The Darzens Glycidic Ester Condensation[1]

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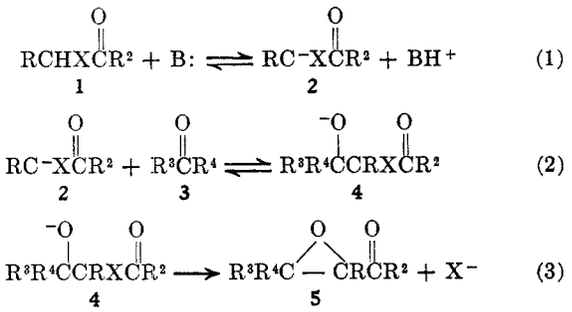
Benzaldehyde, acetophenone, and isobutyrophenone were condensed with the methyl, ethyl, isopropyl, and *t*-butyl esters of chloroacetic acid. The glycidic esters formed were analyzed for *cis/trans* isomer ratios. The chlorohydrin from acetophenone and *t*-butyl chloroacetate was treated with base in the presence of *p*-nitrobenzaldehyde and found to give a mixture of glycidic esters resulting from cyclization and from dealdolization and condensation with the *p*-nitrobenzaldehyde. A new mechanism for the Darzens glycidic ester condensation is proposed.

Although the Darzens glycidic ester condensation has been known for many years, there has not as yet been a satisfactory mechanism postulated for this reaction which explains all Darzens and Darzens-like condensations. The sequence of reactions is now generally accepted to be as shown in eq 1–3.



The reaction has been conclusively demonstrated to be noncarbenoid[3] and the intermediacy of a halohydrin has been shown by modifications of the conditions such that the cyclization step is essentially blocked. This can be done by using fluoride as the halogen since fluoride is notoriously unreactive in SN2-type displacements. When ethyl fluoroacetate was condensed with benzaldehyde, the fluorohydrin was isolated in 20% yield along with other products resulting from the halohydrin, such as α-fluorocinnamates and the free acids.[4] A second method for interrupting the sequence is the use of diisopropylamino magnesium bromide as the base.[5] This reaction depends on the formation of a rather insoluble sludge of the magnesium salt of the halohydrin which does not react further. Unfortunately, these same conditions are also responsible for rather low yields of the halohydrin.

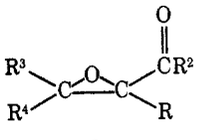
The difficulties in interpreting the mechanism are (1) the kinetic problem of whether step 2 or 3 is the rate-determining step, and (2) the conformational problem which determines the *cis/trans* isomer ratio of the resulting glycidic esters. We will deal with these problems one at a time.

The kinetic question is easily solved. There already exists sufficient evidence in the literature to draw the correct conclusion, *i.e.*, that the rate-determining step is a function of the reactants, and that one can go from the extreme of step 2 being rate determining[6] to that where step 3 is rate determining.[3] Unfortunately no condensations of intermediate reactivity have been previously demonstrated.

The method used for deducing the rate-determining step has been to treat the intermediate halohydrins with a base in the presence of a highly reactive aldehyde acceptor (either *m*- or *p*-nitrobenzaldehyde) and analyze the products of the reaction. Should aldolization be rate determining, then cyclization would be fast and only the glycidic ester resulting from direct cyclization would be found. Such was the case when Ballester treated the halohydrin from benzaldehyde and phenacyl chloride with base in the presence of *p*-nitrobenzaldehyde.[6] On the other hand, if cyclization is the slow step, then the aldolization–dealdolization preequilibrium would generate the carbanion **2** which would then condense with the more reactive aldehyde and lead to a different product from that from the starting halohydrin. An example of this type was shown by Zimmerman when he treated ethyl 2-chloro-3-hydroxy-2,3-diphenylpropionate with potassium *t*-butoxide in the presence of *m*-nitrobenzaldehyde.[3] There was isolated only the glycidic ester resulting from the *m*-nitrobenzaldehyde.

We have now observed for the first time a Darzens condensation in which the rate constants for the aldolization–dealdolization preequilibrium and cyclization are sufficiently close that one finds products from both direct cyclization and carbanion trapping. The halohydrin mixture from acetophenone and *t*-butyl chloroacetate was prepared by the method of Munch-Peterson[5] and treated with potassium *t*-butoxide in the presence of *p*-nitrobenzaldehyde. The glycidic esters from this reaction were analyzed by gas phase chromatography and found to consist of 87% product from direct cyclization and 13% glycidic ester from *p*-nitrobenzaldehyde.

A much more serious difficulty arises in predicting the stereochemistry of the final products. These products can exist as the geometrically related *cis* and *trans* isomers **6** and **7**. Based on the ratios of these isomers, or, more frequently, on the isolation of a single



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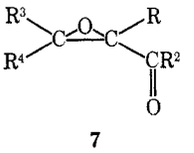

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(1) Presented in part at the 50th Annual Conference of the Chemical Institute of Canada, Toronto, Canada, June 1967.

(2) (a) Taken from the Ph.D. Thesis of R. K. Bansal, University of Calgary, 1968. (b) National Research Council of Canada student fellow, 1966–1968.

(3) H. E. Zimmerman and L. Ahramjian, *J. Amer. Chem. Soc.*, **82**, 5459 (1960).

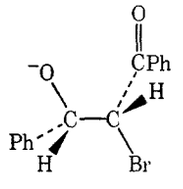
(4) V. F. Martynov and M. I. Titov, *J. Gen. Chem. USSR*, **30**, 4107 (1960).

(5) J. Munch-Peterson, *Acta. Chem. Scand.*, **7**, 1041 (1953).

(6) M. Ballester, *Chem. Rev.*, **55**, 283 (1955).

isomer, at least three different mechanisms for addition have been proposed.[3,7-9]

A sterically controlled reaction is favored by Cromwell and Setterquist[7] wherein the important factor is the conformation of the halohydrin anion leading to cyclization. In their work the condensation between benzaldehyde and phenacyl bromide gave predominantly or exclusively the *trans* isomer. They suggest that the configurationally unfavorable *threo* isomer **8** fails to cyclize to **9** but instead reverses to the reactants and then re-forms the more favorable *erythro* isomer **10** which can then readily cyclize to give the *trans*-glycidic ester **11**.



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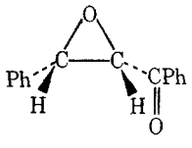

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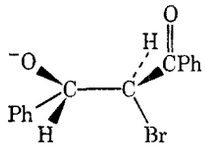

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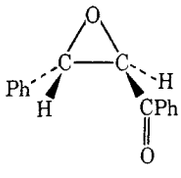

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Kwart and Kirk[8] implied the same argument but suggested in addition that any *cis* isomer found was probably due to base-catalyzed epimerization of the glycidic ester. Such epimerizations have already been well authenticated.[10,11]

A mechanism based on electronic repulsion between the oxyanion and the halogen atom has been proposed by Dahn and Loewe.[9] It is their suggestion that the halogen atom and the carbonyl oxygen which is developing a negative charge be *trans* coplanar in the transition state leading to the halohydrin oxy anion. The remaining groups would orient themselves to give the most favorable conformation. These would correspond to the conformations **8** and **10** where **10** would be the most favored conformation.

The most recent proposal by Zimmerman and Ahramjian[3] is that the stereochemistry of the final product is controlled by an overlap of the carbonyl π orbital of the ester and the developing p orbital at the α-carbon atom in the transition state between the halohydrin anion and the final epoxide. The resulting stereochemistry is based on the idea that in the condensation of benzaldehyde with ethyl α-chlorophenylacetate the carbethoxy group prefers to be *trans* to the phenyl group in spite of the fact that this places two phenyl groups *cis* to each other in the suggested transition state. There are logical arguments to support this suggestion.[3]

The mechanisms of Cromwell and Dahn and Loewe do not explain the product from benzaldehyde and ethyl α-chlorophenylacetate. Zimmerman's mechanism holds as long as the products are predominantly those in which the carbonyl group is *trans* to the larger group on the epoxide. This is usually a phenyl group. In view of several recent reports[12,13] of 50% or greater amounts of the isomer in which the carbonyl group appears *cis* to the phenyl group, the last mechanism also becomes suspect. Speziale and Frazier[12] condensed N,N-diethyl chloroacetamide with acetophenone and found that the glycidic amide consisted of approximately a 50% mixture of the *cis* and *trans* forms. This was not due to epimerization since the product was stable to epimerization conditions. Reinvestigation of a number of Darzens reaction products by Valente and Wolfhagen[13] showed significant amounts of *cis* isomer with one exception,[14] and in the case of ethyl 3-methyl-3-phenylglycidate the *cis* isomer predominated.

In a condensation between acetophenone and *t*-butyl chloroacetate we obtained a mixture of glycidic esters in which the isomer with the carboalkoxyl group *cis* to the phenyl group predominated to the extent of 62%. This is a significant excess over the *trans* isomer and is in direct contrast to what would be predicted by any of the previously discussed mechanisms. This prompted us to investigate the Darzens condensation further. We prepared a series of glycidic esters using benzaldehyde, acetophenone, and butyrophenone as the carbonyl component and the methyl, ethyl, isopropyl, and *t*-butyl esters of chloracetic acid as the carbanion source. Potassium *t*-butoxide in *t*-butyl alcohol were used as the base and solvent media as these have been shown to give the least elimination to cinnamates and give good yields of the glycidic esters.[15,16] In the examples using other than *t*-butyl esters, some transesterification does take place. This has been noted before[13] but will not effect the argument. In one case, it was possible to separate the *cis* and *trans* isomers by fractional distillation through an 18-in. spinning-band column. In this manner *t*-butyl *cis*-α-methyl-β-phenylglycidate (**19**) was obtained as a colorless liquid distilling at 77–78° (0.1 mm) and the *trans* isomer which remained in the distilling pot crystallized. This was then recrystallized from ethanol giving a white solid melting at 55–57°. These were identified by preparing the authentic *trans* isomer by epoxidation of *t*-butyl β-methylcinnamate with *m*-chloroperbenzoic acid, a reaction which is known to give stereospecifically *cis* addition.[13] The *cis* isomer was identified by elemental analysis and infrared and nmr spectra. The chemical shifts of the *t*-butyl protons appear at higher field in all of the *cis* isomers than in the *trans* isomers. This is because the *t*-butyl protons in the *cis* isomer spend part of their time in the shielding field of the aromatic ring.[17]

Chromatography of the crude reaction products on alumina gave mixtures of the glycidic esters which were suitable for analysis by nmr or gas chromatography. However, most of the reactions were analyzed directly by gas chromatography without any preliminary separation. The nmr method was only suitable for the

(7) N. H. Cromwell and R. A. Setterquist, *J. Amer. Chem. Soc.*, **76**, 5752 (1954).
(8) H. Kwart and L. G. Kirk, *J. Org. Chem.*, **22**, 116 (1957).
(9) H. Dahn and L. Loewe, *Chimia*, **11**, 98 (1957).
(10) H. O. House and R. S. Ro, *J. Amer. Chem. Soc.*, **80**, 2428 (1958).
(11) H. H. Wasserman and N. E. Aubrey, *ibid.*, **77**, 590 (1955).
(12) A. J. Speziale and H. W. Frazier, *J. Org. Chem.*, **26**, 3176 (1961).
(13) V. R. Valente and J. L. Wolfhagen, *ibid.*, **31**, 2509 (1966).
(14) The exception was ethyl 2,3-diphenylglycidate which is the model used by Zimmerman for his proposed mechanism.
(15) L. Field and C. G. Carlile, *ibid.*, **26**, 3170 (1961).
(16) W. S. Johnson, J. S. Belew, L. J. Chinn, and R. Hunt, *J. Amer. Chem. Soc.*, **75**, 4995 (1953).
(17) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p 126.

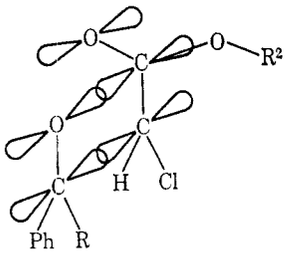
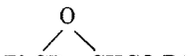


Figure 1.

analysis of the *t*-butyl glycidic esters from benzaldehyde and acetophenone. It was not possible to get satisfactory integrations of the remainder of the glycidic esters. The results of these analyses are shown in Table I.

TABLE I

cis/trans ISOMER RATIOS FROM DARZENS CONDENSATIONS



R	R^2	Compound	% *cis*	% *trans*	*cis/trans*
H	CH_3	12	21	79	0.27
	C_2H_5	13	26	74	0.35
	$CH(CH_3)_2$	14	33	67	0.49
	$C(CH_3)_3$	15	54	46	1.2
CH_3	CH_3	16	43	57	0.75
	C_2H_5	17	49	51	0.96
	$CH(CH_3)_2$	18	60	40	1.5
	$C(CH_3)_3$	19	62	38	1.6
$CH(CH_3)_2$	CH_3	20	73	27	2.7
	C_2H_5	21	75	25	3.0
	$CH(CH_3)_2$	22	79	21	3.7
	$C(CH_3)_3$	23	75	25	3.0

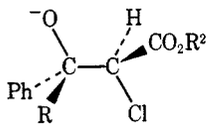
Examination of Table I shows two interesting trends; as the size of the alkyl radical attached to the benzoyl group increases, or the size of the ester alkoxyl group increases, the *cis/trans* isomer ratio increases.[18] That this is not due to epimerization of the glycidic esters was demonstrated by attempting to epimerize both the *cis* and *trans* forms of *t*-butyl β-methyl-β-phenylglycidate with potassium *t*-butoxide in *t*-butyl alcohol. The results are shown in Table II. As expected, the *trans* isomer is the thermodynamically more stable. Since the condensation reactions were completely homogeneous and since most of the products were liquids, there was no chance for an insoluble isomer to be separated by precipitation. This has occurred in a previous study[8] and led to erroneous conclusions.

TABLE II

EPIMERIZATION OF *t*-BUTYL β-METHYL-β-PHENYLGLYCIDATE WITH POTASSIUM *t*-BUTOXIDE IN *t*-BUTYL ALCOHOL

	Room temp for 170 hr		70° for 24 hr	
Starting isomer	% *trans*	% *cis*	% *trans*	% *cis*
trans	100	0	100	0
cis	0	100	32	68

Alternatively, epimerization of the intermediate halohydrin must be considered. If one looks at the preferred conformations of these halohydrins, one sees that **24** is the preferred conformation for cyclization and leads to the *trans*-glycidic ester. In spite of this, increasing the size of R^2 leads to the formation of more of the *cis* isomer which must come from conformation **25**. Therefore, epimerization of these intermediates must be slow compared with cyclization.



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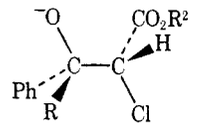

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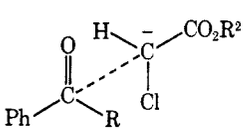
One is now forced to the conclusion that the stereochemistry of the final product is fixed by the aldolization step (step 2). Let us consider the possible conformations of the transitions state leading to formation of the *trans* isomer. If we look at the normally accepted skew forms **26–28** we find that, when R = H, **26** is the



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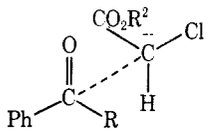

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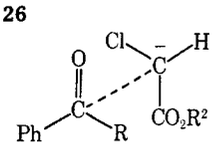

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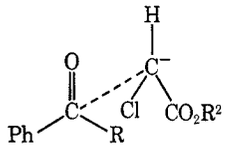
most acceptable both on steric grounds and, as has also been suggested, because of repulsive forces between the halogen atom and the developing oxy anion. It is conceivable that increasing the steric bulk of R would cause a new conformation favoring the *cis* isomer, but we have some difficulty in explaining why increasing the size of R^2 causes a greater amount of the *cis* isomer to be formed when, in fact, this conformation would predict that the *trans* isomer should increase. There is no compelling reason to consider either form **27** or **28** since **27** would not explain the results and **28** would certainly not be a stable conformation.

Eclipsed conformations are usually not considered because of the additional energy introduced by van der Waals repulsive forces.[19] However, they can exist in cases where some additional bonding forces come into play. Looking at the eclipsed conformations **29–31** we see that such an additional bonding force is in fact possible in conformation **30**. Here, the electron pair



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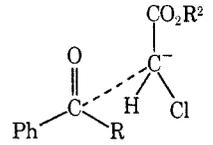

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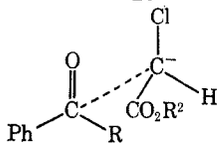

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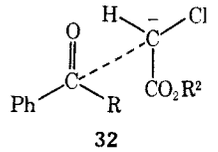

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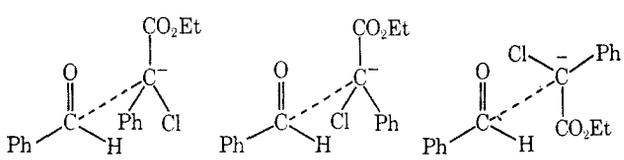
(18) There is an apparent discrepancy in the case of compound **23**. Whether this is due to experimental error or to some further effect we do not know. We tend to favor the former since the difference in ratio in all four adducts with isobutyrophenone is small.

(19) E. L. Eliel, N. L. Allinger, S. J. Angyal, and S. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1966, Chapter 1.

on the developing oxy anion can overlap with the π orbital of the ester carbonyl carbon atom in what amounts to a nucleophilic attack on this center. This is shown in Figure 1. Accepting this conformation as a working hypothesis one sees that increasing the size of either R or R^2 increases the repulsive energy of the eclipsed groups until it exceeds that of the overlap energy and thus forces the transition state out of the eclipsed conformation. When the overlapping orbitals are forced out of linearity a new force comes to the fore, a repulsive force between the developing oxy anion and the partial negative charge on the carbonyl oxygen of the ester group which is present because of the resonant anion. This repulsive force must be more important than that between the oxy anion and the halide atom and one would predict that these two groups would try to get as far apart from each other as possible, *i.e.*, into a *trans* coplanar conformation. Consideration of the remaining groups predict that conformation **32** would then be favored. This conformation gives the *cis* isomer after cyclization.

The mechanism which we here propose satisfactorily explains all of the examples which we have presently been able to find. Perhaps the least obvious case is of that of Zimmerman[8] between benzaldehyde and ethyl α-chlorophenylacetate. Accepting our mechanism one sees that either a phenyl group or a chlorine atom must eclipse a phenyl group to give the glycidic ester from the overlap conformation in Figure 1 (**33** or **34**). Alternatively using the *trans* skew conformation one would predict **35** to be the preferred conformation. This now leads to the glycidic ester with the phenyl groups *cis* to each other as is found experimentally.



Experimental Section[20]

All Darzens condensations were run under identical conditions. A model run is described for the preparation of methyl β-phenylglycidate.

Methyl β-Phenylglycidate (12).—To a mixture of 15 g (0.14 mol) of benzaldehyde and 15.1 g (0.14 mol) of methyl chloroacetate there was added dropwise a solution of 15.7 g (0.14 mol) of potassium *t*-butoxide in 150 ml of *t*-butyl alcohol under a nitrogen atmosphere over a period of 1.5 hr at room temperature. The reaction was stirred for an additional 3.5 hr. The *t*-butyl alcohol was then removed *in vacuo* and the residue was treated with ether and washed with water. The aqueous phase was extracted with two 100-ml portions of ether and the ether extracts were combined. The organic extract was washed with saturated sodium chloride solution and water and dried ($MgSO_4$). The ether was removed by distillation and the residue was distilled through an 18-in. spinning-band column to give 10.7 g (42.5% yield) of a colorless liquid (**12**): bp 73–74° (0.02 mm); $n^{25}D$ 1.5235 [lit.[21] bp 121–122° (4 mm)].

Ethyl β-Phenylglycidate (13).—From 15 g (0.14 mol) of benzaldehyde and 17.1 g (0.14 mol) of ethyl chloroacetate there was obtained 15.8 g (58.2%) of glycidic ester **13**: bp 86–88° (0.02 mm); $n^{25}D$ 1.5149 [lit.[22] bp 96° (0.5 mm); $n^{25}D$ 1.5131].

Isopropyl β-Phenylglycidate (14).—From 15.0 g (0.14 mol) of benzaldehyde and 19.1 g of isopropyl chloroacetate a yield of 17.9 g (66%) of glycidic ester **14** was obtained: bp 87–88° (0.03 mm); $n^{25}D$ 1.5053; ir (CCl_4) 1754, 1730 cm^{-1} (C=O).[23]

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.90; H, 6.79. Found: C, 70.21; H, 6.82.

***t*-Butyl β-Phenylglycidate (15).**—The reaction of 15 g (0.14 mol) of benzaldehyde and 21.07 g (0.14 mol) of *t*-butyl chloroacetate gave 17.2 g (78.2%) of glycidic ester **15**: bp 82° (0.02 mm); $n^{25}D$ 1.4981; ir (CCl_4) 1754, 1730 cm^{-1} (C=O); nmr ($CDCl_3$)[24] *cis* isomer, τ 8.85 [s, $C(CH_3)_3$], 6.35 (d, J = 5 Hz, α H), 6.60 (d, J = 5 Hz, β H); *trans* isomer, τ 8.53 [s, 9, $C(CH_3)_3$], 6.50 (d, 1, J = 2 Hz, α H), 6.01 (d, 1, J = 2 Hz, β H).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.85; H, 7.36.

Methyl β-Methyl-β-phenylglycidate (16).—From 12.0 g (0.10 mol) of acetophenone and 11.0 g (0.10 mol) of methyl chloroacetate there was obtained 8.2 g (42.7%) of glycidic ester **16**: bp 75–77° (0.2 mm); $n^{25}D$ 1.5109; ir (CCl_4) 1766, 1738 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.25. Found: C, 68.56; H, 6.19.

Ethyl β-Methyl-β-phenylglycidate (17).—Acetophenone (12.0 g, 0.10 mol) and ethyl chloroacetate (11.4 g, 0.10 mol) yielded 12.8 g (62.1%) of glycidic ester **17**: bp 98–99° (0.01 mm); $n^{25}D$ 1.5029 [lit.[25] bp 138° (6 mm); $n^{25}D$ 1.5027].

Isopropyl β-Methyl-β-phenylglycidate (18).—Acetophenone (12.0 g, 0.1 mol) and isopropyl chloroacetate (13.0 g, 0.1 mol) afforded glycidic ester **18** in a yield of 11.5 g (52.3%): bp 80–81° (0.07 mm); $n^{25}D$ 1.4961 [lit.[21] bp 112–114° (2.5 mm)].

***t*-Butyl β-Methyl-β-phenylglycidate (19).**—Acetophenone (18.0 g, 0.15 mol) was condensed with *t*-butyl chloroacetate. Distillation of the crude product yielded 19.5 g (51%) of *t*-butyl *cis*-β-methyl-β-phenyl glycidate (**19**): bp 77–78° (0.1 mm); $n^{25}D$ 1.4938; ir (CCl_4) 1755, 1722 cm^{-1} (C=O); nmr ($CDCl_3$) τ 8.91 [s, 9, $C(CH_3)_3$], 6.50 (s, 1, α H), 8.33 (s, 3, β CH_3).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.73. Found: C, 71.68; H, 7.73.

The residue from the distillation crystallized. Recrystallization from ethyl alcohol yielded 6.7 g (17.5%) *t*-butyl *trans*-β-methyl-β-phenylglycidate (**19**): mp 55–57°; ir (CCl_4) 1755, 1722 cm^{-1} (C=O); nmr ($CDCl_3$) τ 8.51 [s, 9, $C(CH_3)_3$], 6.74 (s, 1, α H), 8.25 (s, 3, β CH_3).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.73. Found: C, 71.62; H, 7.50.

***t*-Butyl *trans*-β-Methyl-β-phenylglycidate (19a).**—*trans*-β-Methylcinnamic acid[26] (35 g, 0.19 mol) and thionyl chloride (113 g, 0.95 mol) were heated on a water bath until the evolution of HCl had ceased. The acid chloride was distilled to give 35.7 g (91.5%) of a colorless liquid: bp 78–80° (0.08 mm). A mixture of 16 g (0.08 mol) of the acid chloride, 10.5 g (0.08 mol) of N,N-dimethylaniline, and 6.4 g (0.08 mol) of *t*-butyl alcohol was refluxed for 12 hr and then allowed to stand at room temperature for 12 hr. Distillation furnished 5.4 g (27.9%) of the ester: bp 69–70° (0.05 mm) [lit.[27] 104.5–108° (1 mm)].

To a solution of *t*-butyl *trans*-β-methylcinnamate (2.0 g, 0.009 mol) in 10 ml of CH_2Cl_2 was added 1.8 g (0.009 mol) of 85% *m*-chloroperbenzoic acid in 10 ml of CH_2Cl_2 and the mixture was refluxed for 70 hr. The reaction was worked up as described elsewhere.[13] The crystalline product was recrystallized from ethanol yielding 1.7 g (63%) of pure *t*-butyl *trans*-β-methyl-β-phenylglycidate: mp 55–57°. This was identical with that isolated from the glycidic ester condensation between acetophenone and *t*-butyl chloroacetate.

Methyl β-Isopropyl-β-phenylglycidate (20).—Isobutyrophenone (10 g, 0.06 mol) and methyl chloroacetate (6.5 g, 0.06 mol) were condensed to yield 8.1 g (54.4%) of glycidic ester **20**: bp 90–92° (0.08 mm); $n^{25}D$ 1.5129; ir (CCl_4) 1765, 1735 cm^{-1} (C=O).

(20) Boiling points and melting points are uncorrected. Elemental analyses were performed by Mrs. S. Swaddle of this department. Infrared spectra were measured on a Perkin-Elmer Model 237B spectrophotometer. Gas–liquid chromatographic analyses were carried out on a Hewlett–Packard Model 402 biomedical gas chromatograph. Nmr were recorded on a Varian A-60-spectrometer.

(21) S. Ishikawa and E. Yamamoto, *Rept. Sci. Res. Inst.* (Japan), **26**, 170 (1950).

(22) H. O. House and J. W. Blaker, *J. Amer. Chem. Soc.*, **80**, 6389 (1958).

(23) This double carbonyl band has been ascribed to rotomers and is not due to the two isomers present.[22]

(24) The pure *trans* isomer was prepared from the oxidation of *trans*-*t*-butyl cinnamate with *m*-chloroperbenzoic acid according to the method of Valente and Wolfhagen[13] and its nmr spectrum was measured. The values for the *cis* isomer were then taken from the mixture of the two isomers.

(25) H. O. House, J. W. Blaker, and D. A. Madden, *ibid.*, **80**, 6386 (1958).

(26) D. Lipkin and T. D. Stewart, *ibid.*, **61**, 3295 (1939).

(27) C. R. Hauser and W. H. Puterbaugh, *ibid.*, **75**, 1068 (1953).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 70.91; H, 7.27. Found: C, 70.68; H, 7.68.

Ethyl β-Isopropyl-β-phenylglycidate (21).—Isobutyrophenone (10 g, 0.06 mol) and ethyl chloroacetate (7.5 g, 0.06 mol) were condensed to yield 10.6 g (67%) of glycidic ester **21**: bp 81–82° (0.03 mm); $n^{25}D$ 1.4933; ir (CCl_3) 1764, 1730 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.80; H, 7.69. Found: C, 71.57; H, 7.90.

Isopropyl β-Isopropyl-β-phenylglycidate (22).—Ten grams (0.06 mol) of isobutyrophenone was condensed with 8.1 g (0.06 mol) of isopropyl chloroacetate to yield 9.8 g (58.5%) of glycidic ester **22**: bp 72.5° (0.05 mm); $n^{25}D$ 1.4881; ir (CCl_4) 1761, 1727 cm^{-1} (C=O).

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.06. Found: C, 72.38; H, 8.16.

***t*-Butyl β-Isopropyl-β-phenylglycidate (23).**—Condensation of 23 g (0.15 mol) of isobutyrophenone and 22.5 g (0.15 mol) of *t*-butyl chloroacetate yielded 24.5 g (64%) of glycidic ester **23**: bp 87–89° (0.1 mm); $n^{25}D$ 1.4915; ir (CCl_4) 1761, 1719 cm^{-1} (C=O).

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.20; H, 8.46.

***t*-Butyl β-(*p*-Nitrophenyl)glycidate.**—*t*-Butyl chloroacetate (19.5 g, 0.13 mol) was condensed with *p*-nitrobenzaldehyde (19.5 g, 0.13 mol) to yield 32.4 g (92%) of crystalline glycidic ester. Recrystallization from ethanol gave 24.2 g (68.5%) of pale yellow crystals: mp 89–91°; ir (CCl_4) 1757, 1730 cm^{-1} (C=O).

Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.87; H, 5.66; N, 5.28. Found: C, 58.88; H, 5.68; N, 5.00.

***t*-Butyl α-Chloro-β-hydroxy-β-phenylpropionate.**—This compound was prepared by the method of Munch-Peterson.[5] The crude product was a brown oil which was partially purified by removing the low boiling components by distillation and chromatographing the residue over silica gel. The fraction containing the chlorohydrins was eluted with 20% ether in hexane. The chlorohydrins could not be induced to crystallize and the mixture was used directly in the cyclization studies. The absence of acetophenone, *t*-butyl chloroacetate, and glycidic esters was readily demonstrated by glpc.

Cyclization of Chlorohydrin Ester in the Presence of *p*-Nitrobenzaldehyde.—To a solution of 2.4 g (8.8 mmol) of chlorohydrin ester and 3.32 g (22 mmol) of *p*-nitrobenzaldehyde in 20 ml of *t*-butyl alcohol was added dropwise a solution of 510 mg (9.1 mmol) of potassium *t*-butoxide in 20 ml of *t*-butyl alcohol under a nitrogen atmosphere. The mixture was stirred for 3.5 hr. At the end of this time water was added and the mixture was extracted with ether. The ether layer was washed with water and dried ($MgSO_4$). Evaporation of the solvent left 3.1 g of a viscous oil. Analysis by glpc showed that the glycidic esters were composed of 13% *t*-butyl β-(*p*-nitrophenyl)glycidates and 87% *t*-butyl β-methyl-β-phenylglycidates (**19**).

Epimerization of *t*-Butyl *cis*-β-Methyl-β-phenylglycidate.—A solution of 2 g of *cis*-glycidate in 50 ml of *t*-butyl alcohol and a catalytic amount of potassium *t*-butoxide was allowed to stand at room temperature for 1 week. After this time the *t*-butyl alcohol was removed *in vacuo* and the residue was treated with a dilute solution of NH_4Cl and extracted with ether. The ether extract was dried ($MgSO_4$) and the solvent was removed by distillation. The residue was analyzed by nmr.

A second sample was treated similarly except that it was heated at 70° for 24 hr.

Epimerization of the *trans* isomer was carried out under the same conditions. The results are listed in Table II.

Analyses of *cis/trans* Glycidic Ester Ratios.—A 2-g sample of the crude ester from a Darzens condensation was chromatographed on alumina (30 g, activity II, neutral) and eluted with 300 ml of petroleum ether (bp 30–60°). The solvent was removed *in vacuo* and the residual mixture was used for analyses. Recovery of material from the column was better than 95% in all cases.

A. Nmr.—The *t*-butyl esters from acetophenone and benzaldehyde could be analyzed by nmr. Both the peaks due to the *t*-butyl group and the α proton were sufficiently separated from other peaks that satisfactory integrations were obtained.

B. Glpc.—Crude samples taken directly from the reaction mixture or samples eluted from the chromatography columns gave the same results within experimental error. The latter were used as it was easier to integrate the results. Injection of samples in ether solution on a 4-ft column of 3.8% SE-30 on Chromosorb W (acid-washed DMCS) at temperatures between 110 and 125° gave clear separations of all *cis–trans* pairs. The relative areas under the peaks were calculated using a Disc integrator. Reproducibility is within ±2%. In all cases, the *trans* isomer preceded the *cis* isomer in elution from the column.

Registry No.—**14**, 21309-17-1; **15** (*cis*), 21309-18-2; **15** (*trans*), 7042-30-0; **16**, 5441-04-3; **19** (*cis*), 21309-20-6; **19** (*trans*), 21309-21-7; **20**, 21297-89-2; **21**, 21297-90-5; **22**, 21297-91-6; **23**, 21297-92-7; *t*-butyl β-(*p*-nitrophenyl)glycidate, 21297-93-8.

Preparation of Olefins by Pyrolysis of O-Alkyl Dimethylthiocarbamates[1,2]

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Pyrolysis of O-alkyl dimethylthiocarbamates which contain a β hydrogen affords olefins in high yield. The temperature required for pyrolysis is somewhat lower than that needed for the pyrolysis of the corresponding xanthates and is much lower than that needed for acetates. The required O-alkyl dimethylthiocarbamates of primary and secondary alcohols were prepared from the corresponding sodium alkoxides and dimethylthiocarbamyl chloride in 80–90% yields. O-Neopentyl dimethylthiocarbamate is recovered unchanged when heated to 300°.

In the course of studies on the rearrangement of O-aryl dimethylthiocarbamates to S-aryl dimethylthiocarbamates on heating,[3] the question arose as to whether a similar rearrangement would occur in the aliphatic series. Since elimination, as in the case of xanthates, would be expected if O-alkyl dimethylthiocarbamates which contained a β hydrogen were used, O-neopentyl dimethylthiocarbamate (I) was prepared. Even when heated to 30° for 20 min, I was recovered mostly unchanged. Thus, the oxygen to sulfur rearrangement occurs readily only in the aryl series.[4] This result stands in contrast to that obtained on pyrolysis of O-2,2,6,6-tetramethylcyclohexyl-S-methyl

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(2) Taken from the M.S. thesis presented to The Ohio State University, 1967, by F. W. H.

(3) M. S. Newman and H. S. Karnes, *J. Org. Chem.*, **31**, 3980 (1966).

(4) Professor D. Horton, The Ohio State University, in a private communication, has reported to us that certain dimethylthiocarbamates in the protected sugar series do give small yields of the corresponding S-alkyl dimethylthiocarbamates on heating in the region of 300°. Also, photochemical treatment leads to the S-alkyl derivatives in small yield. These results will be published at a later date. For similar reactions in the sugar field, see D. Horton and D. H. Hutson, *Advan. Carbohyd. Chem.*, **18**, 160 (1963).