The Darzens Condensation. II. Reaction of Chloroacetamides with Aromatic Aldehydes

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N,N-Dialkyl-α-chloroacetamides undergo the Darzens condensation at relatively low temperatures with aromatic aldehydes to give *cis*- and *trans*-epoxyamides in essentially equal amounts. In the presence of potassium *t*-butoxide the sterically favored *trans*-epoxide does not undergo epimerization whereas the *cis* isomer epimerizes at relatively high temperature. The Darzens condensation with amides is viewed as proceeding *via* a slow irreversible aldolization followed by a rapid cyclization step. The configurational assignment of the isomeric epoxy amides is confirmed by n.m.r. spectra and by an unambiguous synthesis of the *trans*-epoxyamides. The reliability of n.m.r. in the quantitative determination of a mixture of *cis*–*trans*-epoxides is demonstrated. Infrared data of the *cis*–*trans*-epoxyamides are also reported.

In continuing our studies on the Darzens condensation,[1] we undertook the investigation of the reaction of N,N-disubstituted α-chloroacetamides with aromatic aldehydes. Although a few reactions with amides were reported previously,[2] their stereochemical products were not isolated or identified. Of particular interest to us were the observations that only *trans*-epoxides were formed from benzaldehyde and ethyl chloroacetate[3] or chloroacetone[4] under normal Darzens conditions. However, Linstead[5] reported the formation of the *cis*-epoxide from benzaldehyde and methyl α-chloroacetate and, recently, Field[6] also reported the probable formation of the *cis*-epoxide from benzaldehyde and ethyl chloroacetate.

Normally the Darzens condensation leads to a mixture of *cis*- and *trans*-epoxy diastereoisomers. However, depending on the reaction conditions either or both isomers can be isolated. The kinetically (or sterically) favored *trans*-epoxide (carbonyl group *trans* to substituent in 3-position) is initially formed but on prolonged contact with the basic media, epimerization[7,8] occurs with the crystallization of the less soluble *cis* isomer.[7,9]

Several investigators have dealt with the stereochemistry of the Darzens condensation. Ballester and Perez-Blanco[10a] have demonstrated that the base-catalyzed condensation of *m*-nitrobenzaldehyde and 2,4,6-trimethoxyphenacyl chloride affords the two isomeric chlorohydrins and each of these under usual Darzens condensation conditions gives the same, and only one, epoxy isomer. This isomer is also the sole product in Darzens condensation from the same reactants. Ballester and Bartlett[10b] indicated that the aldolization step in the Darzens condensation from benzaldehyde and the phenacyl chloride is irreversible. Zimmerman and Ahramjian[11] also have noted that each of the diastereoisomers of ethyl 2-chloro-3-hydroxy-2,3-diphenylpropionate under Darzens conditions, affords only one epoxide. However, in contrast to Ballester,[10b] they concluded that the Darzens condensation proceeds *via* an initial rapidly reversible aldolization–dealdolization prequilibrium followed by a rate-limiting and stereochemically controlled cyclization. As a consequence of overlap control, that epoxide is formed in which the carbonyl group occupies an unhindered position with respect to the 3-phenyl group in the transition state.

We have reported previously[1] that acetophenone and N,N-diethyl-α-chloroacetamide under Darzens conditions gave both *cis*- and *trans*-epoxides in about equal amounts. However, in contrast to the reaction of ethyl chloroacetate[3] or methyl chloroacetate[5] with benzaldehyde, N,N-diethyl-α-chloroacetamide and N,N-diallyl-α-chloroacetamide with benzaldehyde each gave a mixture of the *cis* and *trans* diastereoisomers in essentially equal amounts. Similar results were also obtained for substituted aromatic aldehydes with N,N-diethyl-α-chloroacetamide (Table I). One would expect as a consequence of overlap control in the transition state[11] that 2,6-dichlorobenzaldehyde would provide a system where the *trans* isomer might predominate. This, however, under Darzens conditions gave a mixture of the *cis*- and *trans*-epoxyamides in equal quantities. The formation of the *cis*-epoxyamide could result from the base-catalyzed epimerization of the *trans*-epoxyamide in the reaction medium. However, this interpretation is rejected in that equal quantities of both isomers were obtained in all cases and the *trans*-epoxyamide is not epimerized even under more drastic conditions (Table V).

Our first attempt in the investigation of the configuration of the isomers obtained in Darzens condensation was the synthesis of *trans*-Ia through the known stereospecific epoxidation of *trans*-IIa with peracid.[12] Unfortunately, *trans*-IIa did not give any epoxidation product with monoperphthalic acid. The *trans* bromo-

(1) A. J. Speziale and H. W. Frazier, *J. Org. Chem.*, **26**, 3176 (1961).

(2) M. S. Newman and B. J. Bagerlein, *Org. Reactions*, **5**, 438 (1949).

(3) (a) H. O. House, J. W. Baker, and D. A. Madden, *J. Am. Chem. Soc.*, **80**, 6386 (1958); (b) H. O. House and J. W. Baker, *ibid.*, **80**, 6389 (1958).

(4) H. Kwart and L. G. Kirk, *J. Org. Chem.*, **32**, 116 (1957).

(5) (a) R. P. Linstead, L. N. Owen, and R. F. Webb, *J. Chem. Soc.*, 1218 (1953). (b) There is some doubt as to the stereochemical homogeneity of the methyl 3-phenylglycidate prepared by these workers. The glycidate distilled over a 10° range and the elemental analysis for carbon was 3% lower than the calcd. value. Our work on the Darzens condensation from benzaldehyde and methyl α-chloroacetate clearly indicate a mixture of *cis*- and *trans*-glycidates.

(6) L. Field and C. G. Carlile, *J. Org. Chem.*, **26**, 3170 (1961).

(7) N. H. Cromwell and R. A. Setterquist, *J. Am. Chem. Soc.*, **76**, 5752 (1954).

(8) H. O. House and R. S. Ro, *ibid.*, **80**, 2428 (1958).

(9) (a) H. Jorlander, *Ber.*, **50**, 1457 (1917); (b) S. Bodforss, *ibid.*, **51**, 192 (1918); (c) J. H. Berson, *J. Am. Chem. Soc.*, **74**, 5175 (1952); *Chem. Ind.* (London), 814 (1957); (d) H. H. Wasserman, N. E. Aubrey, and H. E. Zimmerman, *J. Am. Chem. Soc.*, **75**, 96 (1953); (e) H. H. Wasserman and H. E. Aubrey, *ibid.*, **77**, 590 (1955); (f) H. Dahm and L. Loewe, *Chimia*, **11**, 98 (1951); (g) recently N. H. Cromwell, F. H. Schumacher, and J. L. Adelfang [*J. Am. Chem. Soc.*, **83**, 974 (1961)] have shown that when sufficient solvent is used *cis*-2-nitro chalcone oxide undergoes base-catalyzed epimerization to form the thermodynamically stable *trans* isomer.

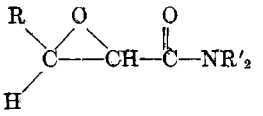
(10) (a) M. Ballester and D. Perez-Blanco, *J. Org. Chem.*, **23**, 652 (1958); (b) M. Ballester and P. D. Bartlett, *J. Am. Chem. Soc.*, **75**, 2042 (1953).

(11) H. E. Zimmerman and L. E. Ahramjian, *ibid.*, **82**, 5459 (1960), also references to other work.

(12) (a) S. Winstein and R. B. Henderson in R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 1; (b) D. Swern, *Chem. Rev.*, **45**, 30 (1949); (c) D. Swern; *Org. Reactions*, **7**, 378 (1953).

TABLE I

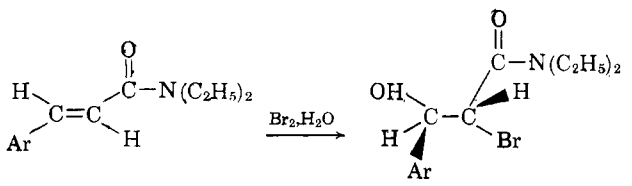
cis- AND *trans*-N,N-DIALKYLGLYCIDAMIDES



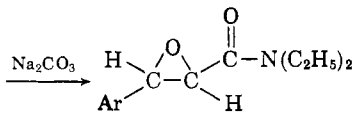
I

			cis			*trans*		
I	R	R′	Yield, %	M.p. or b.p., °C.	$n^{25}D$	Yield, %	M.p. or b.p., °C.	$n^{25}D$
a	Phenyl	C_2H_5	35.4	52.4–53.0		31.8	88.0–88.4	
b	2,6-Dichlorophenyl	C_2H_5	26.0	112–113		35.5		1.5505
c	2,4-Dichlorophenyl	C_2H_5	21.4	98–100		24	142–147 (0.14 mm.)	1.5523
d	*m*-Nitrophenyl	C_2H_5	36.7		1.5452	34.5	122.4–123.0	
e	Phenyl	$CH_2CH{=}CH_2$	43.0	88.6–90		43.0	147–150 (0.2 mm.)	1.5448

acetoxylation[13] of a *trans* olefin with N-bromosuccinimide–acetic acid followed by ring closure to give a *trans*-epoxide with base was also unsuccessful for *trans*-IIa. Only tarry material was obtained. However, conclusive evidence for the configurational assignment of the isomeric epoxyamides was obtained from an unambiguous synthesis of *trans*-Ia,b from *trans*-IIa,b, on the basis of the known *trans* addition of hypohalous acid to α,β-unsaturated carbonyl compounds followed by intramolecular S_N2 displacement at the halogen-bearing carbon atom.[14]



trans-IIa,b *erythro*-IIIa,b



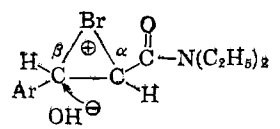
trans-Ia,b

a. Ar = phenyl
b. Ar = 2,6-dichlorophenyl

Thus, *trans*-IIa,b gave *erythro*-bromohydrin IIIa,b which, followed by treatment with base, gave *trans*-epoxyamides Ia,b. The identity of this *trans*-Ia to the high melting solid (m.p. 88.0–88.4°) and *trans*-Ib to the oil ($n^{25}D$: 1.5505) from the Darzens condensation was demonstrated by mixture melting point determination (for Ia), n.m.r. spectrum[15] (Tables II–IV), and transparency in their infrared spectrum. The assignment of configuration for Ia and Ib was further investigated by an alternate synthesis.

(13) A. Jovtscheff, *Ber.*, **93**, 2048 (1960).

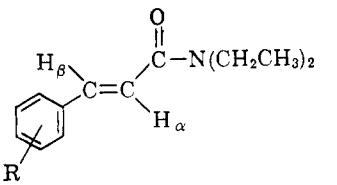
(14) The bromohydrins IIIa,b are assigned the α-bromo-β-hydroxy structures since attack of hydroxide ion on the bromonium ion intermediate would be expected to occur on the β-carbon atom because a lower electron density would be expected on that carbon atom than on the α-carbon atom and the positive character at reaction site would be more stabilized by the phenyl group (β-carbon) than by the carbonyl group (α-carbon). See (a) A. Feldstein and C. A. Vander Werf, *J. Am. Chem. Soc.*, **76**, 1626 (1954); (b) H. O. House and R. L. Wasson, *ibid.*, **78**, 4394 (1956); (c) N. H. Cromwell and R. E. Bambury, *J. Org. Chem.*, **26**, 997 (1961).



(15) C. A. Reilly and J. D. Swalen, *J. Chem. Phys.*, **32**, 1378 (1960).

TABLE II

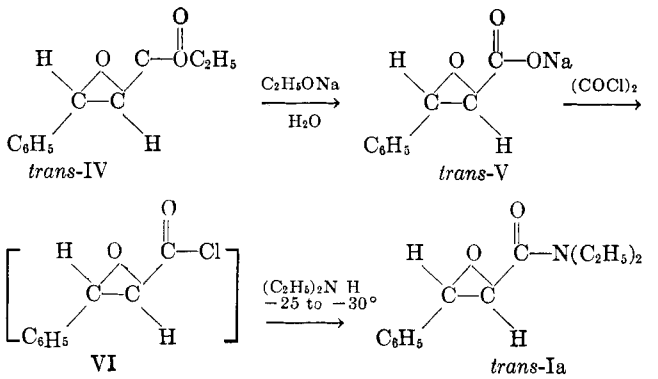
CHEMICAL SHIFTS[a] AND SPIN–SPIN COUPLING CONSTANTS OF CINNAMAMIDES



trans-II

	Chemical shifts, τ						
Compound R	CH_2 triplet	CH_2 quartet	H_α doublet	H_β doublet	Coupling constants, c.p.s. J_{CH_2}	J_{CH_2}	$J_{H_\alpha H_\beta}$[b]
H	8.78	6.50	3.18	2.25	7.5	7.5	16.0
2,6-Dichloro	8.85	6.66	3.31	2.60	7.5	7.5	15.5

[a] N.m.r. spectra were measured at 60 Mc./sec. on a modified Varian Model A-60 spectrometer. The samples contained tetramethylsilane (TMS) as internal reference. [b] J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 238.



trans-IV *trans*-V

VI *trans*-Ia

Ethyl 3-phenylglycidate (IV) which has been assigned the *trans* configuration[16] was converted by the sequence (IV→Ia) to *trans*-N,N-diethyl-3-phenylglycidamide (m.p. 88.0–88.4°) in 62% yield. Although the epimerization of epoxides by base is well known,[7,8] IV did not epimerize upon treatment with sodium ethoxide. This is supported by n.m.r. data of V whose coupling constant for α,β-hydrogens (2.0 c.p.s.) is the same as that observed for IV.[16]

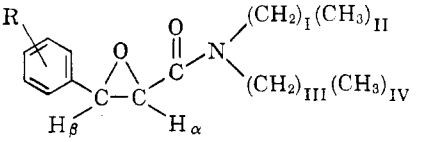
Cis-hydroxylation[17] of *trans*-IIa,b with neutral permanganate gave *threo*-VIIa (m.p. 72°) and *threo*-VIIb (m.p. 113–114°), respectively. Treatment of the high

(16) The configuration of (IV) was assigned by House, *et al.*, as *trans* (see ref. 3). This was further confirmed by n.m.r. spectrum in our laboratory. The coupling constant for α,β hydrogens is found to be 2.0 c.p.s. and is in full agreement with known data (see ref. 15).

(17) J. Boeseken, *Rec. trav. chim.*, **47**, 683 (1928).

TABLE III

CHEMICAL SHIFTS[a] AND SPIN–SPIN COUPLING CONSTANTS OF *cis*-N,N-DIETHYLGLYCIDAMIDES FROM DARZENS CONDENSATION

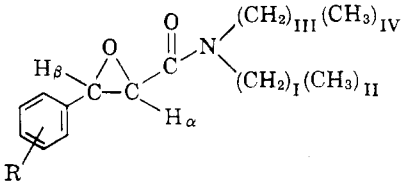


Compound R	Chemical shifts, τ: $(CH_3)_{II}$ triplet	$(CH_3)_{IV}$ triplet	Δδ, c.p.s.	$(CH_2)_I$ quartet	$(CH_2)_{III}$ quartet	Δδ c.p.s.	Hα doublet	Hβ doublet	Coupling constants, c.p.s.: J_{CH_3}	J_{CH_2}	$J_{H_\alpha H_\beta}$[15]
H	9.24	8.97	16.2	6.88	6.72	9.6	6.13	5.75	7.2	7.2	5.0
2,6-Dichloro-	9.03	8.70	19.8	6.80	6.34	12.0	5.97	5.76	7.2	7.2	5.0
2,4-Dichloro	9.22	8.86	21.6	7.00	6.68	19.2	6.13	5.64	7.2	7.2	5.0
m-Nitro	9.20	8.84	21.6	6.80	6.60	12.0	5.95	5.55	7.2	7.2	5.0
N,N-Diallyl 3-phenylglycidamide							6.10	5.72			5.0

[a] N.m.r. spectra were measured at 60 Mc./sec. on a modified Varian Model A-60 spectrometer. The samples contained tetramethylsilane as internal reference.

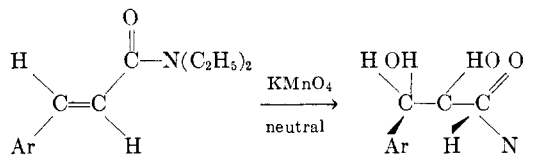
TABLE IV

CHEMICAL SHIFTS[a] AND SPIN–SPIN COUPLING CONSTANTS OF *trans*-N,N-DIETHYLGLYCIDAMIDES FROM DARZENES CONDENSATION



Compound R	Chemical shifts, τ: $(CH_3)_{II}$ triplet	$(CH_3)_{IV}$ triplet	Δδ, c.p.s.	$(CH_2)_I$ quartet	$(CH_2)_{III}$ quartet	Δδ, c.p.s.	Hα doublet	Hβ doublet	Coupling constants, c.p.s.: J_{CH_3}	J_{CH_2}	$J_{H_\alpha H_\beta}$[15]
H	8.84	8.80	2.4	6.55		0	6.43	5.94	7.2	7.2	2.0
H[b]	8.85	8.80	3.0	6.56		0	6.43	5.94	7.2	7.2	2.0
2,6-Dichloro	8.88	8.76	7.2	6.66		0	6.34	5.92	7.2	7.2	2.0
2,6-Dichloro[b]	8.80	8.68	7.2	6.50		0	6.15	5.65	7.2	7.2	2.0
2,4-Dichloro	8.93	8.82	6.6	6.71		0	6.60	5.93	7.2	7.2	2.0
m-Nitro	8.80	8.73	4.2	6.58	6.50	4.8	6.35	5.76	7.2	7.2	2.0
N,N-Diallyl 3-phenylglycidate							6.40	6.03			2.0

[a] N.m.r. spectra were measured at 60 Mc./sec. on a modified Varian model A-60 spectrometer. The samples contained tetramethylsilane as internal reference. [b] From bromohydrin method.



IIa,b — VIIa, m.p. 72°; VIIb, m.p. 113–114°

Higher melting isomeric epoxy amide of Ia (m.p. 88.0–88.4) $\xrightarrow[\text{dioxane}]{H_2SO_4}$ VIII *erythro*-diol, m.p. 58–59°

cis-trans-Ib $\xrightarrow[\text{dioxane}]{H_2SO_4}$ IX *erythro*-diol, m.p. 148–149° + *cis*-Ib, m.p. 112–113°

melting isomeric epoxy amide of Ia with sulfuric acid in aqueous dioxane afforded a diol VIII (m.p. 58–59°). Since VIII is different from *threo*-VIIa, the configuration for VIII can be assigned as *erythro* which would be derived from the ring opening of *trans*-Ia, (m.p. 88.0–88.4°) with inversion of configuration.[18] Consequently the low melting solid (m.p. 52.4–53.0°) from the Darzens condensation of benzaldehyde and N,N-diethyl-α-chloroacetamide is *cis*-Ia. Similarly when *cis–trans* mixture of Ib was treated with sulfuric acid in aqueous dioxane at 45–50°, there was isolated a diol IX (m.p. 148–149°) and a solid (m.p. 112–113°) which was identical in its infrared spectrum with that isolated from *cis-trans*-Ib from Darzens condensation. The mixed melting point showed no depression. By following the same reasoning for the assignment of *trans*-Ia from VIII, the diol IX is assigned as *erythro* which would be derived from the ring opening of *trans*-Ib (oil, $n^{25}D$: 1.5505). Consequently the solid Ib (m.p. 112–113°) is the *cis* isomer. The resistance to ring opening of the *cis*-epoxyamide Ib in acid media was also observed for other *cis*-epoxyamides and this interesting finding is under further investigation.

Since *trans*-IV did not undergo epimerization upon treatment with base, alkaline epimerization of the *cis*-epoxide was undertaken. Each of the isomeric N,N-diallyl 3-phenylglycidamides was dissolved in *t*-butyl alcohol in the presence of catalytic amount of potassium *t*-butoxide. The results of these experiments, as shown in Table V, indicated that the sterically favored *trans*-epoxide does not undergo epimerization whereas the *cis*-epoxide epimerizes to the *trans* isomer to the extent of 31.8% (calculated from n.m.r. spectrum). Furthermore the extent of epimerization does not change upon further heating. To indicate that epimerization

(18) The ring opening of epoxides in acid media is expected to proceed by an SN2 mechanism with the inversion of configuration [R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959)], although ring openings with retention of configuration are also reported. [See (a) R. Kuhn and F. Ebel, *Ber.*, **58**, 919 (1925); (b) J. Boeseken, *Rec. trav. chim.*, **41**, 199 (1922); (c) H. H. Wasserman and N. E. Aubrey, *J. Am. Chem. Soc.*, **78**, 1726 (1956).]

TABLE V

EPIMERIZATION OF *cis*- AND *trans*-N,N-DIALLYL-3-PHENYLGLYCIDAMIDE IN PRESENCE OF POTASSIUM *t*-BUTOXIDE[a]

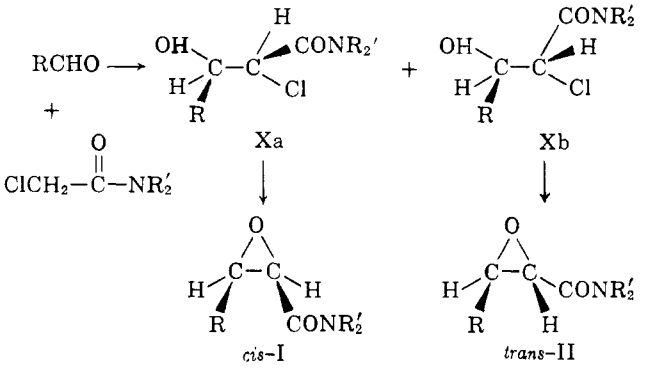
	After standing at room temperature for 6 days		After 2 hr. at 60°		After 25 hr. at 60°	
	trans	*cis*	*trans*	*cis*	*trans*	*cis*
trans	100	0	100	0	100	0
cis	0	100	32	68	32	68
cis[b]	...	...	...	..	...	100

[a] Yields were calculated from n.m.r. spectrum. [b] Without potassium *t*-butoxide.

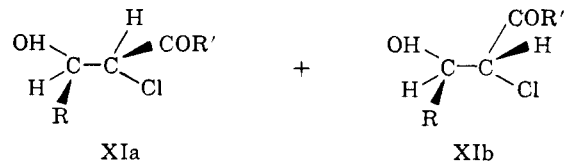
did not result from heat alone, the *cis* isomer was recovered unchanged after fifteen hours at 60°.

In general the Darzens condensation should give diastereoisomeric halohydrin intermediates in essentially equal quantities. The ratios and stereochemistry of the epoxides derived from these halohydrins are determined by epimerization of the chlorohydrin anions and/or epoxides, or, as reported in one instance, the reversibility of the aldolization step.[11]

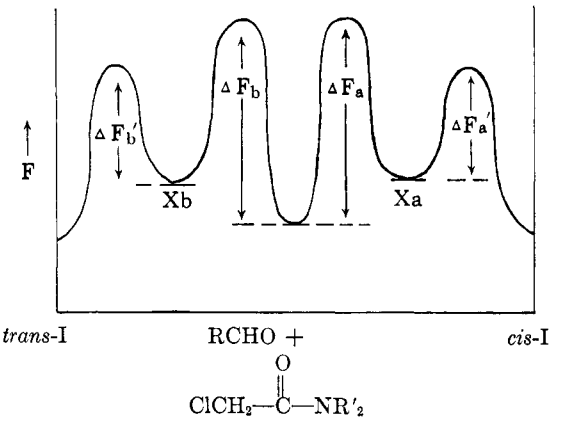
Since our epimerization conditions were more drastic than those in the Darzens condensation and the *trans*-epoxides did not isomerize to the *cis*, the formation of *cis*- and *trans*-epoxyamides in the Darzens condensation undoubtedly arise from ring closure of the diastereoisomeric chlorohydrins Xa and Xb.



The epimerization of the chlorohydrins (leading to only one epoxide) would be controlled by the acidity of the α-hydrogen atom. Since the α-hydrogen of an amide is less acidic than the α-hydrogen of an ester[19] and probably also of a ketone, epimerization of the chlorohydrin Xa to the less sterically hindered Xb *via* base-catalyzed enolization did not occur. Consequently both *cis*- and *trans*-epoxyamides were produced from the cyclization of Xa and Xb despite the fact that the formation of the *cis* isomer was derived from the unfavored conformer Xa. In the condensation of aromatic aldehydes with ethyl chloroacetate,[3] phenacyl chloride,[9e] chloroacetone,[4] and 2,4,6-trimethoxyphenacyl chloride,[10a] the diastereoisomeric chlorohydrins XIa and XIb were presumably formed. However, due to the greater acidity of their α-hydrogens as compared to Xa and Xb, epimerization of the chlorohydrin to the less sterically hindered conformer XIb took place and hence the *trans* isomer was the sole or major product.



In contrast to the reversible aldolization–dealdolization prequilibrium reported by Zimmerman and Ahramjiam,[11] the formation of the aldolization products Xa and Xb (from α-chloroacetamides and aromatic aldehydes) must be the rate controlling step followed by a rapid cyclization to the isomeric epoxides. The free energy of aldolization ΔF_a and ΔF_b (to form Xa and Xb) must be greater than their respective free energies of cyclization $\Delta F_a'$ and $\Delta F_b'$.



The n.m.r. spectra for *cis*- and *trans*-epoxyamides were analyzed in detail (Tables III and IV). The coupling constant for α-β hydrogen ($JH_\alpha H_\beta$) in the *cis*-epoxyamides is 5.0 c.p.s. and for the *trans* isomer ($J_{H_\alpha H_\beta}$) 2.0 c.p.s. These are in agreement with published data[15] for simple epoxides. The n.m.r. spectra for the *cis* isomers showed two nonequivalent methyl and methylene groups with a difference of chemical shift ranging from 16.2–21.6 c.p.s. for methyl and 9.6–19.2 c.p.s. for the methylene group. The nonequivalency of the ethyl groups is clearly due to the restricted rotation about the CN bond at room temperature.[20] Consequently their environments, particularly with regard to the 3-aryl group, are different. Although rotation about CN bond is still restricted in the corresponding *trans* isomer, the nonequivalency of these groups with respect to the 3-aryl group is reduced due to the greater distance. The difference in chemical shift is, therefore, diminished. Thus, for the olefinic compounds (Table II) the distances between the alkyl amido groups and 3-aryl group are sufficiently far apart that no difference in chemical shift is observed. The assignment of $(CH_2)_I$ and $(CH_2)_{II}$ at higher field than $(CH_2)_{III}$ and $(CH_2)_{IV}$ (for *cis*- and *trans*-epoxyamides) is based on the assumption that the average environment of the former is nearer the 3-aryl group. Hence the shielding effect of the phenyl ring should be greater. The assignment of the α-hydrogen at a higher field than that of the β is based on previous n.m.r. spectra of ethyl α-bromocinnamate and ethyl cinnamate.[19] In these two compounds the α-hydrogen is at higher field than the β.

The reliability of n.m.r. spectra in quantitative determination of *cis*–*trans*-epoxyamides is demonstrated as follows. An authentic mixture of 49.1% of *cis*-Ia

(19) A. J. Speziale and C. C. Tung, *J. Org. Chem.*, **28**, 1353 (1963).

(20) The n.m.r. spectra of *cis*-Ia at 85° exhibited only one triplet for two methyl groups and one quartet for two methylene groups.

and 50.9% of *trans*-Ia showed 51% of *cis*-Ia and 49% of *trans*-Ia, respectively, by measuring the area of one doublet, $J_{H_\alpha H_\beta}$ = 5.0 c.p.s. (H_β) for *cis*-Ia and another doublet, $J_{H_\alpha H_\beta}$ = 2.0 c.p.s. (H_β) for *trans*-Ia. Also, the *cis–trans* mixture of Ia before chromatographic separation from Darzens condensation (m.p. 43–47°) was found to consist of 50% *cis* and 50% *trans* by the same method of n.m.r. analysis. The isolated yields were 52.7% *cis* and 47.3% *trans* (actual yield is 35.4% *cis* and 31.8% *trans*). Thus, n.m.r. spectra serve as a very convenient means to determine the per cent of *cis*- and *trans*-epoxyamides from Darzens condensation without involving the tedious process of separation. For example, reaction of 0.20 mole each of *o*-methylbenzaldehyde, N,N-diethyl-α-chloroacetamide under Darzens conditions gave 31.6 g. of distilled liquid, b.p. 140–145°, (0.72 mm.), and 6.5 g. of liquid boiling at 145–149° (0.72 mm). Both products gave correct elemental analysis for the desired epoxyamide. However, n.m.r. spectrum of the oil, b.p. 145–149° (0.72 mm.), indicated only one pair of doublets with a coupling constant of 2.0 c.p.s. for the *trans*-epoxyamide whereas the spectrum of the oil, b.p. 140–145° (0.72 mm.), revealed two pairs of doublets with coupling constants of 5.0 c.p.s. (*cis*) for one pair and 2.0 c.p.s. (*trans*) for the other. The area of the doublet with a coupling constant 5.0 c.p.s. (*cis*) and that of the other doublet with a coupling constant 2.0 c.p.s. (*trans*) was found to be 53.7% and 46.3%, respectively. Thus, we concluded that the products from Darzens condensation contain 55.5% of *trans*- and 44.5% of *cis*-epoxyamide in a total yield of 82.0%. Similarly, the 3,4-dichlorobenzaldehyde and N,N-diethyl-α-chloroacetamide gave a product which distilled at 170–180° (0.2 mm.) in 69.2% yield. It gave correct elemental analysis for the desired epoxy amide and from its n.m.r. spectrum, the product consisted of 50–50 *cis*- and *trans*-epoxyamide, respectively.

The infrared data for *cis*- and *trans*-epoxyamides are shown in Table V. These have characteristic bands attributable to the epoxy group in the 8-, 11-, and 12-μ region.[1] In general, the *cis* isomers showed absorption at 12-μ region whereas this band was absent in the corresponding *trans* isomer. The n.m.r. data, therefore, serves to corroborate the diagnostic importance of the 12-μ band for the *cis* isomer and its absence for the *trans* isomer.

Experimental

cis–trans-**N,N-Diethyl 3-phenylglycidamide (Ia).**—A solution of potassium *t*-butoxide (16 g., 0.41 g.-atom of potassium and 400 ml. of *t*-butyl alcohol, dried by distilling from sodium) was added to a mixture of 42.4 g. (0.40 mole) of benzaldehyde and 59.8 g. (0.40 mole) of N,N-diethyl-α-chloroacetamide under an atmosphere of nitrogen at 5–10° during 1.5 hr. The mixture was stirred at 10° for 1 hr. and the alcohol was removed at 50° (40 mm.). The residue was treated with 300 ml. of ether and sufficient water to dissolve the potassium chloride. (Potentiometric titration: 0.40 mole Cl^-.) The ether layer was removed, washed with saturated sodium chloride solution, dried with magnesium sulfate, and evaporated to dryness. The crude viscous oil (87.1 g., 99.5% yield) was treated with 150 ml. of ether and 300 ml. of hexane and cooled to 0–5°. The white crystals were filtered, wt. 77 g.; 88.4% yield, m.p. 43–47°. Ten grams of this material was fractionally crystallized from hexane. The less soluble fractions (3.6 g., 31.8% yield) melted at 88.8–90°, was identified as the *trans* isomer and the more soluble fractions (4.0 g., 35.4 yield) melted at 52.4–53°, was identified as *cis* isomer.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.39. Found (*trans*): C, 71.27; H, 7.77; N, 6.52. Found (*cis*): C, 71.27; H, 7.92; N, 6.32.

cis–trans-**N,N-Diethyl-3-(2,6-dichlorophenyl)glycidamide (Ib).**—This glycidamide was prepared from a solution of 35.0 g. (0.20 mole) of 2,6-dichlorobenzaldehyde (Chemical Procurement Laboratories, Inc., College Point, N. Y.), 29.9 g. (0.20 mole) of the chloroacetamide in 100 ml. of ether and 0.20 mole of potassium *t*-butoxide in 250 ml. of *t*-butyl alcohol as described before. The crude epoxyamide, 57.8 g. (theory, $n^{25}D$ 1.5505) was distilled at 165–175° (0.15 mm.); 36.5 g. (63.4% yield, $n^{25}D$ 1.5536).

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_2$: N, 4.86; Cl, 24.60. Found: N, 4.89; Cl, 25.08.

Seven and two-tenths grams of this distilled epoxyamide was chromatographed on alumina. The first six fractions on elution with benzene–hexane mixture afforded 4.0 g. (35.5% yield) of an oil (*trans*) $n^{25}D$ 1.5505. Further elution with benzene afforded 3.0 g. (26.0% yield) of solid (*cis*) m.p. 112–113° after recrystallization from hexane.

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_2$: C, 54.18; H, 5.25; N, 4.86; Cl, 24.61. Found (*cis* solid): C, 53.72; H, 5.28; N, 4.96; Cl, 24.82. Found (*trans* oil): C, 54.16; H, 5.51; N, 5.03; Cl, 24.57.

cis–trans-**N,N-Diethyl-3-(2,4-dichlorophenyl)glycidamide (Ic).**—The glycidamide was prepared from a solution of 35.0 g. (0.20 mole) of 2,4-dichlorobenzaldehyde, 29.9 g. (0.20 mole) of the chloroacetamide in 100 ml. of ether and 0.20 mole of potassium *t*-butoxide in 250 ml. of *t*-butyl alcohol as described in the previous experiment. The crude epoxyamide was obtained in 99.4% yield. Upon recrystallization from hexane it gave a colorless solid (*cis*), m.p. 98–100°, wt. 12.3 g. (21.4% yield). The solvent was removed under vacuum and the residue was distilled to obtain the *trans* isomer, b.p. 142–147° (0.12 mm.), 13.8 g. (23.9% yield).

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_2$: C, 54.18; H, 5.25; N, 4.86; Cl, 24.61. Found (*cis*): C, 53.94; H, 5.24; N, 4.80; Cl, 24.50. Found (*trans*): C, 54.55; H, 5.05; N, 5.14; Cl, 24.63.

cis–trans-**N,N-Diethyl-3-(*m*-nitrophenyl)glycidamide (Id).**—From 22.5 g. (0.15 mole) of *m*-nitrobenzaldehyde, 22.5 g. (0.15 mole) of chloroacetamide in 200 ml. of ether, and 0.15 mole of potassium *t*-butoxide in 150 ml. of *t*-butyl alcohol, there was obtained 27.9 g. of crude glycidamide. Recrystallization from methanol gave 7.9 g. of colorless solid, m.p. 122.4–123°. On further evaporation of the mother liquor, an additional 5.8 g. of same material was obtained. Total weight of solid was 13.7 g. (*trans*), 34.5% yield. The filtrate was evaporated to dryness and chromatographed and eluted with 20–80% chloroform–ether solvent, 14.6 g. of an oil (*cis*), 36.7% yield, $n^{25}D$ 1.5452, was obtained.

Anal. Calcd. for $C_{13}H_{16}N_2O_4$: C, 59.10; H, 6.05; N, 10.58. Found (*cis*): C, 59.05; H, 6.22; N, 10.89. Found (*trans*): C, 58.88; H, 6.04; N, 10.24.

cist–trans-**N,N-Diallyl-3-phenylglycidamide (Ie).**—The Darzens condensation was carried out as described for the diethyl analog (Ia). The crude epoxy amide was recrystallized from ether–hexane mixture. There was obtained 31.6 g. (43.0% yield) of solid, *cis*, m.p. 86–87° and 41.2 g. (56.4%) of oil, *trans*, $n^{25}D$ 1.5376–1.5428, from concentration of the mother liquors. The solid, recrystallized from ethyl acetate–hexane, melted at 88.6–90°. The oil was distilled, b.p. 147–150° (0.2 mm.), $n^{25}D$ 1.5448; 31.2 g., (43% yield).

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.05; N, 5.79 Found (*trans*, oil): C, 74.66; H, 7.55; N, 6.20. Found (*cis*, solid): C, 74.51; H, 7.33; N, 5.97.

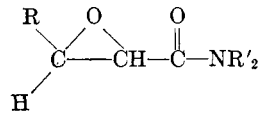
cis–trans-**N,N-Diethyl-3-*o*-tolyl-glycidamide.**—The Darzens condensation from 0.20 mole of *o*-methylbenzaldehyde and N,N-diethyl-α-chloroacetamide as described for Ia gave 46.1 g. (98.7% yield) of crude product. Distillation gave the following two fractions; b.p. 140–145° (0.72 mm.), wt. 31.6 g. (contains 53.7% *cis* and 46.3% *trans* from n.m.r. spectrum), b.p. 145–149° (0.72 mm.), wt. 6.5 g. (pure *trans* from n.m.r. spectrum). Total yield was 82.0% with 44.5% *cis* and 55.5% *trans* isomer.

Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.20; H, 8.21; N, 6.00. Found (*trans*): C, 71.95; H, 8.09; N, 6.24. Found (*cis trans*): C, 71.98; H, 8.26; N, 6.09.

cis–trans-**N,N-Diethyl-3(3,4-dichlorophenyl)glycidamide.**—Treatment of 0.20 mole of 2,4-dichlorobenzaldehyde with N,N-diethyl-α-chloroacetamide under Darzens conditions afforded

TABLE VI

INFRARED SPECTRA[a] OF *cis*- AND *trans*-N,N-DIALKYLGLYCIDAMIDES



			Absorption wave length (μ)				
				Epoxide			
R	R′	Isomer	C=O	8.0-μ region	11.0-μ region	12.0-μ region	Other region
C_6H_5	CH_2CH_3	*cis*	6.00 (s)	7.92 (s); 8.19 (m)	10.94 (s); 11.10 (m)	12.03 (m)	6.75 (s); 6.83 (s); 8.72 (m); 9.09 (m); 9.71 (w); 10.50 (w); 10.71 (w)
C_6H_5	CH_2CH_3	*trans*	6.00 (s)	7.93 (s); 8.20 (m)	10.95 (w); 11.13 (m)		6.73 (s); 6.82 (s); 8.75 (s); 9.11 (m); 9.75 (w); 10.50 (w); 11.65 (w)
2,6-$Cl_2C_6H_3$	CH_2CH_3	*cis*	6.02 (s)	7.95 (m)	10.85 (m); 11.10 (w); 11.20 (w)	11.90 (m)	3.37 (m); 6.40 (m); 6.82 (m); 6.97 (s); 7.25 (m); 7.67 (w); 8.75 (m); 9.17 (m); 10.50 (w)
2,6-$Cl_2C_6H_3$	CH_2CH_3	*trans*	6.06 (s)	7.95 (m)	11.00 (m); 11.55 (w)		3.40 (m); 6.40 (m); 6.98 (s); 8.75 (m); 9.15 (m); 10.55 (w)
2,4-$Cl_2C_6H_3$	CH_2CH_3	*cis*	6.05 (s)	7.92	10.86 (m); 11.00 (m)	11.89 (s); 12.20 (m)	3.36 (s); 6.76 (s); 6.83 (s); 10.50 (m) 11.54 (m)
2,4-$Cl_2C_6H_3$	CH_2CH_3	*trans*	6.05 (s)	7.90 (m)	11.00 (m); 11.40 (m)		3.32 (m); 6.81 (s); 7.20 (m); 8.70 (m); 9.05 (m); 10.50 (w)
m-$NO_2C_6H_4$	CH_2CH_3	*cis*	6.10 (s)	7.90 (m); 8.21 (m)	10.99 (m); 11.40 (m)	12.00 (m); 12.30 (m)	3.35 (m); 6.60 (s); 7.40 (s); 8.71 (m); 9.10 (m); 9.25 (m); 10.45 (m); 13.20 (s); 13.50 (s)
m-$NO_2C_6H_4$	CH_2CH_3	*trans*	6.12 (s)	7.90 (m); 8.25 (m)	10.99 (w); 11.35 (m); 11.75 (m)		3.40 (s); 6.60 (s); 7.40 (s); 8.70 (m); 9.10 (m); 9.25 (m); 10.45 (m); 12.75 (m); 13.65 (m)
C_6H_5	$CH_2CH{=}CH_2$	*cis*	5.96 (s)	7.80 (m); 8.18 (s)	10.80 (s); 10.91 (m)		3.25 (w); 3.35 (w); 3.43 (w); 6.95 (s); 7.04 (s); 8.38 (m); 9.01 (w); 10.07 (s)
C_6H_5	$CH_2CH{=}CH_2$	*trans*	6.00 (s)	7.80 (m); 8.15 (s)	10.80 (s)	11.96 (w); 12.28 (w)	3.25 (w); 3.35 (w); 3.43 (w); 7.08 (s); 8.87 (m); 10.07 (m)
o-$CH_3C_6H_4$	CH_2CH_3	*trans*	6.05 (s)	7.93 (s)	11.11 (m)		3.36 (s): 6.73 (s); 6.82 (s)

[a] All spectra in 3% chloroform.

39.7 g. (69.2% yield), $n^{25}D$ 1.5538, of *cis*–*trans*-epoxyamide, b.p. 170–180° (0.2 mm.). Attempts at purification by crystallization from solvents were unsuccessful. Its composition, by n.m.r. was shown to be a mixture of equal amounts of *cis* and *trans* isomers.

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_2$: C, 54.18; H, 5.24; N, 4.86; Cl, 24.60. Found: C, 54.18; H, 5.52; N, 4.84; Cl, 24.60.

***trans*-N,N-Diethyl-3-phenylglycidamide (Ia) (Authentic).** (a) **From *erythro*-N,N-Diethyl-α-bromo-β-phenyl-β-hydroxypropioamide (IIIa).**—To a stirred solution containing 32.0 g. (0.20 mole) of bromine in 250 ml. of 9% sulfuric acid at 0° was added dropwise a solution of 33.0 g. (0.20 mole) of silver nitrate in 80 ml. of water until the solution was just decolorized. To the above stirred solution at 0°, 20.3 g. (0.10 mole) of *trans*-N,N-diethylcinnamide (IIa)[19] in 500 ml. of dioxane was added dropwise over a period of 1.5 hr. The reaction mixture was allowed to warm to room temperature and heated at 50° for 10 min. The reaction mixture was filtered to remove silver bromide (40.8 g., theory) and the filtrate was poured into 2 l. of water. The product was extracted with ether, washed with cold water and dried over anhydrous magnesium sulfate. The solvent was evaporated to dryness to give 30.1 g. (50.0% yield) of oil which solidified on cooling. An analytical sample crystallized from hexane–benzene and recrystallized from cyclohexane gave colorless solid (IIIa), m.p. 137.2–138°.

Anal. Calcd. for $C_{13}H_{18}BrNO_2$: C, 52.10; H, 6.04; Br, 26.65; N, 4.67. Found: C, 52.18; H, 6.12; Br, 27.00; N, 4.69.

A mixture of 3.47 g. (0.0115 mole) of IIIa and 9.10 g. (0.0865 mole) of sodium carbonate in 80 ml. of water was heated to reflux for 1 hr. After cooling the reaction mixture to room temperature, the oily product was extracted with two 100-ml. portions of ether, washed with water and dried over anhydrous magnesium sulfate. The ether was removed *in vacuo*, there was obtained 2.33 g. (92.5% yield) of colorless oil, which solidified on standing. This solid has identical n.m.r. (Table IV) and infrared spectrum (Table VI) with the high melting solid Ia obtained from Darzens condensation. Mixture melting point showed no depression.

(b) **From Ethyl *trans*-3-Phenylglycidate (IV).**—To a solution of sodium ethoxide in ethanol at 0–5° (3.1 g., 0.1355 g.-atom of sodium and 70 ml. of absolute ethanol), there was added 25.6 g. (0.1355 mole) of ethyl *trans*-3-phenylglycidate (IV)[21] in 0.5 hr. The clear yellow solution was treated dropwise at 0–5° with 2.17 g. (0.1355 mole) of water. The sodium salt precipitated immediately. The mixture was filtered after stirring 0.5 hr. and then dried at 100° to obtain 20.8 g., (83% yield) of sodium *trans*-3-phenylglycidate[5a] (V). A small amount was recrystallized from ethanol and the samples did not differ in their infrared spectra: 6.15 μ (carbonyl) and 8.00, 11.24, 12.17 μ (epoxide).

A suspension of 20.8 g. (0.112 mole) of sodium *trans*-3-phenylglycidate (V) in 100 ml. of dry benzene and 5 drops of pyridine was cooled to 0–5° and treated with 18.9 g. (0.15 mole) of oxalyl chloride in 50 ml. of benzene during the course of 1 hr. The mixture was stirred for 0.5 hr. at 0–5° and the benzene removed *in vacuo* below 15°. A fresh 100 ml. of dry benzene was added and then distilled *in vacuo* below 15°. The crude epoxy acid chloride was dissolved in ether, cooled to −25 to −30°, and treated with 16.4 g. (0.224 mole) of diethylamine in 50 ml. of ether during 0.75 hr. The mixture was stirred for 1 hr. at −20°, allowed to warm to −10°, and treated with 20 ml. of water. The ether layer was removed immediately and, while drying with magnesium sulfate, the solvent was removed *in vacuo* below 0°. Fresh ether was added and again removed *in vacuo* to dryness at 0°. The crude epoxyamide was recrystallized from hexane; wt. 13.6 g., m.p. 84–87°. A mixture melting point with the *trans*-epoxyamide (m.p. 88.0–88.4°) isolated from the Darzens condensation was not depressed and the two spectra were superimposable.

Hexane other liquor was concentrated to dryness *in vacuo*. The oil (6.2 g.) was chromatographed on alumina. There was isolated 1.6 g. of the *trans*-epoxyamide (total yield: 15.2 g., 62%), several other fractions which showed OH and COOH absorption in the infrared and 1.9 g. of oil (last fraction) which showed weak OH band and may have contained a small amount of the *cis*-epoxyamide by infrared analysis.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.39. Found: (84–87°) C, 70.91; H, 8.11; N, 6.43.

***trans*-N,N-Diethyl-3-(2,6-dichlorophenyl)glycidamide (Ib) (Authentic).** (a) **From *erythro*-N,N-Diethyl-α-bromo-β-(2,6-dichlorophenyl)-β-hydroxypropioamide (IIIb).**—The procedure for the preparation of IIIa afforded a crude product in 90.8% yield which was recrystallized from hexane–benzene to give 12.0 g. (65.3% yield) of colorless solid, m.p. 156–157°.

Anal. Calcd. for $C_{13}H_{16}BrCl_2NO_2$: C, 42.30; H, 4.37; Br, 21.69; Cl, 19.20; N, 3.79. Found: C, 42.50; H, 4.32; Br, 21.17; Cl, 18.97; N, 3.77.

The same procedure for the treatment of IIIa with base was employed. From 3.0 g. (0.00814 mole) of IIIb and 6.4 g. (0.061 mole) of sodium carbonate in 70 ml. of water, there was obtained 2.22 g. (94.8% yield), $n^{25}D$ 1.5478 of crude *trans*-Ib. The crude product was chromatographed on alumina and eluted with benzene–chloroform to give 2.2 g. (94.0% yield) of *trans*-Ib, $n^{25}D$ 1.5455.

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_2$: C, 54.18; H, 5.25; N, 4.86; Cl, 24.61. Found: C, 54.25; H, 5.21; N, 5.00; Cl, 24.93.

This *trans*-Ib has identical n.m.r. spectrum (Table IV) and infrared spectrum (Table VI) with the liquid, $n^{25}D$ 1.5505, obtained from Darzens condensation.

***threo*-N,N-Diethyl-2,3-dihydroxy-3-phenylpropionamide (VIIa).**—The procedure employed by Boeseken[17] was followed. A solution of 20.3 g. (0.1 mole) of *trans*-N,N-diethylcinnamide (IIa) m.p. 71–72°, in 1 l. of ethanol was cooled to −40°. A solution of 18.0 g. (0.12 mole) of potassium permanganate and 20.0 g. (0.08 mole) of magnesium sulfate heptahydrate in 600 ml. of water was then added at −40° in 5 hr. The cooling bath was removed and the reaction mixture allowed to stir to room temperature. It was filtered and evaporated to one-third its original volume and then extracted with ether. Evaporation of the ether left 15.5 g. (65.4% yield) of oil. The infrared spectrum and analysis indicated this material to be a mixture of unreacted amide and diol. The oil was chromatographed on alumina. Elution with benzene afforded 5.4 g. (26.5% recovery) of starting amide, m.p. 71–72°. Elution with 95 and 80% ethanol gave 5.8 g. of oil (24.5% yield; 33% conv.) $n^{25}D$ 1.5320–1.5305. Several recrystallizations of the oil from hexane afforded a white solid (4.4 g.) m.p. 72°. It depressed the melting point of starting cinnamamide.

Anal. Calcd. for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90; OH, 14.33. Found: C, 65.94; H, 7.41; N, 6.15; OH, 14.52. Infrared spectrum showed absorption at 2.80, 2.90 and 9.45 μ (hydroxy) and at 6.15 μ (amide).

***threo*-N,N-Diethyl 3-(2,6-dichlorophenyl)-2,3-dihydroxypropionamide (VIIb).**—A solution of 13.6 g. (0.05 mole) of *trans*-N,N-diethyl-2,6-dichlorophenylcinnamide (IIb) in 500 ml. of ethanol was cooled to −40° and treated with a solution of 9.0 g. (0.06 mole) of potassium permanganate and 10.0 g. (0.04 mole) of magnesium sulfate heptahydrate during 5 hr. The mixture was allowed to warm to room temperature, filtered, and the filtrate reduced in volume and extracted with ether. The ether solution was evaporated to dryness to give 12.3 g. (80.4% yield) of crude solid. This was recrystallized from benzene–hexane to give the *threo*-diol, wt. 5.5 g. (36% yield) m.p. 112–113°. Recrystallization from hexane afforded pure diol amide, m.p. 113–114°. A mixture melting point with authentic *cis*-epoxy amide (m.p. 112–113°) was depressed. Infrared spectrum showed absorption at 2.84, 2.95 and 9.23 μ (OH) and 6.10 μ (amide). Bands at 11.77 and 12.23 μ characteristic for the epoxy amide were absent.

Anal. Calcd. for $C_{13}H_{17}Cl_2NO_3$: C, 50.99; H, 5.60; Cl, 23.16; N, 4.58; OH, 11.10. Found: C, 50.71; H, 5.67; Cl, 23.51; N, 4.66; OH, 11.47. The benzene–hexane mother liquors after removal of the *threo*-diol were evaporated to dryness to give 5.1 g. of unidentified oil, $n^{25}D$ 1.5674. No OH absorption was present in its infrared spectrum.

***erythro*-N,N-Diethyl-2,3-dihydro-3-phenylpropionamide (VIII).**—A solution of 5.0 g. (0.023 mole) of high melting isomer of N,N-diethyl-3-phenylglycidamide (m.p. 87–88°) in 50 ml. of acetone and 100 ml. of 30% sulfuric acid was heated at 40–45° for 2 hr. It was poured into water, extracted with ether and the ether solution dried and evaporated. There remained 4.0 g., 74% yield, of oil; $n^{22}D$ 1.5320. This was chromatographed on alumina and eluted with ethanol–ether mixture. The eluent afforded a solid which was recrystallized from hexane, m.p. 58–59°.

Anal. Calcd. for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90; OH, 14.33. Found: C, 65.72; H, 7.88: N, 6.43; OH, 14.13. Infrared spectrum showed absorptions identical with that of *threo* isomer VIIa.

***erythro*-N,N-Diethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropionamide (IX).**—A solution of 9.0 g. (0.315 mole) of *cis–trans*-N,N-diethyl-3-(2,6-dichlorophenyl)glycidamide (Ib) ($n^{25}D$ 1.5536) in 75 ml. of acetone, 75 ml. of water and 15 ml. of concentrated sulfuric acid was heated at 45–50° for 28 hr. and allowed to stand at room temperature for 3 days. The acetone was removed and the mixture extracted with ether, washed with bicarbonate, dried, and evaporated. There remained an oil, wt. 8.1 g. (90% yield) $n^{22}D$ 1.5542. It was chromatographed on alumina and eluted with benzene and ethanol–hexane mixture. The benzene eluents afforded unchanged *cis*-epoxyamide, m.p. 112–113°; 3.4 g. (38% recovery). The ethanol–hexane eluent afforded 3.0 g. (34.5%) of the diol, m.p. 146–147°. Its melting point was was raised to 148–149° after recrystallization from hexane.

Anal. Calcd. for $C_{13}H_{17}Cl_2NO_3$: C, 50.99; H, 5.60; Cl, 23.16; N, 4.58; OH, 11.10. Found: C, 51.38; H, 5.99; Cl, 23.26; N, 4.59; OH, 11.00. Infrared spectrum showed absorptions at 2.95 μ (hydroxy) and 6.12 μ (amide).

Attempted Epimerization of *trans*-N,N-Diallyl-3-phenylglycidamide with Potassium *t*-Butoxide in *t*-Butyl Alcohol.—A solution of 18.4 g. of *trans*-epoxyamide, 0.2 g. of potassium *t*-butoxide in 55 ml. of *t*-butyl alcohol was allowed to stand at room temperature for 6 days and followed by heating at 60° for 2 hr. The solvent was evaporated to dryness *in vacuo* to give an oil which was pure unchanged *trans*-epoxyamide by n.m.r. The sample remained unchanged after it was redissolved in 55 ml. of *t*-butyl alcohol and heated at 60° for 13 hr.

Epimerization of *cis*-N,N-Diallyl-3-phenylglycidamide. (a) **Potassium *t*-Butoxide in *t*-Butyl Alcohol.**—A solution of 9.2 g. of *cis*-epoxyamide, 0.1 g. of potassium *t*-butoxide in 185 ml. of *t*-butyl alcohol was treated as described previously. The results are tabulated in Table V.

(b) **In the Absence of Potassium *t*-Butoxide.**—A solution of 1.5 g. of *cis*-epoxyamide in 50 ml. of *t*-butyl alcohol was heated at 60° for 15 hr. After removal of the solvent, 1.5 g. of *cis*-epoxy-

(21) Sample was prepared according to the method of W. S. Johnson, J. S. Belew, L. J. Chinn, and R. H. Hunt, *J. Am. Chem. Soc.*, **75**, 4995 (1953). For assignment of configuration, see ref. 16.

amide, m.p. 88.6–90° was recovered. Its n.m.r. spectrum was identical to the starting *cis* isomer.

trans-**N,N-Diethyl-2,6-dichlorophenylcinnamide (IIb).**—A solution containing 16.5 g. (0.076 mole) of 2,6-dichlorocinnamic acid[22] (m.p. 193.7–194.2°) and 18.0 g. (0.152 mole) of thionyl chloride in 100 ml. of benzene was heated to reflux for 1 hr. The solvent was evaporated to dryness to give a colorless solid, m.p. 68–69°. The yield was 17.2 g. (96.3% yield). One recrystallization from hexane crystals, m.p. 69.2–70.1°.

Anal. Calcd. for $C_9H_5Cl_3O$: Cl, 42.25. Found: Cl, 42.68.

To a stirred solution of 16.0 g. (0.068 mole) of 2,6-dichlorocinnamoyl chloride in 120 ml. of ether was added 12.5 g. (0.17 mole) of diethylamine over a period of 10 min. Stirring at room temperature was continued for 1 hr. The diethylamine hydrochloride salt (7.8 g., theory) was removed and the filtrate was evaporated *in vacuo* to dryness to yield 17.8 g. of light brown viscous oil. The distilled product, b.p. 170–171° (0.5 mm.), $n^{25}D$ 1.5791, was obtained in 15.2 g. (82.2% yield). The compound was identified as *trans* from n.m.r. spectrum (Table II).

Anal. Calcd. for $C_{13}H_{15}Cl_2NO$: Cl, 26.05; N, 5.15. Found: Cl, 26.02; N, 4.64.

Attempted Epoxidation of *trans*-IIa with Monoperphthalic Acid.—The procedure of Wheeler[23] was followed. A solution of 610 ml. of an ether solution containing 0.44 mole of monoperphthalic acid[24] and 14.0 g. (0.07 mole) of *trans*-N,N-diethylcinnamamide (IIa) was allowed to stand at 5° for 35 days. Water was added to destroy the peracid and the filtered solution was evaporated to dryness *in vacuo*. The residue was extracted with chloroform and chloroform extract was washed with aqueous sodium bicarbonate solution. After being dried over anhydrous magnesium sulfate, solvent was removed to give 12.1 g. (86.5% recovery) of starting *trans*-cinnamamide (IIa), m.p. 70–71°.

Attempted Bromoacetoxylation of *trans*-IIa with N-Bromosuccinimide–Acetic Acid.—The procedure of Jovtscheff[13] was followed. A solution of 10.0 g. (0.05 mole) of *trans*-N,N-diethylcinnamide (IIa) an 18.0 g. (0.10 mole) of N-bromosuccinimide in 500 ml. of glacial acetic acid was stirred at room temperature in a dark flask for a period of 1.5 hr. The reaction mixture was poured into 500 ml. of water containing 30 g. of potassium iodide and the liberated iodine was destroyed by aqueous sodium thiosulfate. The mixture after being extracted with ether, dried over anhydrous magnesium sulfate, evaporated to dryness *in vacuo* gave a dark brown tarry material. Attempts to purify this material by crystallization and chromatography were unsuccessful.

(22) F. Böck, G. Lock and K. Schmidt, *Monatsh.*, **64**, 399 (1934).

(23) K. W. Wheeler, M. G. Van Campen, Jr., and R. S. Shelton, *J. Org. Chem.*, **25**, 1021 (1960).

(24) H. Böhme, *Org. Syn.*, **20**, 70 (1940).

Reaction of Amides and Esters of α,β-Dibromopropionic Acids with Triphenylphosphine

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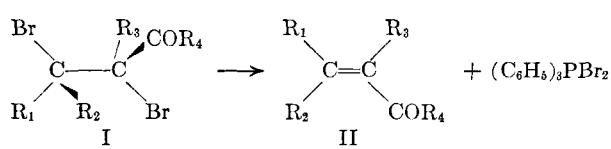
The debromination of the dibromides derived from ethyl methacrylate, methyl acrylate, and N,N-diethyl 3,3-dimethylacrylamide with triphenylphosphine is reported. However, 2,3-dibromopropionamide with triphenylphosphine underwent displacement of the α-bromine atom and dehydrohalogenation to produce the ylid (VI).

In connection with our work on the debromination of *erythro*-N,N-diethylcinnamamide dibromide with bases,[1] the reaction of amides and esters of α,β-dibromopropionic acid with triphenylphosphine was undertaken. Abramov and Ilyina[2] in their investigation of the mechanism of the Arbuzov rearrangement of methyl α,β-dibromopropionate with tributylphosphite, reported a small quantity of by-product whose constants agreed with those of methyl acrylate. Very recently, Dershowitz and Proskauer[3] reported the debromination of dibromides of cinnamic acid, chalcone and *trans*-dibenzoylethylene with one mole equivalent of trialkylphosphite. They also stated that diphosphonates were formed when two mole equivalents of trialkylphosphite were employed.

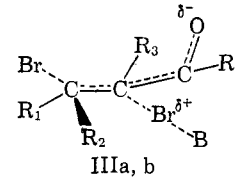
We have found that ethyl methacrylate dibromide (Ia) and methyl acrylate dibromide (Ib) with one mole equivalent of triphenylphosphine gave theoretical yields of triphenylphosphine dibromide and 49.5% yield of ethyl methacrylate (IIa) and 64.0% yield of methyl acrylate (IIb), respectively, were obtained.



I II

a. $R_1 = R_2 = H$; $R_3 = CH_3$; $R_4 = OC_2H_5$
b. $R_1 = R_2 = R_3 = H$; $R_4 = OCH_3$
c. $R_1 = R_2 = CH_3$; $R_3 = H$; $R_4 = N(C_2H_5)_2$

When two mole equivalents of triphenylphosphine were employed, the debromination of Ia,b to IIa,b proceeded with the recovery of one mole equivalent of the unchanged triphenylphosphine. The elimination of bromine can be reasonably explained[1] *via* a favored *trans*-coplanar transition state IIIa,b in which the incipient negative charge on the α-carbon atom can be stabilized by resonance with the carbonyl group.



IIIa, b

Dehydrobromination of Ib or SN2 displacement of the α or β-bromine atoms of Ia,b by triphenylphosphine was not observed. The elimination of hydrogen bromide from Ib would involve the unfavored conformer Ib'.[4]

The reaction of N,N-diethyl 3,3-dimethylacrylamide dibromide (Ic) with triphenylphosphine was also found to give the debrominated product IIc. However, reaction of acrylamide dibromide IV with two moles of triphenylphosphine gave a product $C_{21}H_{19}BrNOP$ in 85% yield and triphenylphosphonium bromide in 90% yield. The product was water soluble and its aqueous

(1) A. J. Speziale and C. C. Tung, *J. Org. Chem.*, **28**, 1323 (1963).

(2) V. S. Abramov and N. A. Ilyina, *J. Gen. Chem., USSR* (Eng. Trans.), **26**, 2245 (1956).

(3) S. Dershowitz and S. Proskauer, *J. Org. Chem.*, **26**, 3595 (1961).

(4) The difference of 33 kcal./g.-bond between C–Br and C–H would favor C–Br bond breaking.