mass spectrum (70 eV), m/e 196 (M^+).

Anal. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.16. Found: C, 85.40; H, 6.21.

Carvomenthone (20). A solution of *l*-carvone (**19**; 23.0 g, 153 mmol) in ethanol (230 mL) containing 1.75 g of palladium on carbon (5%) was hydrogenated (1 kg/cm^2) until the calculated amount of hydrogen (2 equiv) was absorbed. The mixture was filtered, and the solvent was evaporated in vacuo. Distillation of the residue gave 19.5 g (83%) of the product **20**: bp 101-103 °C (21 mm); IR (neat) 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.70-1.23 (m, 9 H), 1.23-2.00 (m, 6 H), 2.00-2.67 (m, 3 H).

8a-Hydroxy-5-isopropyl-8-methyl-3-(phenylthio)-2-decalone (21). Carvomenthone (**20**; 12.0 g, 78 mmol) was added to a stirred solution of LDA (86 mmol) in dry THF (140 mL) at -78 °C under N_2, and stirring was continued for 2 h. The butenone **7** (13.9 g, 78 mmol) in dry THF (80 mL) was added dropwise to the mixture, and the resulting solution was stirred for 2 h at -78 °C, allowed to warm to room temperature for 6 h, and then stirred at 40 °C for 2 h. After addition of 10% hydrochloric acid (20 mL), the mixture was extracted with ether, washed with brine, dried over sodium sulfate, and concentrated to give 26.9 g of yellow oil. The oily residue (10 g) was chromatographed on silica gel (benzene-ether, 1:1) to give 8.48 g (88%) of the ketol **21**: mp 157-159 °C (hexane-benzene); IR (Nujol) 3450, 1710 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 0.90-1.07 (m, 9 H), 1.07-3.10 (m, 12 H), 3.33 (s, 0.7 H, OH), 3.83 (br, 1 H), 4.20 (s, 0.3 H, OH), 7.13-7.87 (m, 5 H).

Anal. Calcd for $C_{20}H_{28}O_2S$: C, 72.26; H, 8.49. Found: C, 72.54; H, 8.40.

5-Isopropyl-8-methyl-5,6,7,8-tetrahydro-2-naphthol (22). A solution of the ketol **21** (1.20 g, 3.6 mmol) and *p*-toluenesulfonic acid monohydrate (171 mg, 0.9 mmol) in benzene (150 mL) was refluxed for 6 h. After cooling, the mixture was poured into 10% aqueous sodium bicarbonate solution, extracted with benzene, dried over sodium sulfate, and concentrated in vacuo. Kugelrohr distillation afforded 0.60 g (81%) of the naphthol **22**: bp 130 °C (3 mm); IR (neat) 3350, 1610, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71, 0.75, 0.91, 1.00 (4 d, J = 6.5, 6.5, 7.0, 7.0 Hz, respectively, total 6 H), 1.23 (d, J = 7.0 Hz, 3 H), 1.40-3.03 (m, 7 H), 4.47 (br, 1 H, OH), 6.47-7.67 (m, 3 H).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.61; H, 9.87.

1-Isopropyl-4-methyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (23). A solution of the naphthol **22** (200 mg, 0.98 mmol), dimethyl sulfate (189 mg, 1.5 mmol), and powdered potassium carbonate (621 mg, 4.5 mmol) in dry acetone (40 mL) was refluxed for 3 h. The mixture was filtered and concentrated. Kugelrohr distillation gave 173 mg (81%) of the naphthalene **23**: bp 130 °C (3 mm); IR (neat) 1605, 1570, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71, 0.75, 0.97, 1.00 (4d, J = 6.5, 6.5, 7.0, 7.0 Hz, respectively, total 6 H), 1.26 (d, J = 7.0 Hz, 3 H), 1.40-3.07 (m, 7 H), 3.77 (s, 3 H), 6.53-7.37 (m, 3 H); mass spectrum (70 eV), m/e 218 (M^+).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.89; H, 9.89.

5-Acetylbicyclo[2.2.2]octan-2-one (25). 2-Cyclohexen-1-one (0.96 g, 10 mmol) in dry THF (10 mL) was added to a stirred solution of LDA (11 mmol) and HMPA (11 mmol) in dry THF (10 mL) at -50 °C under N_2, and stirring was continued for 1 h. The butenone **7** (1.78 g, 10 mmol) in dry THF (10 mL) was added dropwise to the mixture, and the resulting solution was allowed to stir for 1 h at -50 °C and then for 12 h at room temperature. The mixture was quenched by addition of saturated aqueous ammonium chloride solution (20 mL), and the organic layer was separated. The water layer was extracted with ether, and the combined extracts were washed with brine, dried over sodium sulfate, and concentrated. The residue was chromatographed on silica gel to give 1.40 g (84%) of the octanone **25**: IR (neat) 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.08-2.13 (m, 7 H), 2.22 (s, 3 H), 2.27-3.17 (m, 4 H); mass spectrum (70 eV), m/e 166 (M^+).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.91; H, 8.30.

8a-Hydroxy-2-decalone (26). The ketol **14a** (0.90 g, 3.3 mmol) was treated with excess Raney Ni in ethanol (60 mL) under reflux for 26 h. After filtration, the mixture was concentrated to give 0.50 g (91%) of crystals: mp 151-152 °C (hexane-acetone); IR (Nujol) 3300, 1700 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 0.95-1.83 (m, 11 H), 1.93-2.63 (m, 4 H), 3.33 (s, 0.75 H, OH), 4.20 (s, 0.25 H, OH); mass spectrum (70 eV), m/e 168 (M^+).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.72; H, 9.50.

Registry No. **7**, 13522-48-0; **11**, 19718-58-2; **12**, 77202-27-8; **13**, 61203-07-4; **14a** (isomer 1), 80485-41-2; **14a** (isomer 2), 80485-42-3; **14b** (isomer 1), 80485-43-4; **14b** (isomer 2), 80485-44-5; **14c** (isomer 1), 80485-45-6; **14c** (isomer 2), 80485-46-7; **15a**, 77202-26-7; **15b** (isomer 1), 80485-47-8; **15b** (isomer 2), 80485-48-9; **16**, 77202-25-6; **17a**, 1125-78-6; **17b**, 80485-49-0; **17c**, 1470-94-6; **17d**, 1659-93-4; **17e**, 79144-22-2; **18**, 77202-24-5; **19**, 6485-40-1; **20** (isomer 1), 5206-83-7; **20** (isomer 2), 7065-48-7; **21**, 80485-50-3; **22**, 80485-51-4; **23**, 32178-69-1; **25** (isomer 1), 80485-52-5; **25** (isomer 2), 80513-96-8; **26** (isomer 1), 20591-71-3; **26** (isomer 2), 20721-86-2; phenyl vinyl sulfide, 1822-73-7; phenyl α-bromovinyl sulfide, 80485-53-6; acetaldehyde, 75-07-0; diphenyl disulfide, 882-33-7; phenylsulfenyl chloride, 931-59-9; 2-acetyl-6-methyl-3,4-dihydro-2*H*-pyran, 28450-02-4; 3-(phenylthio)-$\Delta^{1(9)}$-2-octalone, 80485-54-7; 8a-hydroxy-3-(phenylsulfonyl)-2-decalone, 80485-55-8; 2-cyclohexen-1-one, 930-68-7; cyclohexanone, 108-94-1; 4-*tert*-butylcyclohexanone, 98-53-3; cyclopentanone, 120-92-3; cycloheptanone, 502-42-1; α-tetralone, 529-34-0.

Dianions Derived from α-Halo Acids. The Darzens Condensation Revisited

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The dianions of α-halo carboxylic acids are readily generated by the addition of the acids to 2 equiv of lithium diisopropylamide at low temperatures. When the mixture warms to room temperature dimeric products are formed. When aldehydes and ketones were added to the cooled solutions of the dianions and the reaction mixtures were allowed to warm to room temperature, followed by acid quench, glycidic acids were formed. The glycidic acids, per se, were often too unstable to be isolated and purified but could be analyzed by conversion to their methyl esters with diazomethane. When the reactions were quenched prematurely, α-chloro-β-hydroxy carboxylic acids were isolated. Homologated aldehydes and ketones were obtained from the glycidic acids by catalytic and thermal decarboxylation methods.

Extensions of the carbon backbone of aldehydes and ketones are important transformations in synthetic chemistry. The Darzens glycidic ester condensation[1] (eq 1) provided one of the early methods for carbonyl homolo-

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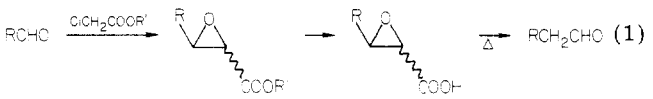
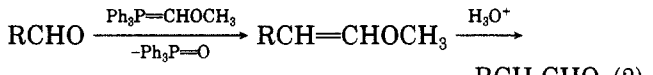


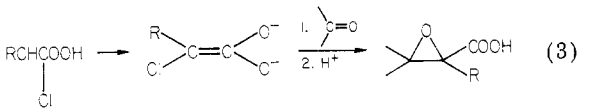
gation.[2] A more modern, yet classic, approach utilizes the Wittig reaction (eq 2). The latter method suffers from



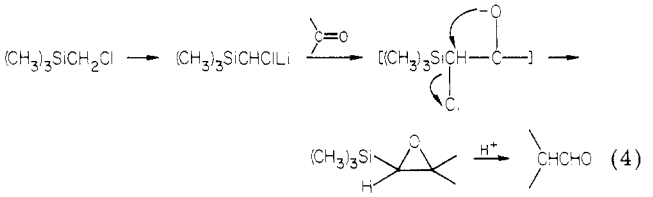
poor yields, reagent instability, and difficulty of separation of the vinyl ethers and triphenylphosphine oxide. A Horner–Wittig modification based on (α-methoxyalkyl)-diphenylphosphine oxide offers considerable improvement.[4] Reagents for the Wittig and Horner–Wittig methods are synthesized from chloromethyl methyl ether which has been shown to be a severe carcinogen.[5] Many other variations of the Wittig reaction have been examined; reagents used include [(phenylthio)methylene]triphenylphosphorane[6] and carbanions derived from diethyl [(methylthio)methyl]phosphonate[7] and α-aminophosphonates.[8] A method based on a boron reagent—lithium bis(ethylenedioxyboryl)methide—has also been examined, but the reagent is not easily accessible.[9]

In view of the above noted disadvantages we decided to reexamine the Darzens reaction (eq 1). A major complication encountered in this procedure is premature epoxide cleavage during ester hydrolysis. This results in carboxylic acid products which do not decarboxylate in the appropriate manner. In an attempt to alleviate the necessity for ester hydrolysis, Büchi and Blanchard[10] investigated the pyrolysis of *tert*-butyl glycidic esters to isobutene and glycidic acids with subsequent decarboxylation under the pyrolysis conditions. The method did not result in a significant improvement in overall yield although it did simplify the procedure. Another procedure designated to improve the Darzens method was developed by Johnson and co-workers.[11] Treatment of the sodium glycidate with excess anhydrous hydrogen chloride gave α-hydroxy-β-chloro carboxylic acids which, when deprotonated, underwent a facile decarboxylation with concomitant loss of chloride. However, the above modification does not eliminate the ester hydrolysis but does result in a slight improvement in yield. The moderate success of these two modifications leaves much room for an improved glycidic acid synthesis.

The utilization of dianionic reagents is of current interest exemplified by several recent reviews.[12] The second site to be metalated is the more nucleophilic anion. Reactions occur regiospecifically at that position with generally no reaction at the initial site of metalation even in the presence of excess electrophile. This current interest in dianion chemistry led to the idea of using the dianion of a-halo carboxylic acids in place of the monoanion of the corresponding esters. This procedure would produce glycidic acids directly without the necessity of the troublesome ester hydrolysis (eq 3).

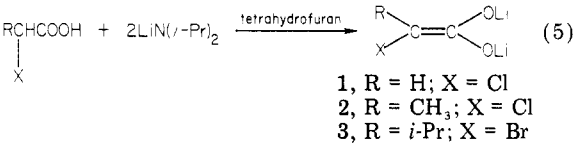


During the course of this study Magnus and co-workers described a carbonyl homologation method based on a silyl-stabilized carbanionic reagent.[13] The method (eq 4) which is convenient and efficient is mechanistically related to the Darzens reaction.



Results and Discussion

Dianion Generation and Stability. Generation (eq 5) of the dianion of chloroacetic acid (dianion 1) was very



1, R = H; X = Cl
2, R = CH_3; X = Cl
3, R = *i*-Pr; X = Br

fast even at −80 °C. The addition of the acid in tetrahydrofuran (THF) (cooled to −80 °C) to lithium diisopropylamide (LDA) in THF (cooled to −80 °C) proved to be the most effective. When a THF solution of dianion 1 at −80 °C was poured into ice, the only product recovered was chloroacetic acid. However, if dianion 1 is warmed to room temperature before quenching, a byproduct was observed along with chloroacetic acid. When dianion 1 was warmed to 50 °C for several hours, poured into acidic water, and methylated with diazomethane, methyl chloroacetate and the byproduct, now as the methyl ester, were isolated. ^{1}H NMR and IR spectra of the ester are consistent with dimethyl 2-chlorobutanedioate. The byproduct, lithium 2-chlorobutanedioate, could arise by an S_N2 attack of dianion 1 on lithium chloroacetate (eq 6).[14] This explains why reverse addition proceeds most efficiently. The excess base insures rapid dianion formation with little monoanion present.

$$1 + ClCH_2COOLi \rightarrow LiOOCCHClCH_2COOLi + LiCl \quad (6)$$

A similar reaction occurs with the dianion of 2-chloropropanoic acid (dianion 2). If dianion 2 is quenched at −80 °C, 2-chloropropanoic acid is the only product. If the dianion is warmed to room temperature and quenched with

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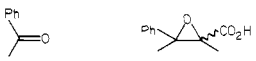
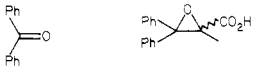
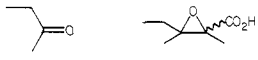
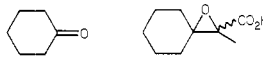
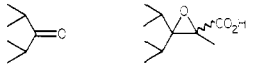
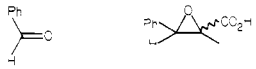
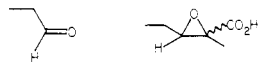
(13) Berford, C.; Cooke, F.; Ehlinger, E.; Magnus, P. *J. Am. Chem. Soc.* **1977**, *99*, 4536.
(14) The reaction of lithium α-lithio carboxylates with lithium α-halo carboxylates to produce succinate derivatives has been recently reported (Petragnani, N.; Yonashiro, M. *Synthesis* **1980**, 710).

Table I. Addition of Dianion 2 to Ketones and Aldehydes

carbonyl	glycidic acid	E/Z	methyl glycidate yields,[a] %	halohydrin ester yields,[b] %
		65:35	93	90
			76	
		50:50	96	96
			74	92
			47	93
			77	
			0	
		96:4	90	
		67:33	34	36

[a] Formed by esterification of glycidic acid with diazomethane. Yields based on isolated esters. [b] Produced by quenching the reaction mixture at −80 °C followed by methylation with diazomethane. Yields based on isolated esters.

water followed by acidification, the major product isolated is 2,3-dimethylmaleic anhydride. This could arise in the same manner proposed for dimerization of dianion 1.

The dianion of 2-bromo-3-methylbutanoic acid (dianion 3) proved to be much more stable than the previous two dianions. Reactions with this dianion could be carried out at 0 °C with little observed dimerization. However, warming a solution of dianion 3 to room temperature followed by methylation with diazomethane resulted in the complete disappearance of starting acid and the appearance of the dimerized products, dimethyl 2-bromo-2,3-diisopropylbutanedioate and dimethyl 2-isopropyl-3-isopropylidenebutanedioate, which results from dehydrohalogenation of the first product.

Addition of Dianions to Ketones and Aldehydes. The results from addition of the dianion of 2-chloropropanoic acid (dianion 2) to various ketones and aldehydes are given in Table I. The yields shown represent isolated methyl esters made for characterization and analytical purposes from the acids with diazomethane. This was necessary because it was difficult, if not impossible, to isolate and purify many of the glycidic acids directly. When the glycidic acids were to be used in a homologation sequence, they were not methylated, purified, or in many cases, even isolated but decarboxylated directly with as little handling as possible.

Dianion 2 and acetophenone react very efficiently, giving a 94% yield of the corresponding glycidic acid. The purity of this acid is attested to be a 93% yield of the methyl ester. The remaining material (6%) was the corresponding chlorohydrin. Methylation allowed the separation of these two compounds chromatographically as well as the separation of the *E* and *Z* isomers of the glycidic ester by crystallization. When the solution was allowed to stand the most abundant isomer crystallized. Filtration and recrystallization afforded a white solid, whose ^{1}H NMR showed four singlest [δ 1.18 (α-methyl), 1.60 (β-methyl), 3.79 (*O*-methyl), 7.26 (phenyl)]. The ^{1}H NMR of the oily isomer showed four singlets [δ 1.65 and 1.67 (α,β-methyls), 3.25 (*O*-methyl), 7.24 (phenyl)]. The IR spectra of the two isomers were similar. Models of the two isomers indicate severe crowding of the phenyl ring, unless it is out of plane with respect to the epoxide carbon–carbon bond. This would then direct the deshielding cone of the aromatic ring at the cis α substituent. Therefore, the oil with a methyl ester absorption at δ 3.25 (shielded from a value of δ 3.72 for the crystalline isomer) must be the *Z* isomer and the crystalline solid having a shielded methyl absorption (δ 1.18 compared to δ 1.6 for the oily *Z* isomer) must be the *E* isomer. These values correspond to the literature value for the α-methyl groups of (*E*)- and (*Z*)-ethyl 2,3-dimethyl-3-phenyl-2-oxiranecarboxylate of δ 1.3 and 1.6, respectively.[15]

If the reaction mixture, at −80 °C, is poured into aqueous acid 30 s after the addition of acetophenone, the only product (90% yield) isolated, after workup and methylation, is the α-chloro-β-hydroxy methyl ester. A 2:3 ratio of diastereomeric alcohols was ascertained by comparison of the two alcohol peaks at δ 3.80 and 4.13, respectively. Monitoring the reaction of removal of aliquots showed that the alkoxide did not close to the epoxide at −80 °C even after 4 h. When the reaction mixture warmed, epoxide began to appear at about −15 °C and was almost completely formed by the time the reaction mixture reached 25 °C. Prolonged reaction time resulted in the appearance of a small quantity (about 5%) of an unknown highly polar material.

Results of reaction of dianion 2 with other ketones are summarized in Table I. To assess steric effects on the addition reaction, we investigated the reactions of diisopropyl ketone and di-*tert*-butyl ketone with dianion 2. Addition to diisopropyl ketone proceeded with reasonable efficiency, affording 77% of the corresponding methyl glycidate after methylation with diazomethane. This represents a somewhat lower yield (19% less) than observed for 2-butanone, indicating some steric inhibition. Di-*tert*-butyl ketone failed to react.

Aldehydes also react with dianion 2 with varying degrees of efficiency. Reaction with benzaldehyde affords a 90% yield of the corresponding glycidic acid with the remaining 10% consisting of 2-chloro-3-hydroxy-2-methyl-3-phenylpropanoic acid. Treatment of a second reaction mixture with diazomethane produced a 96:4 *E*/*Z* mixture of methyl glycidate; the spectral assignments correspond to literature values given by Roux-Schmitt and Seyden-Penne.[16] Again, when the group in the α position is cis to the phenyl ring, it is farther upfield than when it is trans.

In the case of propanal a 36% yield of methyl 2-chloro-3-hydroxy-2-methylpentanoate is obtained after the reaction is quenched at −80 °C with 25% H_2SO_4. The amount of halohydrin is almost equal to the amount (34%) of glycidic acid isolated at room temperature, indicating that once the initial addition takes place, the closure proceeds efficiently upon warming.

The results from addition of the dianion of 2-bromo-3-methylbutanoic acid (dianion 3) to several ketones and aldehydes are shown in Table II. The yields obtained with this dianion are consistently lower than those for dianion

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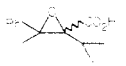
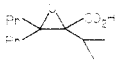
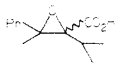
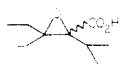
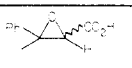
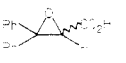
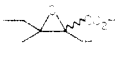
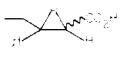
(16) Roux-Schmitt, M. C.; Seyden-Penne, J. *Tetrahedron* **1972**, *28*, 4965.

Table II. Addition of Dianion 3 to Ketones and Aldehydes

carbonyl	glycidic acid	% yield of methyl ester[a]
		79
		68
		74
		67
		37

[a] Prepared by treatment of glycidic acid with diazomethane. Yields based on isolated esters.

Table III. Addition of Dianion 1 to Ketones and Aldehydes

carbonyl	glycidic acid	% yields of glycidate methyl ester[a]	chlorohydrin methyl ester[b]
		59	53
		38	59
		52	55
		41	48

[a] Formed by treatment of reaction mixture with diazomethane. [b] Reaction quenched at -80 °C and treated with diazomethane.

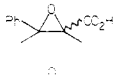
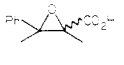
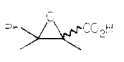
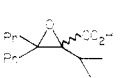
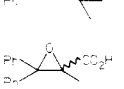
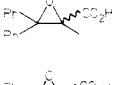
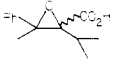
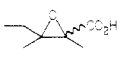
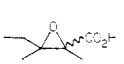
2. This may be a result of the increased bulk of dianion 3.

The results of addition of the dianion of 2-chloroacetic acid (dianion 1) to several ketones and aldehydes are shown in Table III. Considerably lowered yields were observed for dianion 1 than for either dianion 2 or 3. This is a result of a more facile condensation of dianion 1 with the monoanion of α-chloroacetic acid than was observed for the corresponding condensation with dianions 2 or 3. The amount of halohydrin isolated by quenching the reactions at -80 °C is comparable to the yield of glycidic acid isolated at room temperature for all carbonyls treated with dianion 1. Methylation of all of the glycidic acids resulting from reactions with dianion 1 was necessary for isolation and characterization.

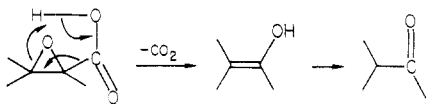
The reaction of acetophenone and dianion 1 afforded (after methylation) a 59% yield of methyl 3-methyl-3-phenyl-2-oxiranecarboxylate as a mixture of isomer. Medium-pressure chromatography on silica gel, using 10:1 hexane/ethyl acetate, successfully separated some of the *E* isomer pure. The adsorption of the α proton in the *E* isomer is upfield of that for the *Z*, δ 3.45 and 3.64, respectively.

Quenching the reaction at -80 °C 30 s after the addition of acetophenone by pouring the cold reaction mixture into 25% H_2SO_4 produced a 53% yield of methyl 3-hydroxy-2-chloro-3-phenylbutanoate (after methylation with diazomethane). From the similarity in yield of halohydrin and glycidic ester, it appears that once dianion 1 adds to a carbonyl, the resulting intermediate closes efficiently to the oxirane upon warming.

Table IV. Pyrolytic Decarboxylation of Glycidic Acids

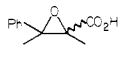
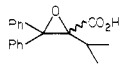
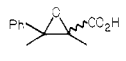
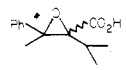
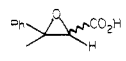
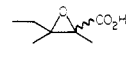
	glycidic acid	method	ketone	% yield
1		oven pyrolysis (300 °C)		62
2		oven pyrolysis (350 °C)		72
3		dropping pyrolysis ($CHCl_3$, 200-210 °C)		71
4		oven pyrolysis (310 °C)		97
5		oven pyrolysis (340 °C)		98
6		oven pyrolysis (310 °C)		98
7		oven pyrolysis (360 °C)		73
8		dropping pyrolysis (CH_2Cl_2, 150 °C)		46
9		dropping pyrolysis (CH_2Cl_2, 200-220 °C)		65

Rearrangements. The established procedure for rearrangement of glycidic acids has been the thermally initiated decarboxylation.[1] Loss of CO_2 can be pictured as proceeding by a concerted process (eq 7) or by a stepwise


(7)

process involving initial protonation of the oxirane oxygen. Generally, neat glycidic acids were heated until gas evolution had ceased; the homologated ketone was isolated by distillation. Two alternative methods of thermal decarboxylation were investigated in this study. The first method was very similar to the classical method but incorporated simultaneous distillation of the homologated product. The glycidic acid was placed in a preheated oven (300–360 °C) and the homologated ketone was collected as it distilled out following decarboxylation. This method required isolation of the glycidic acid, which must always be done with care to avoid epoxide opening prior to decarboxylation. The second method developed to eliminate the isolation difficulty is a dropping pyrolysis method. A dilute solution of glycidic acid was dropped down a preheated column, using a slight argon pressure, and the homologated ketone and solvent were collected on a dry ice cold finger. This method gave comparable yields as well as being much more easily scaled up. The largest scale used in the pyrolysis oven procedure was 11 mmol of glycidic acid, while in the dropping pyrolysis method 500 mmol of glycidic acid was easily decarboxylated. All glycidic acids investigated decarboxylated efficiently with the pyrolytic methods described above (Table IV). However, temperatures of at least 210 °C and upward to 360 °C must be used to obtain good yields of homologated carbonyl compounds. Entries 4–6 in Table IV represent the decarboxylation of pure crystalline glycidic acids which decarboxylate in greater than 97% yields in all three cases. Yields in all of the other entries are based on the amount

Table V. Catalytic Decarboxylation (Dowex 50W Ion-Exchange Resin)

entry	glycidic acid	product	% yield
1			77 (based on starting ketone)
2			77 (based on starting ketone)
3			100 (based on crystalline glycidic acid)
4			100 (based on crystalline glycidic acid)
5			36 (based on starting ketone)
6			0 (based on starting ketone)

of starting carbonyl, without determining the yield of glycidic acid. These somewhat lower values incorporate the less than quantitative yields in glycidic acid formation as well as the yield for decarboxylation.

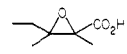
When the glycidic acid in entry 6 was decarboxylated by the traditional method—heating the glycidic acid in an oil bath until carbon dioxide evolution had ceased followed by distillation of the homologated carbonyl—a yield of 41% of the homologated ketone was obtained. The oven pyrolysis method more than doubles this yield.

The conditions required for pyrolytic decarboxylation are rather severe. For this reason several catalytic methods were investigated. The range of catalysts tried included Lewis acids (aluminum chloride, stannic chloride, boron trifluoride etherate), organic and mineral acids (acetic acid, formic acid, sulfuric acid, hydrochloric acid), several inorganic salts (lithium bromide, zinc chloride, lithium carbonate, magnesium bromide, calcium chloride), and several polymeric and/or surface catalysts (neutral alumina, acidic alumina, Dowex 50W ion-exchange resin, Nafion H resin). Relatively few of these catalysts were effective in promoting the desired decarboxylation.

Dowex 50W (H^+), a sulfonated cross-linked polystyrene resin, was a convenient catalyst for decarboxylation of glycidic acids bearing an aromatic group β to the carbonyl (Table V). Addition of this catalyst to a dry chloroform, benzene, or methylene chloride solution of the glycidic acid followed by overnight reflux afforded the homologated ketone. For best results the catalyst must also be dry. This was accomplished with a drying pistol and P_2O_5. Removal of the catalyst from the decarboxylation reaction mixture was accomplished by simple filtration. Any acidic byproducts which might be present can be easily separated by silica gel chromatography, distillation, or bicarbonate washing. Presumably the catalyst functions by proton-catalyzed ring opening of the epoxide to yield a "benzylic" carbonium ion which undergoes eliminative decarboxylation.

A complete lack of decarboxylation is observed with alkyl glycidic acids, using catalysts that decarboxylate aromatic glycidic acids efficiently. Boron trifluoride etherate as well as aluminum chloride and stannic chloride produce little or no homologated ketone with complete loss of glycidic acid. Addition of catalyst at −80 °C or prior complexation with pyridine did not afford homologation product. Finally, it was discovered that lithium bromide, when stirred for several days with the glycidic acid, 3-ethyl-2,3-dimethyl-2-oxiranecarboxylic acid, produced a good yield of 3-methyl-2-butanone. If 3Å molecular sieves were added to scavenge trace amounts of water, this yield could be raised to 73%. Other attempts which showed minor success were the use of acetic and formic acids. Addition of these catalysts to a solution of glycidic acid and 2,3-dimethyl-3-phenyl-2-oxiranecarboxylic acid followed by overnight reflux afforded the homologated carbonyl in 31% and 15% yield, respectively. A summary is given in Table VI.

Table VI. Miscellaneous Catalytic Decarboxylation Methods

glycidic acid	ketone	catalyst	% yield	comments
		neutral alumina	63	benzene reflux
a	*a*	BF_3 etherate	81	chloroform reflux
		LiBr	61	room temperature
a	*a*	BF_3 etherate	trace	−80 °C
a	*a*	BF_3/ pyridine	0	glycidic acid recovered
a	*a*	$AlCl_3$/ pyridine	0	glycidic acid not recovere recovered
a	*a*	$SnCl_4$	0	vigorous reaction
a	*a*	$AlCl_3$	0	vigorous reaction
a	*a*	LiBr + molecular sieves	73	room temperature
a	*a*	CH_3CO_2H	31	reflux
a	*a*	HCO_2H	15	chloroform reflux

[a] Same as above.

Although the dianion method described here circumvents the troublesome ester hydrolysis step in the classic Darzens condensation, the synthetic potential of the reaction for homologation of carbonyl compounds remains limited due to ineffective general methods for mild and rapid decarboxylation.

Experimental Section

Generation and Reactions of α-Chloro Acid Dianions 1 and 2. Lithium diisopropylamide (LDA) was generated under argon in an oven-dried flask equipped with a septum by the addition of 35 mL of 1.6 M butyllithium in hexane (50 mmol) to diisopropylamine (7 mL, 50 mmol) in 150 mL of tetrahydrofuran (THF, freshly distilled from $LiAlH_4$) at −80 °C (dry ice/diethyl ether). The light yellow LDA solution was stirred at −80 °C for 15–20 min. Then the α-chloro acid (25 mmol) dissolved in 10–15 mL of dry THF and cooled to −80 °C was added over ca. 5 min, using a stainless steel double-tipped transfer needle. The resulting dianion was stirred for 5 min at −80 °C before the carbonyl compound (25 mmol), dissolved in an equal volume of THF, was added from a syringe. After 5 min, the cooling bath was removed; the reaction mixture, after warming to room temperature, was quenched with 30 mL of water or saturated ammonium chloride solution. The organic layer was separated and washed twice with 30-mL portions of water and once with aqueous saturated sodium chloride solution. Unreacted carbonyl can be recovered from this organic layer. The combined aqueous portions were washed once with diethyl ether and cooled with vigorous stirring in a dry ice/diethyl ether bath until ice appeared on the side of the beaker. At this point the solution was acidified to pH 2 with cold 25% H_2SO_4 and removed from the cold bath. Dichloromethane (25 mL) was added and the mixture stirred until all of the ice melted. The layers were separated, and the aqueous layer was extracted 3 times with 10-mL portions of dichloromethane. The combined

organic layers were washed once with a small portion of water, dried over anhydrous magnesium sulfate, filtered, layered with argon, and sealed from the atmosphere. The glycidic acid can be stored with minimal decomposition at this stage. Isolation of the glycidic acid from the dichloromethane solution was done in one of the following ways, depending on the glycidic acid and the purpose for its synthesis: (A) for accurate yield and spectral analysis the dichloromethane solution of glycidic acid was treated with diazomethane, concentrated, and chromatographed on silica gel or (B) dropping pyrolysis decarboxylation reactions were performed with the unconcentrated solution and oven pyrolysis were performed on partially concentrated solutions, using the rotary evaporation apparatus at room temperature. Several glycidic acids, particularly those derived from bulky and/or symmetrical ketones, could be crystallized by overnight evacuation of the partially concentrated solution, using a vacuum pump, or crystallized by addition of pentane or hexane to the partially concentrated glycidic acid solution. The application of heat during rotary evaporation of dichloromethane resulted in significant glycidic acid decomposition which severely hindered subsequent crystallization attempts. Also recrystallization of either the solidified or crystallized glycidic acid resulted in a drastic reduction in yield with, in most cases, little increases in purity.

Generation and Reactions of Dianion 3 from 2-Bromo-3-methylbutanoic Acid. The procedure for the generation and reaction of dianion 3 was the same as that described above for dianion 1 and 2 except temperatures of 0 °C (rather than −80 °C) were used. The dianion can be generated at −80 °C as determined by deuterium oxide quenching at this temperature, but it reacts very sluggishly at low temperatures.

Reaction of dianion 2 with acetophenone afforded a ca. 3:2 mixture of (*E*)- and (*Z*)-2,3-dimethyl-3-phenyl-2-oxiranecarboxylic acid as a viscous oil (94%). Methylation with diazomethane gave the methyl esters (65:35) as an oil, bp 95 °C (0.4 mm). Upon standing methyl (*E*)-2,3-dimethyl-3-phenyl-2-oxiranecarboxylate crystallized. Recrystallization from carbon tetrachloride gave white crystals: mp 71–71.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 3 H, α-Me), 1.60 (s, 3 H, β-Me), 3.79 (s, 3 H, OMe), 7.26 (s, 5 H, Ph). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.61; H, 6.89. The *Z* isomer was a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.65, 1.67 (s, 3 H each, α- and β-Me's), 3.25 (s, 3 H, CO_2Me), 7.24 (s, 5 H, Ph).

Quenching the above reaction 30 s after addition of acetophenone by pouring the −80 °C reaction mixture into 25% H_2SO_4 afforded, after extraction with dichloromethane, drying over anhydrous magnesium sulfate, and methylation with diazomethane, an 85% yield of methyl 3-hydroxy-2-chloro-3-phenylbutanoate: ^{1}H NMR ($CDCl_3$) δ 1.72, 1.75 (3 H), 1.84, 1.85 (3 H) [two sets of overlapping singlets are the four methyls of the two diastereomers in an approximate ratio of 3:2], 3.63 (s, 3 H, CO_2Me), 3.80 and 4.13 (2 s, 1 H, diastereomeric alcohols in a 3:2 ratio, both disappear upon addition of D_2O), 7.35 (m, 5 H, Ph). Anal. Calcd for $C_{12}H_{15}ClO_3$: C, 59.39; H, 6.22. Found: C, 59.51; H, 6.22.

2-Methyl-3,3-diphenyl-2-oxiranecarboxylic Acid. The addition of benzophenone to the dianion 2 afforded an 84% yield of an off-white solid, mp 112–120 °C. Recrystallization from hexane afforded only a 29% recovery of white crystalline glycidic acid: mp 125–126.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3 H, α-Me), 7.3 (m, 10 H, Ph), 9.16 (s, 1 H, CO_2H). Direct methylation of a reaction mixture afforded methyl 2-methyl-3,3-diphenyl-2-oxiranecarboxylate: 76% yield; mp 78–79 °C; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3 H, α-Me), 3.41 (s, 3 H, CO_2Me), 7.5 (m, 10 H, Ph). Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 75.94; H, 5.98.

Methyl 3-Ethyl-2,3-dimethyl-2-oxiranecarboxylate. Reaction of dianion 2 and 2-butanone afforded a mixture of glycidic acids which could not be isolated. Treatment of the unisolated glycidic acid with diazomethane afforded a 1:1 mixture of (*E*)- and (*Z*)-methyl 3-ethyl-2,3-dimethyl-2-oxiranecarboxylate (96%) as a clear oil: bp 49 °C (0.9 mm); ^{1}H NMR ($CDCl_3$) singlets at δ 1.05, 1.30, 1.36, 1.55, 1.50, 3.80. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.97; H, 8.72.

Quenching the reaction by pouring the −80 °C reaction mixture into 25% H_2SO_4 30 s after the addition of 2-butanone afforded, after extraction with dichloromethane, drying over anhydrous magnesium sulfate, and methylation with diazomethane, a 97% yield of methyl 2-chloro-3-hydroxy-2,3-dimethylpentanoate: ^{1}H NMR ($CDCl_3$) δ 1.0 (t, 3 H, *J* = 3.3 Hz, CH_2CH_3), 1.26 (2 s 0.5 Hz apart, 3 H, α-Me diastereomers), 1.70 (m, 2 H, *J* = 3.3 Hz, CH_2CH_3 overlapping quartets due to diastereomers), 1.83 (2 s 5 Hz apart), 3 H, β-Me diastereomers), 3.5 (s, 1 H, OH, disappears upon addition of D_2O), 3.85 (s, 3 H, CO_2Me). Anal. Calcd for $C_8H_{15}ClO_3$: C, 49.36; H, 7.76. Found: C, 49.19; H, 7.59.

2-Methyl-3,3-diisopropyl-2-oxiranecarboxylic Acid. The reaction mixture of 2,4-dimethyl-3-pentanone with dianion 2 was worked up according to the prior procedure but divided into two equal portions after it was extracted into dichloromethane. One portion was concentrated, producing the acid (70%) as an off-white solid: mp 58–61 °C; ^{1}H NMR ($CDCl_3$) δ 1.07 (2 overlapping t, 6 H, $(CH_3)_2CH$), 1.62 (s, 3 H, α-Me), 2.93 (m, 2 H, $(CH_3)CH$), 11.48 (s, 1 H, CO_2H). The other portion was methylated with diazomethane, producing the methyl ester (77%) as a clear oil. Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.06. Found: C, 65.76; H, 10.20.

2-Methyl-3-phenyl-2-oxiranecarboxylic Acid. The reaction of the dianion 2 and benzaldehyde afforded, after overnight evacuation to remove the remaining solvent from the partially concentrated product, crude glycidic acid (100%) as a viscous oil which resisted crystallization: ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3 H, αMe), 4.4 (s, 1 H, β-H), 7.35 (s, 5 H, Ph), 10.8 (br s, 1 H, CO_2H).

Performing the above reaction in an identical manner but without sufficient warming produced, after methylation with diazomethane, a mixture which was separated with medium-pressure chromatography on silica gel, using 10:1 hexane/ethyl acetate. The first to come off of the column was the 96:4 mixture of (*E*)- and (*Z*)-methyl 2-methyl-3-phenyl-2-oxiranecarboxylate: ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3 H, *E* and α-Me), 1.70 (s, 3 H, *Z* and α-Me). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.41. Found: C, 68.42; H, 6.24. The second compound to elute was methyl 2-chloro-3-hydroxy-2-methyl-3-phenylpropanoate: mp 43.5–44 °C. Anal. Calcd for $C_{11}H_{13}ClO_3$: C, 57.77; H, 5.73. Found: C, 58.04; H, 6.00.

2-Methyl-3-ethyl-2-oxiranecarboxylic Acid. The reaction of dianion 2 and propanal afforded a product mixture which contained 68% of the desired acid as an *E*/*Z* mixture as well as 9% of 2-chloropropanoic acid and 23% of 2-chloro-2-methyl-3-hydroxypentanoic acid (determined from the ^{1}H NMR of the crude reaction mixture). Attempted separation of the mixture resulted in extensive decomposition. From a similar reaction, followed by treatment with diazomethane, was isolated a 2:1 mixture (*E*)- and (*Z*)-methyl 2-methyl-3-ethyl-2-oxiranecarboxylate: ^{1}H NMR ($CDCl_3$) δ 1.46 and 1.5 (s, *Z* and *E*, α-Me). Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.14; H, 8.85. If the above reaction is not allowed to warm to room temperature, varying amounts of methyl 2-chloro-2-methyl-3-hydroxypentanoate are isolated. Anal. Calcd for $C_7H_{13}ClO_3$: C, 46.54; H, 7.25. Found: C, 46.76; H, 6.98.

Methyl 2-Methyl-1-oxaspiro[2.5]octane-2-carboxylate. The reaction of dianion 2 and cyclohexanone afforded, after methylation and medium-pressure chromatography on silica gel, using 10:1 hexane/ethyl acetate, the methyl ester (74%) as a clear liquid: ^{1}H NMR ($CDCl_3$) δ [1.55 (s, CH_3) overlapping, 1.64 (br s, $(CH_2)_5$, total 13 H], 3.75 (s, 3 H, CO_2Me). Anal. Calcd for $C_{10}H_{16}O_3$: C, 64.19; H, 8.75. Found: C, 64.07; H, 8.73.

Quenching a similar reaction at −80 °C with aqueous acid produced, after methylation with diazomethane, methyl 2-chloro-2-(1-hydroxycyclohexyl)propanate (92%): ^{1}H NMR (CCl_4) δ 1.61 (br s, $(CH_2)_5$, 10 H), 1.79 (s, 3 H, $C(Cl)CH_3$), 2.75 (s, 1 H, OH, disappears upon addition of D_2O), 3.76 (s, 3 H, CO_2Me). Anal. Calcd for $C_{10}H_{17}ClO_3$: C, 54.42; H, 7.76. Found: C, 54.63; H, 7.79.

Methyl 2-Methyl-1-oxaspiro[2.4]heptane-2-carboxylate. The reaction of dianion 2 and cyclopentanone afforded, after methylation and distillation, the methyl ester (47%) as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 1.53 (s, 3 H, CH_3), 1.75 (br s, 8 H, $(CH_2)_4$, 3.73 (s, 3 H, CO_2Me). Anal. Calcd: C, 63.51; H, 8.29. Found: C, 63.21; H, 8.09.

Quenching a similar reaction at −80 °C with aqueous acid produced, after methylation, with diazomethane, methyl 2-chloro-2-(1-hydroxycyclopentyl)propanate (93%) as a clear liquid: ^{1}H NMR (CCl_4) δ 1.8 (s overlapping a br s, $(CH_2)_4$ and $C(Cl)CH_3$, 11 H), 2.78 (s, 1 H, OH, disappears upon addition of D_2O), 3.79 (s, 3 H, CO_2Me). Anal. Calcd for $C_9H_{15}ClO_3$: C, 52.30; H, 7.31. Found: C, 52.20; H, 7.35.

2-Isopropyl-3-methyl-3-phenyl-2-oxiranecarboxylic Acid.

Reaction of dianion 3 and acetophenone afforded the crude glycidic acid (96%) as an oil. Addition of pentane resulted in white crystals, mp 111–114 °C, which were a mixture of *E* and *Z* isomers. Fractional crystallization from pentane resulted in a combined 51% recovery of the less soluble *Z* isomer: mp 126–128 °C; ^{1}H NMR ($CDCl_3$) δ 1.1 (d, 3 H), 1.3 (d, 3 H), 1.9 (m, 1 H), 1.7 (s, 3 H, β-Me), 7.15 (s, 5 H), 8.45 (br s, 1 H, CO_2H). The second isomer to crystallize was the *E* isomer: mp 118–121 °C; ^{1}H NMR ($CDCl_3$) δ 1.0 (6 H, actually 2 overlapping d), 1.25 (m, 1 H), 1.73 (s, 3 H), 7.35 (s, 5 H), 10.3 (br s, 1 H).

Performing the same reaction as above but allowing 2 hours at room temperature before quenching followed by treatment with diazomethane resulted in a 79% yield of a mixture of (*E*)- and (*Z*)-methyl 2-isopropyl-3-methyl-3-phenyl-2-oxiranecarboxylate, bp 109 °C (0.4 mm), the *E* isomer of which crystallized upon standing: mp 55–57 °C; ^{1}H NMR (CCl_4) δ 0.84 and 1.05 (*i*-Pr), 1.60 (s, 3 H, β-Me), 3.85 (s, 3 H, CO_2Me), 7.40 (s, 5 H, Ph).

2-Isopropyl-3,3-diphenyl-2-oxiranecarboxylic Acid. Reaction of dianion 3 and benzophenone afforded the glycidic acid (91%) as an off-white solid after removal of the last traces of solvent by overnight evacuation. Recrystallization from pentane gave a white crystalline solid, mp 143.5–145 °C. Methylation with diazomethane afforded methyl 2-isopropyl-3,3-diphenyl-2-oxiranecarboxylate, mp 70.5–71 °C. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.94; H, 6.54. Only a trace of methyl 2-bromo-3-hydroxy 2-isopropyl-3,3-diphenylpropanate (mp 118–119 °C) was ever observed.

Methyl 2-Isopropyl-3-phenyl-2-oxiranecarboxylate. Reaction of the dianion 3 and benzaldehyde, according to the above procedure followed by methylation with diazomethane, afforded the glycidic ester (67%), bp 112 °C (2 mm), as a 58:42 mixture of *E* and *Z* isomers: ^{1}H NMR (of mixture; $CDCl_3$) δ 0.95 (2 overlapping d, $(CH_3)_2CH$, *Z* isomer), 1.2 (d of d, $(CH_3)_2CH$, *E* isomer). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.64; H, 7.12.

Methyl 2-Isopropyl-3-ethyl-3-methyl-2-oxiranecarboxylate. The addition of 2-butanone to dianion 3 in the usual fashion afforded after methylation with diazomethane a 1:1 *E*/*Z* mixture of glycidic esters (74%) as a clear oil: bp 42 °C (0.1 mm); 300-MHz ^{1}H NMR ($CDCl_3$) δ 1.04 (2 overlapping t, CH_3CH_2), 1.18 (2 overlapping d, $CH(CH_3)_2$, 1.24 and 1.37 (2 s), 1.5 and 1.65 (2 q, CH_3CH_2), 1.77 (heptet, $CH(CH_3)_2$).

Methyl 3-Methyl-3-phenyl-2-oxiranecarboxylate. The addition of acetophenone to dianion 1 afforded, after methylation with diazomethane, the glycidic ester as a 2:1 mixture of *Z* and *E* isomers: ^{1}H NMR of mixture ($CDCl_3$) δ 1.7 and 1.74 (both s, 3 H, *E* and *Z* β-Me). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.94; H, 6.37.

Quenching the above reaction by pouring the −80 °C reaction mixture into 25% H_2SO_4 30 s after addition of acetophenone afforded after workup and methylation with diazomethane a 53% yield of methyl 3-hydroxy-2-chloro-3-phenylbutanoate: ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 3 H, Me), 3.47 (s, 3 H, CO_2Me), 3.94 (br s, 1 H, OH, disappears upon addition of D_2O), 4.5 (s, 1 H, α-CH), 7.3 (m, 5 H, Ph). Anal. Calcd for $C_{11}H_{13}ClO_3$: C, 57.77; H, 5.73. Found: C, 57.71; H, 5.72.

Methyl 3-Ethyl-3-methyl-2-oxiranecarboxylate. The addition of 2-butanone to dianion 1 afforded, after methylation with diazomethane, a mixture (52%) of *E* and *Z* isomers: ^{1}H NMR ($CDCl_3$) δ 1.30 and 1.35 (s, *E* and *Z* β-Me). Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.38. Found: C, 58.54; H, 8.37.

Quenching the above reaction by pouring the −80 °C reaction mixture into 25% H_2SO_4 30 s after addition of 2-butanone afforded after workup and methylation with diazomethane a 56% yield of methyl 2-chloro-3-hydroxy-3-methylpentanoate.

Methyl 3,3-Diphenyl-2-oxiranecarboxylate. The addition of benzophenone to dianion 1 afforded, after methylation with diazomethane, the ester (38%): ^{1}H NMR ($CDCl_3$) δ 3.4 (s, 3 H, CO_2Me), 3.86 (s, 1 H, α-H), 7.3 (br s, 10 H, Ph). Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.38; H, 5.27.

Quenching the above reaction by pouring the −80 °C reaction mixture into 25% H_2SO_4 30 s after addition of benzophenone afforded after methylation methyl 2-chloro-3-hydroxy-3,3-diphenyl propanate (54%): ^{1}H NMR ($CDCl_3$) δ 3.6 (s, 3 H, CO_2Me), 4.45 (br s, 1 H, OH, disappears upon addition of D_2O), 5.1 (s, 1 H, C(Cl)H), 7.4 (br m, 10 H, Ph). Anal. Calcd for $C_{16}H_{15}ClO_3$: C, 66.10; H, 5.20. Found: C, 66.32; H, 5.17.

Methyl 3-Ethyl-2-oxiranecarboxylate. The addition of propanal to dianion 1 afforded, after methylation with diazomethane, the ester (41%) as a mixture of *E* and *Z* isomers: ^{1}H NMR ($CDCl_3$) δ 1.0 (t, 3 H, CH_3CH_2), 1.55 (m, 2 H, CH_3CH_2), 3.05–3.5 (m, 2 H, *E* and *Z* α and β protons), 3.71 (s, 3 H, CO_2Me).

Quenching the above reaction by pouring the −80 °C reaction mixture into 25% H_2SO_4 30 s after addition of propanal afforded after workup and methylation with diazomethane a 48% yield of methyl 2-chloro-3-hydroxy-pentanoate: ^{1}H NMR ($CDCl_3$) δ 1.0 (t, 3 H, CH_3CH_2), 1.61 (m, 2 H, CH_3CH), 3.15 (2 d, C(H)OH, disappears upon addition of D_2O), 3.83 (s, 3 H, CO_2CH_3), 4.3 (m, 2 H, (OH)CHCH(Cl)). Anal. Calcd for $C_6H_{11}ClO_3$: C, 43.26; H, 6.65. Found: C, 43.21; H, 6.50.

General Procedure for Oven Pyrolysis of Glycidic Acids. The dichloromethane solution of glycidic acid was concentrated on the rotary evaporator without the application of heat (complete removal of solvent resulted in appreciable decomposition). The flask was then connected by an elbow to a receiver cooled in a dry ice/acetone bath. The system was connected to a vacuum pump. The pyrolysis flask was inserted into an oven preheated to 300–360 °C.

General Procedure for Dropping Pyrolysis of Glycidic Acids. The unconcentrated dichloromethane (or chloroform) solution of glycidic acid was placed in a pressure-equalizing addition funnel connected to a vertically mounted 80-cm coiled column in a preheated oven (200–250 °C). A cold finger condenser was attached to the bottom of the column and filled with dry ice. The solvent and decarboxylated product were collected in a flask attached to the bottom of the cold finger condenser. A slight argon flow was passed through the system to keep the vapors flowing through the hot column and not up into the addition funnel. The glycidic acid solution was dropped through the column at such a rate that a constant temperature was maintained in the oven. When all of the solution had been pyrolyzed, the cold finger was warmed and rinsed. The solvent was removed at low pressure, and the residual oil chromatographed on silica gel, using 10:1 hexane/ethyl acetate.

General Procedure for Catalytic Decarboxylation. A portion of the chloroform from the unconcentrated solution of glycidic acid was distilled to azeotrope any remaining water. Anhydrous catalyst (dried overnight over P_2O_5 at 100 °C (0.1 mm)), was added and reflux continued until there was no further change in two successive TLC's or NMR's of the reaction mixture. When no further change was observed, the solution was cooled and filtered and the solvent was removed at reduced pressure. When Dowex 50-W resin was used as the catalyst, this was generally all the workup necessary. If acidic products were observed by TLC, the mixture was washed twice with aqueous bicarbonate solution before removal of solvent. Further purification was by medium-pressure chromatography on silica gel or distillation.

3-Phenyl-2-butanone. A. Oven Pyrolysis Method. A concentrated chloroform solution of 2,3-dimethyl-3-phenyl-2-oxiranecarboxylic acid (9.3 mmol theoretically, glycidic acid was not isolated) was placed in a preheated pyrolysis oven (350 °C) and the product collected in the dry ice/acetone cooled receiver. After column chromatography on silica gel, eluting with 10:] hexane/ethyl acetate, the product was obtained in 71% yield.

B. Dropping Pyrolysis Method. A dichloromethane solution of the glycidic acid (theoretically 6.25 mmol) was pyrolyzed by the dropping pyrolysis method previously described. A light yellow solution was obtained which when worked up produced 0.77 g of a mixture, which was separated by column chromatography on silica gel, eluting with 20:1 hexane/ethyl acetate. The homologated ketone was isolated in 71% yield.

C. Catalytic Method. Dowex Resin. A chloroform solution of the freshly prepared glycidic acid (theoretically 4.8 g, 25 mmol; glycidic acid not isolated) was dried and a portion of the chloroform distilled to azeotrope any remaining water. A catalytic amount of dried Dowex resin (one microspatula full) was added and the mixture refluxed overnight. Filtration and removal of solvent at reduced pressure afforded after distillation (bp 50 °C (0.4 mm)) the ketone (2.83 g, 76%).

3-Methyl-2-pentanone. Lithium bromide was added to a chloroform solution of 3-ethyl-2,3-dimethyl-2-oxiranecarboxylic acid (theoretically 1.6 mmol, glycidic acid not isolated) and the

mixture was stirred at room temperature for 6 days to give the 3-methyl-2-pentanone in 61% yield. A similar reaction in which molecular sieves (3Å; to absorb any water present) and lithium bromide were added produced the ketone in 73% yield.

Registry No. 1, 80532-57-6; 2, 80532-58-7; 3, 80532-59-8; acetophenone, 98-86-2; (*E,Z*)-2,3-dimethyl-3-phenyl-2-oxiranecarboxylic acid, 80532-60-1; methyl (*E*)-2,3-dimethyl-3-phenyl-2-oxiranecarboxylate, 14366-95-1; methyl (*Z*)-2,3-dimethyl-3-phenyl-2-oxiranecarboxylate, 14664-76-7; methyl 3-hydroxy-2-chloro-2-methyl-3-phenylbutanoate, 80532-61-2; benzophenone, 119-61-9; 2-methyl-3,3-diphenyl-2-oxiranecarboxylic acid, 24834-34-2; methyl 2-methyl-3,3-diphenyl-2-oxiranecarboxylate, 15309-40-7; 2-butanone, 78-93-3; (*E,Z*)-methyl 3-ethyl-2,3-dimethyl-2-oxiranecarboxylate, 80532-62-3; methyl 2-chloro-3-hydroxy-2,3-dimethylpentanoate, 80532-63-4; 2,4-dimethyl-3-pentanone, 565-80-0; 2-methyl-3,3-diisopropyl-2-oxiranecarboxylic acid, 80532-64-5; methyl 2-methyl-3,3-diisopropyl-2-oxiranecarboxylate, 80532-65-6; benzaldehyde, 100-52-7; 2-methyl-3-phenyl-2-oxiranecarboxylic acid, 25547-51-7; (*E,Z*)-methyl 2-methyl-3-phenyl-2-oxiranecarboxylate, 80532-66-7; methyl 2-chloro-3-hydroxy-2-methyl-3-phenylpropanoate, 80532-67-8; propanal, 123-38-6; (*E,Z*)-2-methyl-3-ethyl-2-oxiranecarboxylic acid, 80532-68-9; 2-chloropropanoic acid, 598-78-7; 2-chloro-2-methyl-3-hydroxypentanoic acid, 80532-69-0; (*E,Z*)-methyl 2-methyl-3-ethyl-2-oxiranecarboxylate, 80532-70-3; cyclohexanone, 108-94-1; methyl 2-methyl-1-oxaspiro[2,5]octane-2-carboxylate, 73039-91-5; methyl 2-chloro-2-(1-hydroxycyclohexyl)propanoate, 80532-71-4; cyclopentanone, 120-92-3; methyl 2-methyl-1-oxaspiro[2,4]heptane-2-carboxylate, 73039-89-1; methyl 2-chloro-2-(1-hydroxycyclopentyl)propanoate, 80532-72-5; (*Z*)-2-isopropyl-3-methyl-3-phenyl-2-oxiranecarboxylic acid, 80532-73-6; (*E*)-2-isopropyl-3-methyl-3-phenyl-2-oxiranecarboxylic acid, 80532-74-7; (*E,Z*)-methyl 2-isopropyl-3-methyl-3-phenyl-2-oxiranecarboxylate, 80532-75-8; (*E*)-methyl 2-isopropyl-3-methyl-3-phenyl-2-oxiranecarboxylate, 80532-76-9; 2-isopropyl-3,3-diphenyl-2-oxiranecarboxylic acid, 80532-77-0; methyl 2-isopropyl-3,3-diphenyl-2-oxiranecarboxylate, 80532-78-1; methyl 2-bromo-3-hydroxy-2-isopropyl-3,3-diphenylpropanoate, 80532-79-2; (*E,Z*)-methyl 2-isopropyl-3-phenyl-2-oxiranecarboxylate, 80532-80-5; (*E,Z*)-methyl 2-isopropyl-3-ethyl-3-methyl-2-oxiranecarboxylate, 80532-81-6; (*E,Z*)-methyl 3-methyl-3-phenyl-2-oxiranecarboxylate, 5441-04-3; methyl 3-hydroxy-2-chloro-3-phenylbutanoate, 80532-82-7; (*E,Z*)-methyl 3-ethyl-3-methyl-2-oxiranecarboxylate, 65492-41-3; methyl 2-chloro-3-hydroxy-3-methylpentanoate, 80532-83-8; methyl 3,3-diphenyl-2-oxiranecarboxylate, 76527-25-8; methyl 2-chloro-3-hydroxy-3,3-diphenylpropanoate, 80532-84-9; (*E,Z*)-methyl 3-ethyl-2-oxiranecarboxylate, 80581-35-7; methyl 2-chloro-3-hydroxypentanoate, 80532-85-0; di-*tert*-butyl ketone, 815-24-7; methyl 2-isopropyl-3-ethyl-2-oxiranecarboxylate, 80532-86-1; 3-phenyl-2-butanone, 769-59-5; 2-methyl-4,4-diphenyl-3-butanone, 7495-04-7; 1,1-diphenyl-2-propanone, 781-35-1; 2-methyl-4-phenyl-3-pentanone, 20474-49-1; 3-methyl-2-pentanone, 565-61-7; 2-phenylpropanal, 93-53-8.

Synthesis of Simple Derivatives of (2*Z*,4*Z*)-3-Methyl-2,4-hexadienedioic Acid

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Methanolysis of 4-methyl-2,7-oxepindione yields a mixture of both monomethyl esters of (2*Z*,4*Z*)-3-methyl-2,4-hexadienedioic acid. 4-Methyl-1,2-benzoquinone is oxidized by lead(IV) acetate in methanol–benzene to give dimethyl (2*Z*,4*Z*)-3-methyl-2,4-hexadienedioate. The 6-monomethyl ester, but not the 1-monomethyl ester or dimethyl ester, spontaneously stereomutates to the 2*Z*,4*E* isomer. The monoesters also cyclize to lactone esters. The disodium salt of (2*Z*,4*Z*)-3-methyl-2,4-hexadienedioic acid, prepared by saponification of the corresponding dimethyl ester or cyclic anhydride, is stable in the presence of excess base but immediately gives (2*Z*,4*E*)-3-methyl-2,4-hexadienedioic acid upon acidification. The results fit the general mechanism of stereomutation of 3-substituted (2*Z*,4*Z*)-2,4-hexadienedioic acids and derivatives.

The 3-methyl-2,4-hexadienedioic (β-methylmuconic) acids, a classical object of stereochemical investigation, were the subject of much past argument because hydrolysis of the cyclic anhydride 1 (Chart I), obtained by Baeyer–Villiger oxidation of 4-methyl-1,2-benzoquinone, unexpectedly yielded the 2*Z*,4*E* isomer **2a** rather than the 2*Z*,4*Z* isomer **3a**.[2-8] Similarly, enzymatic oxidation of 4-methylcatechol at pH 7–8 furnished what appeared to be the dianion of **3a** in solution,[9,10] but the product isolated after acidification was **2a**.[9,11]

The phenomenon that a 3-monosubstituted (2*Z*,4*Z*)-2,4-hexadienedioic acid is stable in base, but very rapidly stereomutates to the 4*E* isomer in acid, was first recognized in the 3-carboxy series.[12] That the isomerization requires a free 1-carboxy group was discovered by Ainsworth and Kirby, who accounted for their observations by a mechanism involving nucleophilic attack of the 1-carboxy group at the 4-position and rotation about the C4–C5 bond before reversion to a 2,4-hexadienedioate.[13] It should follow from this mechanism that not only the dianion but also the 1-esters of **3a** will be capable of retaining the 4*Z* configu-

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