gas was nitrogen, and the column temperature was 160°. The cut-and-weigh technique was used. Good base line separation was observed between (*E*)-**1** and (*Z*)-**1**, and between these compounds and about 5% of a volatile impurity in each tube. Control experiments with known mixtures demonstrated the analyses were good to about ±0.5%. The identical mixture of (*Z*)- and (*E*)-**1** was obtained at each temperature from each starting material.

Attempts to equilibrate the diastereomers in DMF at 100 and 126° for extended periods of time were frustrated by decomposition of the compounds.

Kinetics of Geometric Isomerization of (+)-(*Z*)-1 to (+)-(*E*)-1 and (−)-(*E*)-1, and Accompanying Racemization of (+)-(*Z*)-1 to (±)-(*Z*)-1 in Benzene (Runs 1 and 2). For run 1, a solution of 147 mg of (+)-(*Z*)-**1**, $[\alpha]^{25}{}_{546}$ +167° (*c* 0.255, EtOAc), in 55 ml of benzene (distilled from 4H Sieves) was distributed by syringe among six clean and dry ampoules (20 ml). The tubes were degassed and sealed as in the equilibration experiments and placed in a Lauda constant-temperature bath held at 174.7 ± 0.2°. For run 2, a solution of 168 mg of (+)-(*Z*)-**1**, $[\alpha]^{25}{}_{546}$ +148° (*c* 0.45, EtOAc), in 55 ml of purified benzene was similarly distributed among six ampoules, which were similarly degassed, sealed, and placed in a Lauda constant-temperature bath at 197.3 ± 0.2°. At appropriate times, ampoules were removed from the bath and quenched by rapid cooling. A small fraction of the contents of each tube was analyzed (glc) under the same conditions as in the equilibration experiments. A control run for 48.75 hr in benzene at 197.8° with octadecane as an internal standard established that >94% of the starting material was accounted for by (*Z*)-**1** plus (*E*)-**1** (glc, base line separation). Least-squares, first-order rate constants were calculated for approach of (*Z*)-**1** to the equilibrium mixture at each temperature. From these rate constants and the equilibrium constants at each temperature, k_i values were calculated (Table I). The bulk of the contents of each ampoule was submitted to preparative glc (base line) separation on a 2 ft × 0.25 in. column, 20% SE-30 on 60–80 Firebrick with helium as carrier gas at 160° fitted in a F & M Model 720 instrument. For each point, the sum of the weights of (*Z*)-**1** and (*E*)-**1** condensed accounted for about 50% of the starting material put in each tube. Control experiments with mixtures of optically active (*Z*)- and (*E*)-**1** demonstrated complete separation and complete preservation of the optical purity of each isomer during separation. The rotation of each isomer from each ampoule was taken in ethyl acetate (*c* ∼0.15). From the rotations of the (*Z*)-**1** samples, least-squares, first-order rate constants for racemization ($k_\alpha{}^Z$) were calculated for each temperature (Table I). From the rotations of the (*E*)-**1** samples taken in ethyl acetate (*c* ∼0.15), five-point plots of optical rotations of recovered (*E*)-**1** *vs.* time were made for each temperature. The fraction of (*E*)-**1** in the mixture of (*E*)-**1** plus (*Z*)-**1** was obtained at each time from a least-squares line of a plot of log [(*Z*)-**1**] *vs.* time (data provided by analytical glc for each point). From values taken from these plots and eq 5–7 were calculated [(+)-(*E*)-**1**] − [(−)-(*E*)-**1**] values at times, *t*. From these values, values of $k_\alpha{}^E$ at the two temperatures (see next section) and eq 3 were calculated least-square values of $k_a - k_b$. These values coupled with k_i values and eq 4 gave the k_a and k_b values of runs 1 and 2 of Table I. The activation energy for isomerization (k_i) was E_a = 39.7 kcal/mol. For epimerization at the cyanoacetate carbon (k_a), E_a = 39.0 kcal/mol, and at the benzyl carbon (k_b), E_a = 39.2 kcal/mol. These values were used to extrapolate estimates of k_i, k_a, and k_b at 126° (listed under run 5, Table I).

Kinetics of Racemization of (−)-(*E*)-1 in Benzene (Runs 3 and 4). A solution of 0.100 g of (−)-(*E*)-**1**, $[\alpha]^{25}{}_{546}$ −251° (*c* 0.55, EtOAc), in 35 ml of benzene (distilled from 4A Sieves) was divided as in runs 1 and 2 among ten ampoules. Five of these were placed in a Lauda thermostat at 205.2 ± 0.2° (run 3) and five in a thermostat at 184.4° (run 4). The ampoules after appropriate times were quenched and opened, and the contents were subjected to preparative glc separation as in runs 1 and 2. The rotation of each sample of (*E*)-**1** isolated from each point was taken in ethyl acetate (*c* 0.15), and from the rotations were calculated least-squares, first-order rate constants (k_α) at each temperature (Table I). From the $k_\alpha{}^E$ values of runs 3 and 4 was calculated E_a = 17.8 kcal/mol, which was used to extrapolate $k_\alpha{}^E$ values to the temperatures of runs 1 and 2, under which the extrapolated values are listed (Table I). In runs 3 and 4, too little (*Z*)-**1** was produced for polarimetric examination.

Geometric Isomerization in DMF of (+)-(*Z*)-1 to (+)-(*E*)-1 and (−)-(*E*)-1 (Runs 6 and 7). Reagent grade DMF was distilled from Molecular Sieves, and a center cut was taken. Two solutions of 0.0210 g of optically pure (+)-(*Z*)-**1** of $[\alpha]^{25}{}_{546}$ +175 ± 1° (*c* 0.192, EtOAc) in 10 ml of DMF were prepared and put in two separate ampoules (20-ml capacity), which were prepared, degassed, and sealed as in runs 1 and 2. For run 6, one ampoule was thermostated at 126.0 ± 0.2° for 1 hr and thermally quenched. For run 7, the other ampoule was thermostated at 100.0 ± 0.2° for 17.2 hr, and thermally quenched. In each run, the ampoule's content was shaken with 30 ml of water and ether, and the aqueous phase was washed twice with ether. The combined ether layers were washed with brine, dried over sodium sulfate, and rotary evaporated under vacuum. A small portion of each residue was submitted to analytical glc analysis. From the result and the equilibrium constants for (*Z*)-**1** ⇄ (*E*)-**1** of 10 at 126° and 12 at 100° (see Results section) were calculated one-point, first-order rate constant values for geometric isomerization of (*Z*)-**1** to (*E*)-**1** (Table I). The bulk of the contents of each ampoule was submitted to preparative glc (see runs 1 and 2 for conditions) to give samples of (+)-(*Z*)-**1**, both $[\alpha]^{25}{}_{546}$ +174 ± 1° (*c* 0.265 in run 6 and 0.185 in run 7). The (+)-(*E*)-**1** in run 6 gave $[\alpha]^{25}{}_{546}$ +232° (*c* 0.30, EtOAc) which was of 92.8% maximum rotation ($[\alpha]^{25}{}_{546}$ ±251°). The (+)-(*E*)-**1** in run 7 gave $[\alpha]^{25}{}_{546}$ +245° (*c* 0.40, EtOAc), which was of 97.7% maximum rotation. These samples of (*E*)-**1** exhibited nmr and mass spectra identical with those of authentic samples.

Runs 6′ and 7′ parallel to runs 6 and 7 were made that involved identical concentrations, times, temperatures, and isolation techniques. However, samples of (−)-(*E*)-**1** of $[\alpha]^{25}{}_{546}$ −247° (*c* 0.243, EtOAc) were used in place of (+)-(*Z*)-**1**. The *Z* isomer (∼1%) was not isolated. The *E* isomer isolated from both runs gave $[\alpha]^{25}{}_{546}$ −246 ± 1° (*c* 0.343 in run 6′ and *c* 0.150 in run 7′). In runs 6, 7, 6′, and 7′, the amount of product condensed from the preparative glc runs was about 50% of the total starting material. Control runs on the preparative glc procedure also gave about 50% condensation from the carrier gas.

In a control experiment at 126°, a solution of (*Z*)-**1** in DMF with octadecane as internal standard was run for 1.00 hr. Glc analysis of the product showed that if starting material = 100%, 95% of (*E*)-**1** and (*Z*)-**1** remained.

Kinetics of Racemization of (−)-(*E*)-1 in DMF (Run 8). A solution of 0.086 g of (−)-(*E*)-**1** of $[\alpha]^{25}{}_{546}$ −246° (*c* 0.841, EtOAc) in 25.0 ml of DMF (purified as in runs 5 and 6) was distributed in ampoules that were degassed and sealed as in runs 1 and 2. The tubes were thermostated at 126°, and withdrawn periodically over 12 hr. The first tube for time = 0 was withdrawn after 10 min, chilled, and opened, and the rotation at λ 546 nm of its contents taken in a 1-dm tube thermostated at 25.0°, α_{obsd} −0.781°. Four more tubes were quenched at appropriate times and gave the following rotations: 3.10 hr, −0.771°; 5.40 hr, −0.765°; 8.00 hr, −0.762°; 12.00 hr, −0.726°. From these values, and the assumption that at $t = \infty$, α_{obsd} = 0.000, the $k_\alpha{}^E$ of run 8 was calculated (Table I).

Kinetics of Geometric Isomerization of (+)-(*Z*)-1 to (+)-(*E*)-1 (Runs 9 and 10). A solution of 0.0308 g of optically pure (+)-(*Z*)-**1** of $[\alpha]^{25}{}_{365}$ +477° (*c* 0.137, DMF) in 25.0 ml of DMF was prepared and distributed among ampoules that were degassed and sealed as in runs 1 and 2. Five tubes were thermostated at 125.4 ± 0.02° (run 9) and five at 99.4 ± 0.2° (run 10). At appropriate times, the tubes were thermally quenched, and the rotations of their contents were taken in a thermostated (25.0°), 1-dm polarimeter tube at λ 365 nm. In run 9, the times and observed rotations were as follows: 0 min, 0.615°; 10.0 min, 0.642°; 25.0 min, 0.671°; 45.0 min, 0.715°; 70.0 min, 0.752°. In run 10, the times and observed rotations were as follows: 0 hr, 0.598°; 0.500 hr, 0.612°; 2.00 hr, 0.650°; 4.00 hr, 0.696°; 9.00 hr, 0.766°. A sample of optically pure (+)-(*E*)-**1** gave $[\alpha]^{25}_{365}$ −801° (*c* 0.151, DMF). From this value, the value for optically pure (+)-(*Z*)-**1** (see above), and the equilibrium constants for (*Z*)-**1** $\rightleftarrows$ (*E*)-**1** of 12 at 100° and 10 at 126° were calculated rotations at equilibrium ($t = \infty$) of α^{25}_{365} 0.992° for run 9 and α^{25}_{365} 0.975° for run 10. Integrated first-order rate constants for the approach to equilibrium were calculated for each run. From these rate constants and the equilibrium constants were calculated the k_i values of Table I.

From the k_i values of runs 9 and 10 was calculated $E_a = 19.1 \pm 1.5$ kcal/mol. Extrapolation of k_i to 34° for purposes of comparison of the catalyzed[8a] with noncatalyzed epimerization rate gave $k_i = 7.46 \times 10^{-8}\ \text{sec}^{-1}$.

Photochemical Stereoisomerization Reactions of the Stereoisomers of 1 (Runs 11–14). In runs 11 and 12, 0.500 g of (*Z*)-**1** and (*E*)-**1**, respectively, was dissolved in 200 ml of reagent grade acetone. The solutions were each irradiated for 6 hr with a Hanovia 450-W medium-pressure lamp fitted with a 1-mm Corex ($\lambda > 267$ mm) filter. The solutions were contained in a Pyrex housing in which a water-jacketed quartz well was immersed. Small samples of the resulting solutions were evaporated and submitted to analytical glc (see runs 1 and 2). Each gave [(*E*)-**1**]/[(*Z*)-**1**] = 1.5. An identical experiment with (*E*)-**1** in cyclohexane gave [(*E*)-**1**]/[(*Z*)-**1**] = 19. In run 13, 0.030 g of (+)-(*Z*)-**1** of $[\alpha]^{25}_{546}$ +112° (*c* 0.15, EtOAc) was dissolved in 200 ml of acetone and irradiated as in run 11 for 3 hr. The solutions were then evaporated and submitted to preparative glc as in runs 1 and 2 (analytical glc indicated 25% conversion). The (*Z*)-**1** isolated gave $[\alpha]^{25}_{546}$ +51° (*c* 0.35, EtOAc), and the (*E*)-**1**, $[\alpha]^{25}_{546}$ 0 ± 2° (*c* 0.18, EtOAc). In run 14, 0.153 g of (−)-(*E*)-**1** of $[\alpha]^{25}_{546}$ −251° (*c* 0.62, EtOAc) dissolved in 200 ml of acetone was irradiated as in run 11 for 4 hr. The solution was concentrated and the product submitted to preparative glc (as in runs 1 and 2). Isomer (*E*)-**1** gave $[\alpha]^{25}_{546}$ −19.5° (*c* 0.17, EtOAc), and (*Z*)-**1** gave $[\alpha]^{25}_{546}$ 0.0° (*c* 0.13, EtOAc).

Studies in Stereochemistry. XLVI. Singlet Diradical Transition States in Epimerization Reactions of Substituted Cyclopropanes[1]

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Abstract: Changes in rates and products with changes in solvent polarity have been used to differentiate between singlet diradical and zwitterionic transition states in the epimerization reactions of the stereoisomers of methyl 1,2-diphenylcyclopropanecarboxylate (**1**). The four stereoisomers of **1** were prepared in an optically pure state. Their relative configurations were firmly established, and their absolute configurations were assigned by rotation–configuration correlations. Oil (+)-(*Z*)-**1** has the 1-(*R*)-2-(*R*) configuration, $[\alpha]^{25}_{546}$ + 272° (*c* 0.14, $CHCl_3$); (−)-(*Z*)-**1** (oil) has the 1-(*S*)-2-(*S*) configuration, $[\alpha]^{25}_{546}$ −272° (*c* 0.28, $CHCl_3$). Solid (+)-(*E*)-**1**, mp 98.5–99°, has the 1-(*S*)-2-(*R*) configuration, $[\alpha]^{25}_{546}$ +55.5° (*c* 0.32, $CHCl_3$); (−)-(*E*)-**1**, mp 98.5–99°, has the 1-(*R*)-2-(*S*) configuration, $[\alpha]^{25}_{546}$ −55.7° (*c* 0.55, $CHCl_3$). Equilibrium constants between diastereomers ((Z)-**1** $\rightleftarrows$ (*E*)-**1**) were determined thermally: $K_{164^\circ}{}^{CH_3OH} = 2.15$; $K_{184^\circ}{}^{CH_3OH} = 2.00$; $K_{184^\circ}{}^{C_6H_6} = 1.92$. In methanol and benzene at 184.4°, and in methanol at 164.6°, geometric isomerization of (*Z*)-**1** to (*E*)-**1** followed good first-order kinetics (rate constant k_i). Values of k_i exceeded those of racemization of optically active (*Z*)-**1** or of (*E*)-**1** by over a power of ten. Optically pure (−)-(*Z*)-**1** in benzene and in methanol at 184.4° was partially isomerized to (+)-(*E*)-**1**; the isomers were separated and their optical purities determined. The results coupled with values of k_i allowed calculation of the first-order rate constants for epimerization of (*Z*)-**1** at the benzyl center (k_b) and at the phenylacetate center (k_a) in both solvents at 184.4°. The following rate ratios emerged: $k_b{}^{CH_3OH}/k_b{}^{C_6H_6} \sim 0.8$; $k_a{}^{CH_3OH}/k_a{}^{C_6H_6} \sim 0.8$; $k_b{}^{CH_3OH}/k_a{}^{CH_3OH} = 12.3$; $k_b{}^{C_6H_6}/k_a{}^{C_6H_6} = 13.3$. These data provide the following conclusions. The epimerization reactions at each chiral center must include face-to-edge configurations on their reaction coordinates that the rate-limiting transition states resemble. In these states, the original bonding orbitals are orthogonal, and must be either zwitterionic or singlet diradical, but cannot be a blend. The lack of rate dependence on solvent polarity at each center of system **1** indicates these orthogonal transition states to be singlet diradical rather than zwitterionic. In the absence of polar effects in the orthogonal state, steric factors favor rotation of the benzyl center over the phenylacetate center by a power of ten (hydrogen of the edge turned inward toward the face of the phenylacetate center). These results are contrasted with those of the methyl 1-cyano-2-phenylcyclopropanecarboxylate system (**2**). For the isomers of **2**, rates of epimerization at both the benzyl and cyanoacetate centers decreased by $\sim 10^4$ in passing from dimethylformamide to benzene. In **2**, the cyanoacetate center rotated from 88 to 4 times as fast as the benzyl center. In **2**, the orthogonal transition states were zwitterionic.

In the last paper of this series,[3] an operational criterion was developed for differentiating between zwitterion or singlet diradical transition states for epimerimization reactions of the stereoisomers of methyl 1-cyano-2-phenylcyclopropanecarboxylate (**2**). The singlet reaction path for epimerization must include both face-to-face structures (A) and face-to-edge structures (B or C). In face-to-face structures, orbital overlap between the ends of the opened structure is

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