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** ⇄ (*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 $k_i = 7.46 \times 10^{-8}$ 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 (λ >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** ⇄ (*E*)-**1**) were determined thermally: $K_{164°}^{CH_3OH} = 2.15$; $K_{184°}^{CH_3OH} = 2.00$; $K_{184°}^{C_6H_6} = 1.92$. 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 ~10⁴ 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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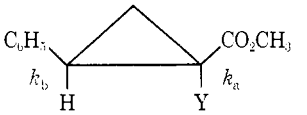
[2] NDEA Title IV Predoctoral Fellow, UCLA, 1966–1969.

[3] N. E. Howe, E. W. Yankee, and D. J. Cram, *J. Amer. Chem. Soc.*, **95**, 4230 (1973).

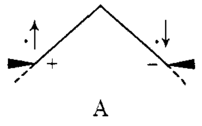
possible, and zwitterionic and diradical character can be blended (A). In face-to-edge structures, the orbitals are orthogonal, and must be either singlet diradical (B) or zwitterionic (C). The transition states for epimerization are probably close to face-to-edge structures.

Epimerization rates of **2** at the cyanoacetate (k_a) and benzyl centers (k_b) were found to decrease by about 10^4 in passing from the polar solvent, dimethylformamide (DMF), to the nonpolar solvent, benzene.[3] Thus, the transition states for the epimerization of the isomers of **2** were zwitterionic, and involved a C-like structure. The cyano and carbomethoxy substituents provide a strong bias for negative charge to concentrate at C-1, and the phenyl a smaller bias for positive charge to concentrate at C-2 of the opened singlet structure derived from **2**.

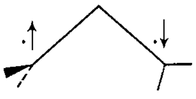
This paper reports the results of a similar study of the stereoisomers of **1**. Systems **1** and **2** differ only in that in **1** the acetate center has a phenyl instead of the cyano substituent of **2**. Phenyl in place of cyano lowers the bias for zwitterionic character that favors transition state C for system **2**. Thus it seemed possible that the epimerization reactions of **1** would have singlet diradical transition states (B) of lower energy than the zwitterionic alternatives (C). Accordingly, the four stereoisomers of **1** were prepared, and their epimerization reaction rates were studied as a function of solvent polarity.



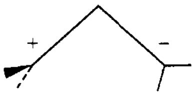
1, Y = C_6H_5
2, Y = CN



A
face-to-face



B
face-to-edge
singlet diradical



C
face-to-edge
zwitterion

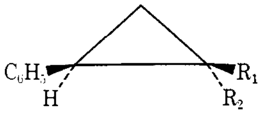
Results

Preparation and Determination of Configurations of the Stereoisomers of Methyl 1,2-Diphenylcyclopropanecarboxylate (1). Addition of dimethyloxosulfonium methylide to methyl α-phenylcinnamate gave (85%) **1** as a mixture of diastereomeric racemates in about equal amounts. Base-catalyzed hydrolysis of the esters gave salts of the corresponding acids (**3**) which were separated by selective precipitation by controlled acidification of the mixture. After crystallization, (*Z*)-**3** (32%) and (*E*)-**3** (31%) were obtained, and were converted with diazomethane to the corresponding esters, (*Z*)-**1** and (*E*)-**1**.[4] The configurational assignments of the racemates of **1** and **3** were based on three grounds. The nmr chemical shift of the methyl proton of (*Z*)-**1** came at δ 3.2, and those of (*E*)-**1** at δ 3.5. Others[5] have correlated methyl ester chemical shifts with their geometric relation to a phenyl group on a β carbon in conformationally constrained systems, and the correlation fitted well with system **2**.[6] The pK_a's of (*Z*)-**3** and (*E*)-**3** were determined potentiometrically in 60% ethanol–water against 0.03 *N* sodium hydroxide in 60% ethanol–water.[7] The pK_a of (*Z*)-**3** came at 6.25, and that of (*E*)-**3** at 6.70. The pK_a's of the structurally related α-phenylcinnamic acids in the same medium are 4.8 for the *Z* and 6.1 for the *E* isomers.[8] Thus, the carboxyl group cis to the phenyl in both the cyclopropane and olefin isomers is the more acidic. At equilibrium at 164.6° in methanol, [(*E*)-**1**]/[(*Z*)-**1**] = 2.15 (see below). Phenyl cis to a carboxylic acid group is less stable than two phenyls cis to one another,[9] and the carbomethoxy group is larger than the carboxylic acid group.

Acid (*Z*)-**3** was resolved through its quinine salt to give (41%) (−)-(*Z*)-**3**, mp 103.5–104°, $[\alpha]^{25}_{546}$ − 302° (*c* 0.66, $CHCl_3$), and (12%) (+)-(*Z*)-**3**, mp 103.5–104°, $[\alpha]^{25}_{546}$ +300° (*c*, 0.45). Diazomethane and (−)-(*Z*)-**3** gave (−)-(*Z*)-**1** (95%) as an oil, $[\alpha]^{25}_{546}$ −272° (*c* 0.28, $CHCl_3$). Similarly, (+)-(*Z*)-**3** gave (95%) (+)-(*Z*)-**1**, $[\alpha]^{25}_{546}$ +272°. Acid (*E*)-**3** was resolved incompletely through its quinine salt, and the crude acids were converted to their methyl esters, which were recrystallized to optically purity. Thus (−)-(*E*)-**3** gave (−)-(*E*)-**1** (15% overall), mp 98.5–99°, $[\alpha]^{25}_{546}$ −55.7° (*c* 0.55, $CHCl_3$), and (+)-(*E*)-**3** gave (+)-(*E*)-**1** (9%) overall), mp 98.5–99°, $[\alpha]^{25}_{546}$ +55.5° (*c* 0.32, $CHCl_3$). At concentrations below *c* 1 in $CHCl_3$, the specific rotations of the four stereoisomers of **1** were independent of concentration.

The relative configurations of the four stereoisomers of **1** were determined by ozonolysis of (+)-(*Z*)-**3** and (−)-(*E*)-**3** to their corresponding optically active 1,1,2-cyclopropanetricarboxylic acids, which were converted to their trimethyl esters (**4**). From (+)-(*Z*)-**3** was obtained (+)-**4**, and (−)-(*E*)-**3** gave (−)-**4**. Thus (+)-(*Z*)-**3** and (+)-(*Z*)-**1** have configurations at the benzyl center identical with those of (+)-(*E*)-**3** and (+)-(*E*)-**1**, respectively. Likewise, (+)-(*Z*)-**3** and (+)-(*Z*)-**1** have configurations at the phenylacetate center opposite to those of (+)-(*E*)-**3** and (+)-(*E*)-**1**, respectively.

The absolute configurations of the four stereoisomers of **1** and **3** were tentatively assigned based on correlations of their signs of rotation with the signs of rotation of a series of 2-phenyl substituted cyclopropanecarboxylic acids, esters, amides, and nitriles of established absolute configuration. Nine 2-phenylcyclopropane derivatives that possess the absolute configuration of **5**



(+)-**5**

R_1 = H, R_2 = CO_2CH_3; R_1 = CO_2CH_3, R_2 = H;[10] R_1 = R_2 = CN;[6] R_1 = CN, R_2 = CO_2CH_3;[6] R_1 = CO_2CH_3, R_2 = CN;[6] R_1 = CN, R_2 = $CONH_2$;[6] R_1 = $CONH_2$, R_2 = CN;[6] R_1 = CN, R_2 = CO_2H;[6] R_1 = CO_2H, R_2 = CN[6]

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[4] For *Z* and *E* nomenclature, see J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968).

[5] G. L. Kruger, F. Kaplan, M. Orchin, and W. H. Fauly, *Tetrahedron Lett.*, 3979 (1965).

[6] E. W. Yankee, B. Spencer, N. E. Howe, and D. J. Cram, *J. Amer. Chem. Soc.*, **95**, 4220 (1973).

[7] L. Meites and H. C. Thomas, "Advanced Analytical Chemistry," McGraw-Hill, New York, N. Y., 1958, p 90.

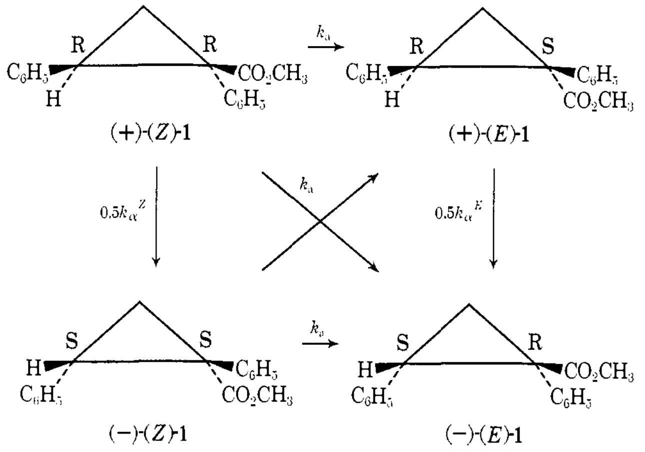
[8] L. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath, Boston, Mass., 1957, pp 182–185.

[9] D. Y. Curtin and B. Luberoff [Abstracts, 13th National Organic Symposium of the American Chemical Society, Ann Arbor, Mich., June 1953, p 40] reported *K* = 6 for *cis*-α-phenylcinnamic acid ⇄ trans isomer.

[10] T. Aratani, Y. Nakanisi, and H. Noyaki, *Tetrahedron Lett.*, 1809 (1969).

at the benzyl carbon possess the same plus sign of rotation. The configurational assignments are strengthened by a calculation of the signs and magnitudes of rotation of the stereoisomers of **3** based on Brewsters rules.[11] The calculated molecular rotation for **3** of the 1-(*R*)-2-(*R*) configuration is [M]D +327°, and that found for (+)-(*Z*)-**3** was $[M]_{546}$ +720°. The calculated molecular rotation for **3** of the 1-(*S*)-2-(*R*) configuration is [M]D +210°, and that found for the most optically pure sample of (+)-(*E*)-**3** obtained was $[M]_{546}$ +160°. Chart I summarizes the configurational assignments.

Chart I



The conclusions of this paper depend only on the validity of assignment of the relative and not absolute configurations.

Geometric Isomerization Equilibria and Kinetics. Geometric isomers (*Z*)- and (*E*)-**1** were equilibrated thermally in sealed, degassed ampoules in dry methanol and benzene. Equilibrium was reached starting with each isomer and 1,1,1-triphenylethane as internal standard in runs 1–4 in methanol at 184.4 and 164.6°. In run 5 in benzene at 184.4°, equilibrium was approached only from (*Z*)-**1** (internal standard). After 22 half-lives of isomerization (see below), the three-component mixtures were analyzed by glc (±0.2%, good base line separation). Less than 3% decomposition of (*Z*)-**1** and (*E*)-**1** was observed, and mixtures of identical composition in runs 1 and 2 and in 3 and 4 were obtained from each isomer. Table I records the results. From the equilibrium constants, the ground state thermodynamic parameters in methanol at 184.4° were calculated for the [(*Z*)-**1** ⇄ (*E*)-**1**] equilibrium: $\Delta G = -0.63$ kcal/mol; $\Delta H = -1.45$ kcal/mol; $\Delta S = -1.8$ eu.

Table I. Equilibrium and First-Order Rate Constants for Geometric Isomerization of (*Z*)- and (*E*)-Methyl 1,2-Diphenylcyclopropanecarboxylates ((*Z*)-**1** and (*E*)-**1**)

Run no.	Starting material Isomer	Starting material Concn, *M*	Solvent	Temp, °C[a]	10^6k_i, $\sec^{-1}$[b]	K_{equil}[c]
1	(*Z*)-**1**	0.032	CH_3OH	184.37		2.00
2	(*E*)-**1**	0.048	CH_3OH	184.37		2.00
3	(*Z*)-**1**	0.032	CH_3OH	164.55		2.15
4	(*E*)-**1**	0.048	CH_3OH	164.55		2.15
5	(*Z*)-**1**	0.037	C_6H_6	184.37		1.92
6[d]	(*Z*)-**1**	0.032	CH_3OH	184.37	9.49 ± 0.12	
7[d]	(*Z*)-**1**	0.032	CH_3OH	164.55	1.408 ± 0.016	
8[e]	(*Z*)-**1**	0.037	C_6H_6	184.37	12.2 ± 0.2	

[a] ±0.02°. [b] Least-squares analyses with limits of error of two standard deviations. [c] Determined after 22 half-lives.

The kinetics of approach of (*Z*)-**1** to the equilibrium mixture was followed for about 3 half-lives in methanol at 184.4 and 164.6° (runs 6 and 7), and in benzene at 184.4° (run 8). The same techniques were used in the kinetic as in the equilibrium experiments. Strict first-order kinetics were observed over the range followed. From the rate data and equilibrium constants were calculated the rate constants (k_i) for geometric isomerization of (*Z*)-**1** → (*E*)-**1**. Table I records the k_i values. Thermodynamic activation parameters based on k_i values in methanol were calculated for 184.4°: $\Delta G^{\ddagger} = 37.7$ kcal/mol; $\Delta H^{\ddagger} = 37.4 \pm 0.5$ kcal/mol; $\Delta S^{\ddagger} = -0.7 \pm 1.2$ eu.

Exploratory runs made with (*Z*)-**1** in methanol, chlorobenzene, and acetonitrile as solvents at 175° with triphenylmethane as internal standard demonstrated extensive loss of both triphenylmethane and (*Z*)-**1** during reaction, and little difference in rate of isomerization in the three media. Additional one-point runs were made in dimethylformamide (DMF) in the absence and presence of 0.10 *M* LiBr. Table II records the latter results. These data indicate that lithium bromide does not catalyze the isomerization, but does catalyze the decomposition of the isomers of **1**, probably by bromide ion attack on the methyl group. Run 13 made in the absence of lithium bromide at 175° showed only 9% loss of material, and 27.1% of the remaining (*Z*)- and (*E*)-**1** was (*E*)-**1**. From the equilibrium constants of runs 1–5, an estimate of *K* in DMF at 175° is 2.07. From this value and the per cent conversion of (*Z*)-**1** to (*E*)-**1** in run 5 at 175° is estimated the one-point rate constant $k_i \sim 2.5 \times 10^{-6}$ $\sec^{-1}$. Interpolation of k_i values obtained in methanol (runs 6 and 7) to 175° gave 3.9×10^{-6} $\sec^{-1}$.

Table II. Isomerization and Decomposition of 0.021 *M* Solutions of (*Z*)-**1** in DMF–0.1 *M* Lithium Bromide and Control Experiments

Run no.	Temp, °C	Time, hr	% (*E*)-**1** produced[a]	% loss ((*Z*)-**1** + (*E*)-**1**)[b]
9	25	0	0.2	0
10	125	24	0.2	8
11	150	24	2.0	40
12	175	23.3	18.0	>95
13[c]	175	23.3	27.1	9

[a] 100[(*E*)-**1**]/([(*E*)-**1**] + [(*Z*)-**1**]). [b] Measured against 1,1,1-triphenylethane as internal standard. [c] Run made in absence of lithium bromide.

Partition of Geometric Isomerization Rate Constants into Epimerization Rate Constants at Two Chiral Centers. In runs 14–17, optically pure samples of (−)-(*Z*)-**1** were allowed to geometrically isomerize 10–30% to (*E*)-**1** at 184.4° in methanol or benzene, and the mixtures were quenched. The per cent conversions were calculated from the rate constants (Table I) and the reaction times. The mixtures were separated by column chromatography into pure (*Z*)-**1** fractions (glc), and mixtures of (*Z*)-**1** and (*E*)-**1** fractions, which could not be completely separated. The rotations of the pure (glc), distilled (*Z*)-**1** fractions were taken and their

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[11] J. H. Brewster, *J. Amer. Chem. Soc.*, **81**, 5433, 5475 (1959).

Table III. Thermal Epimerizations and Racemizations of Optically Pure (−)-(*Z*)-**1** at 184.4°

Run no.	(−)-(*Z*)-**1**, concn, *M*	Solvent	Time, min	% yield (*E*)-**1**[a]	% optical purity recovered (−)-(*Z*)-**1**	% optical purity of produced (+)-(*E*)-**1**
14	0.40	CH_3OH	200	10	100.0 ± 0.5	85 ± 1
15	0.22	CH_3OH	410	20	99.5 ± 0.5	85 ± 1
16	0.40	CH_3OH	717	30	99.0 ± 0.5	83 ± 1
17	0.32	C_6H_6	320	20	99.5 ± 0.5	86 ± 1

[a] Calculated based on times and k_i values of Table I.

optical purities determined. The optical purities of the (*E*)-**1** components of the mixture of (*Z*)- and (*E*)-**1** isomers were determined indirectly. The exact balance of the two isomers in each mixture was determined by analytical glc (±0.2%). Control experiments demonstrated: (1) the rotations of optically active (*Z*)- and (*E*)-**1** were additive over the range involved at several wavelengths; (2) during chromatography or distillation, optically active (*Z*)- and (*E*)-**1** did not optically fractionate or racemize. From these data, the optical purities of the (+)-(*E*)-**1** formed from (−)-(*Z*)-**1** were determined. Table III records the results.

The data of Table III indicate that $k_i > k_\alpha{}^Z$ or $k_\alpha{}^E$ where $k_\alpha{}^Z$ and $k_\alpha{}^E$ are defined as first-order rate constants for racemization of optically active (*Z*)-**1** and (*E*)-**1**, respectively. If the 1% racemization of (−)-(*Z*)-**1** of run 16 is real, then $k_\alpha{}^Z \sim 3 \times 10^{-7}$ sec^{-1}, whereas $k_i = 94.9 \times 10^{-7}$ sec^{-1}. Thus in methanol $k_i/k_\alpha{}^Z \sim 32$. The identical degree of purity of (−)-(*Z*)-**1** (99.5 ± 0.5%) obtained in methanol and benzene after 20% conversion indicates a similar order of magnitude for the ratio in benzene. The optical purity of the (+)-(*E*)-**1** produced changed little with either time or solvent, which indicates $k_i/k_\alpha{}^E \gtrsim 10$. We conclude that the dominant reactions of (−)-(*Z*)-**1** are epimerization at the benzyl center to give (+)-(*E*)-**1** (rate constant k_b), and epimerization at the phenylacetate center (rate constant k_a) to give (−)-(*E*)-**1** (Chart I).

These data allow estimates to be made of k_a and k_b values. To a first approximation, eq 1–4 apply, (3) and (4) of which provide two simultaneous equations in two unknowns. Table IV lists these values and the runs used for their calculations.

Table IV. Estimates of First-Order Rate Constants for Epimerization at the Benzyl Center (k_b) and Phenylacetate Center (k_a) of (+)-(*Z*)-**1** at 184.4°

Runs used	Solvent	$10^6 k_b$, sec^{-1}	$10^6 k_a$, sec^{-1}
6 + 15	CH_3OH	8.78	0.716
8 + 17	C_6H_6	11.3	0.854

$$d[(+)\text{-}(E)\text{-}\mathbf{1}]/dt = k_b[(-)\text{-}(Z)\text{-}\mathbf{1}] \quad (1)$$

$$d[(-)\text{-}(E)\text{-}\mathbf{1}]/dt = k_a[(-)\text{-}(Z)\text{-}\mathbf{1}] \quad (2)$$

$$[(+)\text{-}(E)\text{-}\mathbf{1}]/[(-)\text{-}(E)\text{-}\mathbf{1}] = k_b/k_a \quad (3)$$

$$k_a + k_b = k_i \quad (4)$$

Discussion

Lack of Effect of Solvent Polarity on Geometric Isomerization and Epimerization Rates for Diastereomers of Methyl 1,2-Diphenylcyclopropanecarboxylate (1). The first-order rate constants for geometric isomerization (k_i) of system **1** show trivial change with large changes in solvent character. The rate ratios are listed below. The $k_i{}^{DMF}/k_i{}^{C_6H_6}$ value is derived from the other two ratios. The reasonable assumption is made that the first two ratios listed would not change much with a 9° change in temperature. The rate ratios for methyl 1,2-diphenylcyclopropanecarboxylate (**1**) are all within a factor of 2 of one another as solvent is changed from benzene to methanol to DMF. These three solvents represent extremes of character. Benzene is a hydrocarbon and is nonpolar. Methanol is polar, frequently enters into solvolytic reactions, and is somewhat structured by hydrogen bonding in the liquid state. DMF is an aprotic, dipolar solvent.

$$(k_i{}^{CH_3OH}/k_i{}^{C_6H_6})_{184°} \sim 0.8 \text{ (runs 6 + 8)}$$

$$(k_i{}^{DMF}/k_i{}^{CH_3OH})_{175°} \sim 0.6 \text{ (runs 6, 7 + 13)}$$

$$(k_i{}^{DMF}/k_i{}^{C_6H_6})_{175-184°} \approx 0.5 \text{ (runs 6, 7, 13 + 8)}$$

The absence of isomerization rate dependence on solvent polarity indicates little or no change in the free energies of solvation of (*Z*)-**1** as starting material, and those of the rate-limiting transition states for (*Z*)-**1** → (*E*)-**1**. Those transition states must approach a face-to-edge geometry in which the orbitals are orthogonal to one another, and must be either singlet diradical (B) or zwitterionic (C). A zwitterion such as C should be much more stabilized by solvation than the starting state. A singlet diradical such as B should be solvated to about the same extent as the starting state. Polar solvents like methanol or DMF stabilize zwitterions such as C much more than nonpolar solvents like benzene. Neutral species such as (*Z*)-**1** or diradical B should be stabilized similarly by polar and nonpolar solvents. The proximity of the k_i ratios to unity indicates that diradical B is a good and zwitterion C is a poor model for the rate limiting transition state for (*Z*)-**1** → (*E*)-**1**.

$$(k_b{}^{CH_3OH}/k_b{}^{C_6H_6})_{184°} \sim 0.8 \text{ (runs 6, 8, 15 + 17)}$$

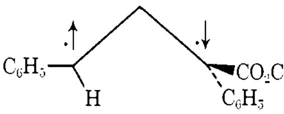
$$(k_a{}^{CH_3OH}/k_a{}^{C_6H_6})_{184°} \sim 0.8 \text{ (runs 6, 8, 15 + 17)}$$

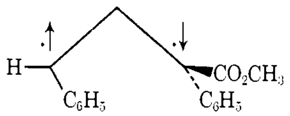
The values of k_b and k_a change little with changes in solvent from methanol to benzene (see k_b and k_a rate ratios). Thus, the conclusions applied generally to the lack of sensitivity of geometrical isomerization rates apply specifically to the epimerization rates at the benzyl and phenylacetate centers.

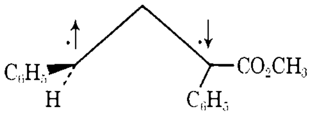
$$(k_b{}^{CH_3OH}/k_a{}^{CH_3OH})_{184°} \sim 12 \text{ (runs 6 + 15)}$$

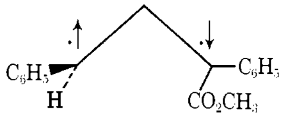
$$(k_b{}^{C_6H_6}/k_a{}^{C_6H_6})_{184°} \sim 13 \text{ (runs 8 + 17)}$$

The values of k_b/k_a listed measure the relative rates of epimerization at the benzyl (k_b rate constant) and at the phenylacetate (k_a rate constant) centers. In both methanol and benzene at 184°, rotation of the benzyl center exceeds that of the phenylacetate center by a factor of 12–13. Edge-to-face orthogonal structure D[12] is less sterically constrained than alternative structure E for rotation at benzyl, or either face-to-edge structures F or G for rotation at the phenylacetate center. There is no basis for ranking F or G as the more stable.


D

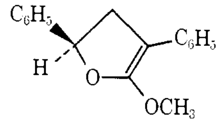

E

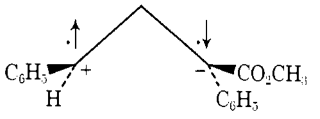

F


G

Ketene acetal, H, is a possible intermediate in the minor reaction, (+)-(Z)-**1** → (+)-(E)-**1** (see Chart I). It is also possible that formation of H from (+)-(Z)-**1** and its decomposition to form (+)-(E)-**1** could be one-transition-state processes. Should such a mechanism apply, the rate constant for decomposition of H would have to be higher valued than that for its formation.

Such an intermediate is impossible for the major reaction, (+)-(Z)-**1** → (−)-(E)-**1**, and provides no explanation for the fact that the major and minor reaction rates show the same response to major changes in medium. Its presence on the reaction path is unlikely.

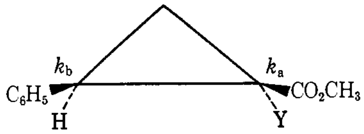

H


J

The question of whether face to-face structures such as J are energy minima on the reaction coordinates is both interesting and hard to answer. The observation that triphenylmethane was consumed somewhat when present in isomerizing reaction mixtures suggests the possibility that intermediates such as J did exist, and could behave like a diradical in hydrogen atom transfer reactions. Only intermediates and not transition states could be intercepted by hydrogen atom donors. Further experimental work is needed before firm conclusions can be reached.

Zwitterionic *vs.* Diradical Transition States in Epimerization Reactions of Substituted Cyclopropanes. The dramatic differences in the behavior of (Z)-**1** and (Z)-**2**[3] to changes in medium provide the strongest evidence for differentiation of zwitterionic and singlet diradical orthogonal structures as transition states on reaction coordinates for epimerization reactions. Chart II[12] summarizes the differences in terms of geometric isomerization rate constant (k_i) ratios, benzyl epimerization (k_b), and acetate epimerization (k_a) rate constant ratios. Rate constants k_i, k_b, and k_a are related by $k_i = k_b + k_a$. The differences in reactivity of **1** and **2** prevented the rate ratios from being compared at the same temperature in most cases.

Chart II



(+)-(Z) isomer

	(+)-(Z)-**1** (Y = C_6H_5)	(+)-(Z)-**2** (Y = CN)
$k_i^{DMF}/k_i^{C_6H_6}$	~0.5 at 175°	~32,000 at 126°
$k_i^{CH_3OH}/k_i^{C_6H_6}$	~0.8 at 184°	
$k_b^{CH_3OH}/k_b^{C_6H_6}$	~0.8 at 184°	
$k_a^{CH_3OH}/k_a^{C_6H_6}$	~0.8 at 184°	
$k_b^{DMF}/k_b^{C_6H_6}$		~7000 at 126°
$k_a^{DMF}/k_a^{C_6H_6}$		~36,000 at 126°
$k_a^{C_6H_6}/k_b^{C_6H_6}$	~0.08 at 184°	~5 at 184°
$k_a^{CH_3OH}/k_b^{CH_3OH}$	~0.08 at 184°	
k_a^{DMF}/k_b^{DMF}		~27 at 126°

For (Z)-**1**, geometric isomerization and epimerization rates at each center were almost independent of solvent polarity. For (Z)-**2**, geometric isomerization and epimerization rates show changes of ~10^4 as solvent polarity is changed, the more polar solvent giving the greater rate.[3] For (Z)-**1**, the benzyl center epimerized faster than the acetate center by a factor ~10, in accordance with anticipated steric effect relationships. For (Z)-**2**, the acetate center epimerized faster than the benzyl center by factors that ranged from 5 to 27, depending on solvent and temperature.[3] This result is the opposite of that expected from steric effects, but in conformity with that expected from polar effects. The product–reactant structural relationships for the two systems are very similar, and thus the reactions of the two systems require similar kinds of geometric reaction paths. Yet the grossly different sensitivity of epimerization rates at both centers of **1** and **2** to solvent polarity changes requires these reactions of **1** and **2** to go by different mechanisms. *All of these facts support a singlet diradical, orthogonal transition state for* **1**, *and a zwitterionic, orthogonal transition state for* **2**.

The products derived from acetone-sensitized photolysis of (+)-(Z)-**2** and (−)-(E)-**2** were completely racemic,[3] in contrast to the products of the thermal reaction of both (+)-(Z)-**1**[12] and (+)-(Z)-**2**. This experiment differentiates triplet and singlet state reaction paths for **2**, and by analogy for **1**. Mechanisms that involve edge-to-edge π-cyclopropane[13] transition states or intermediates can apply only to racemization, and not to epimerization reactions of isomers of **1** and **2**.

Other comparisons bear indirectly on the hypothesis of a zwitterionic reaction coordinate for the thermal reactions of **2**, and a singlet diradical reaction coordinate for **1**. In methanol, both (Z)-**2** and (E)-**2** underwent methanolysis to give open-chain methyl ether, and no epimerization was detected.[6] For the methanolysis reaction of (E)-**2** at 126°, $\Delta H^{\ddagger} = 19.4$ kcal/mol and $\Delta S^{\ddagger} = -32$ eu.[6] In contrast, in methanol, (Z)-**1** only underwent epimerization reactions. For these reactions at 184°, $\Delta H^{\ddagger} = 37.4$ kcal/mol and $\Delta S^{\ddagger} = -0.7$ eu. In DMF–0.1*M* lithium bromide, (Z)-**2** → (E)-**2** at

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[12] For purposes of simplicity for comparing systems 1 and 2, structures are drawn and referred to as if (+)-(Z)-1 rather than (−)-(Z)-1 had been used in runs 14–17.

[13] R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 1475 (1968).

34° with $k_i = 1.1 \times 10^{-4}$ sec^{-1},[6] and bromide ion catalysis produced a rate increase of a factor of ~1500.[6] At 125° in the same medium, (*Z*)-**1** gave no detectable epimerization (run 10), and $k_i < 5.3 \times 10^{-8}$. Even if the 91° temperature difference is disregarded, bromide ion catalysis of geometric isomerization of (*Z*)-**2** is $>10^3$ larger than that reaction for (*Z*)-**1**. Thus, system **2** is much more subject to nucleophilic substitution processes than is system **1**.

Both systems present essentially the same steric environment to potential nucleophiles. Potential reaction intermediates would differ in structure only at the negatively charged acetate center. A cyano substituent attached to that center is able to stabilize negative charge much more than is phenyl. To our knowledge, the relative acidities of methyl phenylacetate and methyl cyanoacetate are not known. However, acetonitrile is an estimated 10 pK_a units more acidic than toluene.[14] Clearly, the vastly greater ability of cyanoacetate as compared to phenylacetate to act as a negatively charged leaving group is the source of the differences in **1** and **2**, both with respect to epimerization and nucleophilic substitution reactions.

Experimental Section

General. Nmr spectra were taken on Varian A-60, A-60D, T-60, or HA-100 spectrometers in 5–10% weight by volume $CDCl_3$ solutions, 1% in tetramethylsilane. Ir spectra were recorded with a Beckman IR-5 machine using chloroform solutions and were calibrated against the polystyrene band at 6.246 μ. The near-infrared spectra were recorded with a Cary 14 spectrometer. Mass spectra were obtained on an Associated Electrical Industries Model MS-9 or Consolidated Electrodynamics Corporation Model 21–491 spectrometer. All melting points were determined in a Thomas-Hoover Unimelt apparatus and are corrected. Organic solutions were dried over anhydrous sodium sulfate. All qualitative and quantitative glc analyses were performed on an Aerograph Model 200 flame ionization detector instrument using a 10 ft × $^1/_8$ in. copper column packed with 5% Carbowax 20M on 110–120 mesh Anakrom A. Nitrogen was the carrier gas and 160–170° the column temperature. For all quantitative analyses (*i.e.*, analyses of the mixtures of (*E*)-methyl 1,2-diphenylcyclopropanecarboxylate ((*E*)-**1**) and (*Z*)-methyl 1,2-diphenylcyclopropanecarboxylate ((*Z*)-**1**) produced in kinetic and equilibration runs), it was demonstrated that the detector response was the same for all the substrates being analyzed. All optical rotations were determined with a Perkin-Elmer Model 141 Polarimeter whose specified accuracy is ±0.002° or 0.2% of the observed rotation (whichever was larger). Thermostated (25.0°) 1-dm cells were used.

Mixture of (*Z*)- and (*E*)-Methyl 1,2-Diphenylcyclopropanecarboxylates ((*Z*)-1 and (*E*)-1). By the usual procedure,[6] α-phenylcinnamic acid[8] and diazomethane gave (*E*)-methyl α-phenylcinnamate, mp 76.5–77°. From 27.0 g of trimethyloxosulfonium iodide in 150 ml of dry dimethyl sulfoxide was prepared the corresponding ylide.[15] The ester (26.6 g) in 50 ml of dry dimethyl sulfoxide was added to the ylide solution stirred under dry nitrogen at 5°. The mixture was heated at 50° for 2 hr, cooled, and shaken with ice-water and ether. After the usual washing procedures, the dried organic layer was evaporated to give 23 g (85%) of crude **1** as a pale yellow oil. The nmr spectrum gave only two methyl proton signals, one at δ 3.17 and the other at 3.52, and the mass spectrum gave a molecular ion peak for **1** at *m*/*e* 252 but none for the starting ester. Glc analysis of the mixture on a 10 ft × $^1/_8$ in. column of 5% Carbowax 20M on 110–120 mesh Anakrom A gave a mixture of (*Z*)-**1** and (*E*)-**1** in about equal amounts with retention times of authentic materials (see below).

(*Z*)- and (*E*)-1,2-Diphenylcyclopropanecarboxylic Acids ((*Z*)-3 and (*E*)-3). The mixture of (*Z*)-**1** and (*E*)-**1** (23 g) was hydrolyzed in 75 ml of ethanol, 175 ml of water, and 12 g of sodium hydroxide at reflux temperature for 10 hr. The mixture was cooled and acidified to pH 1, and the precipitate was washed, collected, and dried, 20.6 g (95% of **3**). Fractional crystallization of the mixture from acetone and 95% ethanol gave low yields of (*Z*)-**3**, mp 150.5–151.5°, and (*E*)-**3**, mp 227–228°. A better separation was accomplished making use of the differences in pK_a's of the two isomers.[8] The mixture of acids (2.0 g) was dissolved in a solution of 1.1 g of potassium hydroxide in 80 ml of water. The pH change of the solution, initially 13, was followed with a Beckman H2 pH meter with a calomel–silver chloride electrode pair. Hydrochloric acid (0.1 *N*) was added to a pH of 6.0, and the precipitate formed was collected and dried, mp 220–225°. Enough acid was added to the filtrate to give a final pH of 2.5, and the new precipitate was collected and dried, mp 140–150°. The scale of the separation could not be increased. From 20 g of the initial crude acid mixture, 6.6 g (31% from crude **1**) of pure (*E*)-**3** was obtained after recrystallizing (collectively) samples from several runs from hot benzene, mp 227–228°. This material gave pK_a = 6.70 in 60% ethanol–water against sodium hydroxide in a potentiometric titration (64 points). The pK_a of benzoic acid was determined as a control in 20% ethanol, and was found to be 4.10 as compared with the published value of 4.19 in water.[16] The nmr spectrum (CD_3SOCD_3) of (*E*)-**3** gave δ 6.7–7.2 (m, 10 H, ArH), 2.9–3.1 (overlapping d, 1 H, Ar CH), and 1.85–2.1 (d, 2 H, CH_2). *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.84; H, 6.02.

From 20 g of initial crude acid mixture was obtained 6.9 g (32% from crude **1**) of pure (*Z*)-**3**, mp 150.5–151.5°, after four recrystallizations from ethanol. The pK_a (determined as for *E* isomer) was 6.25. The nmr spectrum (CD_3SOCD_3) of (*Z*)-**3** gave δ 7.1–7.6 (m, 10 H, Ar H), 2.8–3.0 (overlapping d, 1 H, ArCH), 2.07–2.25 (q, 1 H of CH_2), and 1.37–1.60 (q, 1 H of CH_2). *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.71; H, 5.84.

(*Z*)- and (*E*)-Methyl 1,2-Diphenylcyclopropanecarboxylates ((*Z*)-1 and (*E*)-1). These esters were prepared (~95%) from the carboxylic acids (**3**) with diazomethane by the usual procedure.[6] From (*E*)-**3** was obtained (*E*)-**1**, mp 63–64°, after recrystallization from ethanol. The nmr spectrum gave δ 6.6–7.1 (m, 10 H, Ar H), 3.5 (s, 3 H, CH_3), 2.95–3.35 (overlapping d, 1 H, Ar CH), and 1.7–2.2 (m, 2 H, CH_2). The near-ir spectrum ($Cl_2C{=}CCl_2$) in the region 1.85–1.50 μ gave among the other bands the first overtone of the cyclopropyl hydrogen C–H stretch at 1.63 μ. The ir spectrum gave bands at 1720, 1600, 1500, 1440, 1260, 1165, 1100, 965, 695, and 665 cm^{-1}. The mass spectrum gave a parent ion at *m*/*e* 252. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.87; H, 6.43.

Ester (*Z*)-**1** (from (*Z*)-**3**) after two molecular distillations (90° at 5 μ) remained a colorless oil. Its nmr spectrum gave δ 7.1–7.6 (m, 10 H, Ar H), 3.2 (s, 3 H, CH_3), 2.7–2.95 (overlapping d, 1 H, Ar CH), 2.2–2.4 (q, 1 H of CH_2), and 1.42–1.68 (q, 1 H of CH_2). The near-ir spectrum in the region 1.85–1.50 μ showed the first overtone of the cyclopropyl hydrogen C–H stretch at 1.63 μ. The ir spectrum gave bands at 1720, 1600, 1500, 1450, 1440, 1310, 1280, 1200, 1170, 1120, 910, and 697 cm^{-1}. The mass spectrum showed the parent ion at *m*/*e* 252. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.03; H, 6.41.

Glc analysis of (*Z*)-**1** and (*E*)-**1** samples prepared above showed the presence of <0.2% contamination of either isomer by the other Deliberate contamination at the 0.2% level was easily detected.

Resolution of (±)-(*Z*)-3 and Conversion of Enantiomers to Enantiomers of (*Z*)-1. A mixture of 7.0 g of (*Z*)-**3** and 11.1 g of quinine trihydrate was dissolved in 565 ml of hot ethanol. The precipitate that settled when the solution was cooled was recrystallized once from ethanol to give ~7 g of salt of maximum negative rotation, $[\alpha]^{25}_{546}$ −236° (*c* 0.5, $CHCl_3$). The more soluble salt was obtained (~2.2 g) by careful fractional crystallization from ethanol of the salt in the mother liquors, $[\alpha]^{25}_{546}$ +6.5° (*c* 0.71, $CHCl_3$). Further recrystallizations of either salt gave no change in rotation. The more insoluble salt was shaken with dichloromethane and 6 *N* hydrochloric acid, and (−)-(*Z*)-**3** was obtained in the usual way.

After a recrystallization from pentane, 2.9 g of (−)-(*Z*)-**3** was obtained (41%), mp 103.5–104°, $[\alpha]^{25}_{546}$ −302°, $[\alpha]^{25}_{436}$ −538°, and $[\alpha]^{25}_{365}$ −905° (*c* 0.66, $CHCl_3$). *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.79; H, 5.80. Additional recrystallizations of this material produced no change in either its melting point or rotation.

From (−)-(*Z*)-**3** and diazomethane by the usual procedure[6]

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(14) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 12 and 19.

(15) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).

(16) "The Handbook of Chemistry and Physics," 43rd ed, The Chemical Rubber Publishing Co., Cleveland, Ohio, 1961, p 1753.

(95%) was produced (−)-(*Z*)-**1** as an oil, which was distilled (molecular at 90° and 1 μ), $[\alpha]^{25}_{546}$ −272°, $[\alpha]^{25}_{546}$ −488°, $[\alpha]^{25}_{365}$ −822° (*c* 0.28, $CHCl_3$). *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.77; H, 6.36.

From the more soluble quinine salt (2.2 g) was obtained as above after recrystallization from pentane, 0.84 g (12%) of (+)-(*Z*)-**3**, mp 103.5–104°, $[\alpha]^{25}_{546}$ +300°, $[\alpha]^{25}_{436}$ +534°, $[\alpha]^{25}_{365}$ +900° (*c* 0.66, $CHCl_3$). *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.75; H, 5.82. Additional recrystallizations of this material did not change the melting point or rotation.

From (+)-(*Z*)-**3** and diazomethane was obtained (95%) (+)-(*Z*)-**1** as a molecularly distilled oil, $[\alpha]^{25}_{546}$ +272°, $[\alpha]^{25}_{436}$ +487°, and $[\alpha]^{25}_{365}$ +827° (*c* 0.14, $CHCl_3$). *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.23; H, 6.27.

The nmr and ir spectra of (+)-, (−)-, and (±)-(*Z*)-**1** were identical. The rotations of (+)- and (−)-(*Z*)-**1** were found to be concentration independent up to *c* 1, $CHCl_3$.

Resolution of (±)-(*E*)-3 and Conversion of Enantiomers to Enantiomers of (*Z*)-1. A mixture of 7.0 g of (*E*)-**3** and 11.1 g of quinine hydrate was dissolved in 200 ml of hot methanol. When the filtered solution was cooled, a precipitate separated, which after two recrystallizations from methanol gave salt whose specific rotation ($[\alpha]^{25}_{546}$ −140°, $CHCl_3$) fluctuated randomly upon further recrystallization. The salt of this rotation was converted to (−)-(*E*)-**3** which was recrystallized once from nitromethane to give 3.15 g (45%) of optically impure (−)-(*E*)-**3**, $[\alpha]^{25}_{546}$ −55° (*c* 0.53, $CHCl_3$). Esterification of this material with diazomethane[6] gave crude (−)-(*E*)-**1**, which was recrystallized twice from methanol to give 1.06 g (15% overall) of optically pure material, mp 98.5–99°, $[\alpha]^{25}_{546}$ −55.7°, $[\alpha]^{25}_{546}$ −120°, and $[\alpha]^{25}_{365}$ −261° (*c* 0.55, $CHCl_3$). Additional recrystallizations of (−)-(*E*)-**1** changed neither its melting point or rotation. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.11; H, 6.19.

The more soluble quinine salts in the mother liquor residues (see above) were crystallized from the concentrated methanol solution, and the salt that separated was recrystallized twice from acetone, $[\alpha]^{25}_{546}$ −81.5° (*c* 0.44, $CHCl_3$). This material was converted to crude (+)-(*E*)-**3**, wt 2.24 g (32%), $[\alpha]^{25}_{546}$ +56.7° (*c* 0.54, $CHCl_3$). This material with diazomethane gave impure ester, two recrystallizations of which from methanol gave 0.67 g (9% overall) of optically pure (+)-(*E*)-**1**, mp 98.5–99°, $[\alpha]^{25}_{546}$ +55.5°, $[\alpha]^{25}_{436}$ +121°, and $[\alpha]^{25}_{365}$ +262° (*c* 0.32, $CHCl_3$). Additional recrystallizations of (+)-(*E*)-**1** changed neither its melting point nor rotation. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.85; H, 6.17.

The nmr and ir spectra of (±)-(*E*)-**1**, (+)-(*E*)-**1**, and (−)-(*E*)-**1** were identical. The rotations of (+)- and (−)-(*E*)-**1** were demonstrated to be concentration independent up to *c* 1, $CHCl_3$.

Ozonolysis of (+)-(*Z*)-3. Through a stirred solution of 0.78 g of (+)-(*Z*)-**3**, $[\alpha]^{25}_{546}$ +294° (*c* 0.60, $CHCl_3$), in 50 ml of glacial acetic acid was bubbled a stream of crude ozone from a Welsbach Ozonator (Model T-23) for 10 hr at 25°.[17] About 20 ml of acetic acid was added every 3 hr to compensate for that evaporated. To the resulting solution was added 30 ml of 10% hydrogen peroxide, and the solution was stirred 12 hr at 25°. The solvent was evaporated at 100° under a gentle stream of air, about 10 ml of 10% hydrogen peroxide was added, and the solution was evaporated to dryness at 100° as before. This oxidation procedure was repeated three more times. The last traces of solvent were removed under high vacuum to give 0.423 g (74%) of crude triacid. This gummy solid was triturated with ethyl acetate and filtered. The ethyl acetate filtrate was evaporated and about 0.100 g of the residue was esterified with diazomethane in ether.[6] The ether was carefully evaporated and the residue distilled onto a Dry Ice cooled cold finger in a sublimation apparatus at 80° and 15–20 mm pressure to give triester, (+)-**4**. The mass spectrum of the distillate gave the expected parent ion at *m*/*e* 216. The 100-MHz nmr spectrum ($CDCl_3$) gave two singlets for the methyl ester protons at δ 3.68 and 3.74 (9 H's) and three quartets centered at δ 2.68 (1 H), 1.94 (1 H), and 1.68 (1 H). Glc analysis of the oil indicated it to be >96% **4** (one component). The specific rotations of this material were: $[\alpha]^{25}_{589}$ +102.5°, $[\alpha]^{25}_{546}$ +122°, $[\alpha]^{25}_{436}$ +211°, and $[\alpha]^{25}_{365}$ +336° (*c* 0.52, chloroform). *Anal.* Calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.41; H, 5.49. Because this material was highly volatile, extreme precautions were taken during combustion analysis to prevent large losses before it burned. Without precautions the C and H values obtained were 10% lower than calculated.

Ozonolysis of (−)-(*E*)-3. The above procedure[17] was applied to 0.603 g of optically impure (−)-(*E*)-**3**, $[\alpha]^{25}_{546}$ −47° (*c* 0.50, $CHCl_3$), to give 0.283 g of crude, gummy triacid. This solid was triturated with ethyl acetate and again a small amount of insoluble impurities remained. The ethyl acetate was evaporated and 65 mg of the residue was esterified with diazomethane. Careful evaporation of the ether followed by distillation of the residue onto a Dry Ice cooled cold finger at 75° and 15–20 mm pressure gave (−)-**4** whose mass spectrum showed the parent ion at *m*/*e* 216. The 100-MHz nmr spectrum ($CDCl_3$) was the same as that of (+)-**4** (see above). Glc analysis indicated this material to be >95% one component. The specific rotations of this material were: $[\alpha]^{25}_{589}$ −76.8°, $[\alpha]^{25}_{546}$ −91.5°, $[\alpha]^{25}_{436}$ −158°, and $[\alpha]^{25}_{365}$ −252° (*c* 0.25, $CHCl_3$). *Anal.* Calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.79; H, 5.80.

General Procedure for Equilibration and Kinetic Runs. All runs were carried out starting with pure (Z)-**1** or pure (−)-(*Z*)-**1** as indicated. The cyclopropane ester was dissolved in freshly purified solvent under nitrogen along with the glc internal standard when one was used. Aliquots of solution were syringed into clean, dry, preconstricted, heavy-walled Pyrex ampoules. The ampoule cleaning procedure consisted of consecutive rinses with chromic acid, concentrated ammonium hydroxide, and water. After the water rinse, the ampoules were dried at 200° overnight and stored in a dessicator. The sample solutions were freed of oxygen by a standard freeze–thaw technique (done under vacuum). After five to six freeze–thaw cycles at ~5 μ the ampoules were sealed at 1–5 μ. For runs at all temperatures a Lauda constant-temperature bath, Model NBS, was used. Temperatures were measured with either National Bureau of Standards calibrated mercury thermometers or with a platinum resistance thermometer calibrated by the NBS. Times were measured with a digital electric timer. All tubes were subjected to thermal quenching as soon as they were removed from the rate bath. After the cooled tubes were opened, the contents were either analyzed directly by glc or subjected to a work-up procedure prior to analysis as indicated. The composition of the (*Z*)-**I**–(*E*)-**I** mixture in each tube was taken as the average of three to four glc determinations. Peak areas were determined by a Disc integrator. Rate constants were determined by a manual least-squares analysis of the raw kinetic data using standard equations.

Runs 1–4, 6, and 7 in Methanol. A mixture of exactly 0.250 g of (*Z*)-**1** and 0.138 g of 1,1,1-triphenylethane was dissolved in 31 ml of methanol. Aliquots of 2 ml each were syringed into 14 ampoules which were degassed and sealed. Seven ampoules were placed in the rate bath at 184.37°. One tube was removed every 350 min (run 6) with the exception of the last (run 1) which was removed after 10.3 days (infinity point). The remaining seven tubes were placed in the rate bath at 164.55°. One tube was removed every 2160 min (run 7) with the exception of the last (run 3) which was heated for 9 days at 164.55°, 11 days at 185°, and 39 days at 164.55° (infinity point). The contents of these tubes were analyzed directly by glc (see Table I for the equilibrium and rate constants derived from these analyses). Duplicate infinity point runs (2 and 4) were made at both temperatures starting with pure (*E*)-**1** in methanol. Table I records the concentrations and results. Less than 3% loss [(*Z*)-**1** + (*E*)-**1**] was observed in any of these runs (glc). In an additional run, 0.137 g of (*Z*)-**1** heated in 31 ml of methanol for 20 days at 185° gave 0.130 g (95%) of (*Z*)-**1**–(*E*)-**1** mixture which was pure by glc, nmr, and mass spectrometry.

Runs 5 and 8 in Benzene. A mixture of exactly 0.112 g of (*Z*)-**1** and 53.5 mg of 1,1,1-triphenylethane was dissolved in 12 ml of benzene. Aliquots of 2 ml each were sealed in five tubes. The tubes were heated at 184.37°, and one tube was removed every 350 min (run 8) with the exception of the last one (run 5) which was removed after 10.3 days. After the tubes were opened, the benzene was evaporated and each of the residues dissolved in 2 ml of methanol. The glc analyses were carried out as above. Less than 3% decomposition was observed by glc. Table I records concentrations and results.

Attempts to Observe Lithium Bromide Catalysis of Epimerization of (*Z*)-1 in Dimethylformamide (Runs 9–13). Aliquots of 2 ml of DMF (purified) solution 0.043 *M* in (*Z*)-**1**, 0.021 *M* in 1,1,1-triphenylethane, and 0.1 *M* in lithium bromide were degassed and sealed in ampoules (runs 9–12). The ampoules were treated as indicated in Table II. The quenched solutions were mixed with 10 ml of water and the resulting solution was extracted three times with ether. The ether solutions were dried and the solvent was evaporated. The residues were dissolved in 2 ml of methanol and analyzed by glc. Run 13 was identical to run 12 except the lithium bromide was omitted. Table II records the results.

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[17] This procedure resembles that of Y. Inouye, T. Sugita, and H. M. Walborsky, *Tetrahedron*, 20, 1695 (1964).

Epimerization of Optically Pure (−)-(*Z*)-1 in Methanol and in Benzene (Runs 14–17). **Run 14.** Optically pure (−)-(*Z*)-**1** (0.300 g) in 3 ml of purified methanol was heated in a degassed, sealed ampoule at 185° for 200 min (10% epimerization). The product mixture was chromatographed on 90 g of silica gel (1.9 × 67 cm column) using 5% ether-pentane mixture as eluent and taking 10-ml fractions. Fractions 53–63 were pure (*Z*)-**1** by glc. The materials from these fractions were combined and after distillation had $[\alpha]^{25}_{546}$ −272° (*c* 0.28, $CHCl_3$). Fractions 70–79 were all >50% (*E*)-**1** in composition. These fractions were combined and after distillation had the observed rotation: α^{25}_{546} −0.308° (4.977 mg in 1.00 ml of $CHCl_3$). The composition of the rotation sample was determined by glc to be 34.1% (*Z*)-**1** and 65.9% (*E*)-**1**. The contribution of (−)-(*Z*)-**1** to the observed rotation was calculated to be −0.462°, and the contribution of (+)-(*E*)-**1** to be (+)-0.154°. From these values, the (+)-(*E*)-**1** produced from (−)-(*Z*)-**1** was calculated to be $[\alpha]^{25}_{546}$ +47.0° (*c* 0.328, $CHCl_3$). Internally consistent rotations were obtained at λ 436 and 365 nm. Control experiments are recorded in the following section, and Table III records the results.

Run 15. Optically pure (−)-(*Z*)-**1** (0.113 g) in 2 ml of methanol was heated (see Table III), and the product was glc analyzed and isolated by chromatography (43 g of silica gel). Fractions 29–31 gave pure (*Z*)-**1** (glc), $[\alpha]^{25}_{546}$ −270° (*c* 0.304, $CHCl_3$), and fractions 46–55 were collectively 25.1% (*Z*)-**1** and 74.9% (*E*)-**1**, and gave the observed rotation: α^{25}_{546} −0.094° (2.900 mg in 1.00 ml of $CHCl_3$). The contribution of (−)-(*Z*)-**1** to the observed rotation was calculated to be −0.197°, and that of (+)-(*E*)-**1** to be 0.103°. The rotation of the (+)-(*E*)-**1** produced was calculated to be $[\alpha]^{25}_{546}$ +47.4° (*c* 0.217, $CHCl_3$). Internally consistent results were obtained at λ 436 and 365 nm. Table III records the results.

Run 16. Optically pure (−)-(*Z*)-**1** (0.100 g) in 1 ml of methanol was heated (Table III), and the product was glc analyzed and isolated by chromatography (40 g of silica gel). Fractions 27–32 gave pure (*Z*)-**1** having $[\alpha]^{25}_{546}$ −268.4° (*c* 0.166, $CHCl_3$). Fractions 45–55 were combined. By glc the composite was 17.2% (*Z*)-**1** and 82.2% (*E*)-**1**. The observed rotation was α^{25}_{546} +0.024° (3.060 mg in 1.00 ml of $CHCl_3$). The contribution of (−)-(*Z*)-**1** to the observed rotation was calculated to be −0.141°, and that of (+)-(*E*)-**1** to be +0.117°. The calculated rotation of the (+)-(*E*)-**1** produced was $[\alpha]^{25}_{546}$ +46.2° (*c* 0.253, $CHCl_3$). Internally consistent rotations were obtained at λ 436 and 365 nm. Table III records the results.

Run 17. Optically pure (−)-(*Z*)-**1** (0.164 g) in 2 ml of benzene was treated as indicated in Table III, and the product was glc analyzed and isolated by chromatography (50 g of silica gel). Fractions 24–27 gave pure (glc) (*Z*)-**1**, $[\alpha]^{25}_{546}$ −270° (*c* 0.122, $CHCl_3$). Fractions 39–46 were combined, and the composite was (glc) 15.6% (*Z*)-**1** and 84.4% (*E*)-**1**. Its observed rotation was α^{25}_{546} −0.006° (3.598 mg in 1.00 ml of $CHCl_3$). The contribution (−)-(*Z*)-**1** to the observed rotation was calculated to be −0.151°, and of (+)-(*E*)-**1** to be +0.145°. The rotation of the (+)-(*E*)-**1** produced in the epimerization was calculated to be $[\alpha]^{25}_{546}$ +47.7° (*c* 0.304, $CHCl_3$). Internally consistent rotations were obtained at λ 436 and 365 nm. Table III records the results.

Control Experiments. A sample of (−)-(*Z*)-**1** of $[\alpha]^{25}_{546}$ − 126° was distilled exhaustively onto a Dry Ice cooled cold finger at 90° at 5 μ to give (−)-(*Z*)-**1** of $[\alpha]^{25}_{546}$ −124°. This material was distilled a second time to give $[\alpha]^{25}_{546}$ −127°. Thus (−)-(*Z*)-**1** was optically stable to distillation.

A sample of (−)-(*E*)-**1** of $[\alpha]^{25}_{546}$ −43.1° was subjected to two exhaustive distillations (see above) to give $[\alpha]^{25}_{546}$ −43.1° and $[\alpha]^{25}_{546}$ −43.2° after the first and second distillations, respectively. Thus (−)-(*E*)-**1** was optically stable to distillation.

The additivity of the rotations of (−)-(*Z*)-**1** and (+)-(*E*)-**1** was demonstrated as follows. Optically pure (−)-(*Z*)-**1** (1.165 mg) and (+)-(*E*)-**1** (3.395 mg) were dissolved in 2.00 ml of chloroform, and the solution gave observed rotations of α^{25}_{546} −0.066° and α^{25}_{436} −0.083°. The rotations of the mixture calculated from the amounts of each and their specific rotations were α^{25}_{546} −0.065° and α^{25}_{436} −0.081°. The observed and calculated are within experimental error of one another.

About 240 mg of (−)-(*Z*)-**1**, $[\alpha]^{25}_{546}$ −256° (94% optically pure), was chromatographed on 70 g of silica gel using 5% ether-pentane mixture as eluent. Product was eluted in fractions 36–45. The specific rotations of the (−)-(*Z*)-**1** in fractions 37, 40, 43 and 45 were determined after the material was exhaustively distilled and were all $[\alpha]^{25}_{546}$ −258°, or of 95% optical purity.

About 60 mg of (−)-(*E*)-**1**, $[\alpha]^{25}_{546}$ −44° (79% optically pure), was chromatographed on 70 g of silica gel. The product was eluted in fractions 44–52. The specific rotations of the (−)-(*E*)-**1** in selected fractions were determined after each sample was exhaustively distilled, and were as follows: fraction 45, $[\alpha]^{25}_{546}$ −44.6° (80.5% optically pure); fraction 49, $[\alpha]^{25}_{546}$ −44.8° (80.5% optically pure); fraction 52, $[\alpha]^{25}_{546}$ −43 ± 2° (77.5 ± 3.5% optically pure). So little material was available in fraction 52 that the limits of error were much larger than for the other fractions. These results indicate that no optical fractionation or racemization of (−)-(*Z*)-**1** or (−)-(*E*)-**1** occurs during chromatography.

Stereospecificity of "Retro-Diels–Alder" Fragmentation under Electron Impact

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Abstract: "Retro-Diels–Alder" fragmentation under electron impact and two analogous processes which are accompanied by hydrogen migrations are highly stereospecific in three systems of diketones. The resulting ions a, b, and c are very abundant in the case of cis isomers **3**, **7**, and **9**, but of negligible abundance in trans diketones **4**, **8**, and **10**. The high degree of stereospecificity suggests that no rearrangement of the molecular ions to common structures precedes these fragmentation processes, and that two C,C bonds are cleaved concurrently in the course of retro-Diels–Alder fragmentation and the analogous processes in the examined systems.

The electron-impact-induced "retro-Diels–Alder" fragmentation is one of the most important processes occurring in many organic compounds which contain a double bond in a six-membered ring.[3,4] This process provides a unique method for structure determination in polycyclic compounds of consider-

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(2) Based in part on the D.Sc. Thesis of J. Deutsch, 1971.

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