Ethyl 2,3-epoxy-4,4-dimethylhept-6-eneoate. A solution of 0.5 mole of tetramethylammonium ethoxide in 800 ml. of absolute ethanol[27] was added during 1.5 hr. to 61.3 g. of ethyl chloroacetate and 55.5 g. of redistilled 2,2-dimethyl-4-pentenal.[35] After isolation of product as usual, distillation (36-in. column) provided 16.7 g. (17%) of crude glycidate, b.p. 92.5–102° (4.3 mm.), n_D^{25} 1.4436. Redistillation gave material with a constant n_D^{25} of 1.4447; b.p. 97° (3.0 mm.), d_4^{25} 0.9742, M_D 54.13 (calcd. 53.64).

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.91; H, 9.36.

Also isolated from the reaction was 22.7 g. of ethyl ethoxyacetate (34% yield), b.p. 56° (15 mm.), n_D^{25} 1.4008, d_4^{25} 0.9637 (reported[36] b.p. 155–158°, n_D^{25} 1.4009), M_D 33.29, (calcd. 33.21).

Anal. Calcd. for $C_6H_{12}O_3$: C, 54.52; H, 9.16; Sapon. equiv., 132. Found: C, 54.20; H, 9.40; Sapon. equiv., 131.

A portion of the distillate obtained upon removal of solvent from the reaction mixture was tested with 2,4-dinitrophenylhydrazine; the test was positive; melting point of the precipitate, 117.5–118° (reported[37] for the hydrazone of the pentenal, 117–118°).

Ethyl 2,3-epoxy-4,4-dimethylpentanoate. A solution of 9.2 g. of potassium in 250 ml. of dry *t*-butyl alcohol was added dropwise to 14.3 g. of redistilled pivalaldehyde (Columbia Organic Chemicals, Inc.) and 29.5 g. of ethyl chloroacetate over 2 hr. at 25°. The next day the mixture was treated as usual. Distillation (36-in. column) gave 19.3 g. (67%), b.p. 81° (5–9 mm.), n_D^{25} 1.4232–1.4264. Redistillation provided 8.7 g. (30%) of ethyl 2,3-epoxy-4,4-dimethylpentanoate, b.p. 57–65° (3 mm.), n_D^{25} 1.4253–1.4258. A third distillation gave material of constant n_D^{25} 1.4255, b.p. 68° (4 mm.), d_4^{25} 0.9648, M_D 45.68 (calcd. 44.86). The product gave a positive epoxide test with hydriodic acid and no precipitate with 2,4-dinitrophenylhydrazine.

Anal. Calcd. for $C_9H_{16}O_3$: C, 62.78; H, 9.35; Sapon. equiv., 172. Found: C, 62.70; H, 9.51; Sapon. equiv., 175.

Reaction of benzaldehyde, phenyl chlorothiolacetate, and potassium t-butoxide. Potassium *t*-butoxide (0.09 mole) in *t*-butyl alcohol was added (1 hr.) to benzaldehyde (9.1 g.) and phenyl chlorothiolacetate[38] (16.0 g.) in ether at 0°. After 1 hr., the usual isolation, two distillations (6-in. column), and chilling resulted in 11% of greasy phenyl phenylthiothiolacetate (III). Recrystallization gave colorless III, m.p. 63.5–65°. No other substance was isolated.

With anhydrous potassium acetate in dry ethanol (or methanol) as the base, the yield of recrystallized III, b.p. 185° (0.9 mm.), was 56%, m.p. 64–65°.

Anal. Calcd. for $C_{14}H_{12}OS_2$: C, 64.58; H, 4.65; Sapon. equiv. 130. Found: C, 64.25; H, 5.25; Sapon. equiv. 128.

Interestingly, under the same conditions in the absence of benzaldehyde, no III was isolated.

III was saponified[22] by adding 1 equivalent to 2 g.-atom proportions of sodium in absolute ethanol,[27] followed by 1 equivalent of water. The resulting salt was acidified and the phenylthioacetic acid ($C_6H_5SCH_2CO_2H$) recrystallized (hexane); m.p. and mixture m.p., 64.5–65.5°; anilide, m.p. 81.5–82.5° (Kofler hot stage) (reported,[39] 82–83°); *p*-bromophenacyl ester, m.p. 87–88°.

Anal. Calcd. for $C_{16}H_{13}BrO_3S$: Br, 21.88. Found: Br, 21.46.

For synthesis of III, benzenethiol (2.20 g.) was dissolved in 20 ml. of absolute ethanol containing 0.02 mole of potassium ethoxide, and phenyl chlorothiolacetate (2.00 g.) in 15 ml. of ethanol was added. Potassium chloride was separated. The filtrate was warmed slightly, and cooled. Upon addition of water, III precipitated. After two recrystallizations from hexane, the m.p. was 64–65°, undepressed by the product from the potassium acetate reaction; yield, 10%.

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[35] We wish to thank Dr. J. B. Dickey of the Tennessee Eastman Corp., Kingsport, Tenn., for providing this material.

[36] S. M. McElvain and W. R. Davie, *J. Am. Chem. Soc.*, **73**, 1400 (1951).

[37] K. C. Brannock, *J. Am. Chem. Soc.*, **81**, 3379 (1959).

[38] C. E. Dalgliesh and F. G. Mann, *J. Chem. Soc.*, 559 (1947).

[39] E. Vinkler, *J. prakt. Chem.*, **159**, 115 (1941); *Chem. Abstr.*, **37**, 4072 (1943).

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, AGRICULTURAL CHEMICALS DIVISION, MONSANTO CHEMICAL CO.]

The Darzens Condensation. I. Reaction of Chloroacetamides with Acetone and Cyclohexanone

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Ethyl chloroacetate undergoes the Darzens condensation with acetone or cyclohexanone regardless of basic agents used. In contrast, *N,N*-diethyl-α-chloroacetamide, presumably because of the relatively lower acidity of its α-hydrogens, does not readily undergo the Darzens condensation. Instead, γ-keto amides are produced as the predominant product. These arise from displacement of the chlorine by the enolates of acetone and cyclohexanone when either potassium *t*-butoxide or sodium hydride is used. If either methoxide or ethoxide is used, the same products are formed along with α-alkoxy amides.

The Darzens glycidic ester condensation[1] has been applied to only a few α-chloro amides.[1a,2] However, some discrepancies were noted in some of the glycidamide work. Fourneau[2a] reported a 55% yield of 3,3-dimethylglycidamide (Ia) (m.p. 85–87°) from acetone and chloroacetamide when sodium ethoxide was used as the condensing agent, but von Schickh[2b] reported an 80% yield (m.p. 121°) when metallic sodium was used. Forneau[2a] also stated that 3,3-diethylglycidamide, prepared from diethyl ketone and chloroacetamide, melted at 148°. However, he also reported a melting point

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[1] (a) M. S. Newman and B. J. Magerlein, *Org. Reactions*, **V**, 413 (1949). (b) M. Ballester, *Chem. Revs.*, **55**, 283 (1955).

[2] (a) E. Fourneau, J. R. Billeter, and D. Bonet, *J. Pharm. Chem.*, **49**, (1934); (b) O. von Schickh, *Ber.*, **69**, 967 (1936); (c) S. Bodforss, *Ber.*, **52**, 142 (1919).

of 104° for the same compound obtained from the reaction of the glycidic ester with ammonia.

In view of these reports and our interest in reactions of chloro amides and chloro esters,[3] we decided to investigate the Darzens condensation of acetone and cyclohexanone with chloroacetamides and chloroacetates.[4–6]

Cyclohexanone and *N,N*-diethyl-α-chloroacetamide in the presence of sodium methoxide in ether, sodium ethoxide in toluene, or sodium ethoxide with no solvent gave a mixture or products. In these reactions, 40–56% of the cyclohexanone was recovered unchanged and 20–48% of the chloroamide was converted to the α-alkoxyacetamide. A high boiling fraction which was isolated in 18–35% yield showed infrared absorption at 2.95 μ (OH), 5.85 μ (carbonyl), 6.10 μ (amide), and at 11.58, 12.00 μ (epoxide).

Acetone and *N,N*-diethyl-α-chloroacetamide in the presence of sodium methoxide gave similar results. About 30% of the chloroacetamide was converted to the α-methoxyamide and the epoxy fraction (35% yield) showed infrared absorption similar to the products from the cyclohexanone reaction: 5.83 μ (carbonyl), 6.10 μ (amide), and 10.9 μ (epoxide).

The extensive side reactions (displacement of the α-chlorine atom and formation of carbonyl and hydroxyl containing by-products) clearly indicated that the use of chloroacetamides in the Darzens condensation for the production of glycidamides (Ib and IIa) was considerably more complicated than the glycidic ester synthesis.[1a]

To circumvent the formation of α-alkoxyamides as by-products, our attention was focused on potassium *t*-butoxide[4] and sodium hydride[7] as the condensing agents. Neither of these reagents would be expected to displace the α-chlorine atom and both were shown to be superior to methoxide and ethoxide in glycidic ester formation.

Cyclohexanone or acetone with *N,N*-diethyl-α-chloroacetamide in the presence of potassium *t*-butoxide in *t*-butyl alcohol gave only carbonyl containing fractions. There was no evidence for the formation of the α-*t*-butoxyamide in either reaction. The infrared spectra of the distilled materials were identical with those obtained in the other alkoxide reactions.

In contrast to von Schickh[2b] and Fourneau[2a] acetone and α-chloroacetamide in molar ratios of 2:1, 3.3:1, and 10:1, respectively, with potassium *t*-butoxide (one equivalent) gave 6.5–14.8% yield of Ia (m.p. 124–125°). There was no evidence by infrared for the keto amide. Large amounts of unidentified waxy solids were obtained.

Acetophenone reacted normally with *N,N*-diethyl-α-chloroacetamide to give 60% yield of a mixture of the diastereoisomers of *N,N*-diethyl-3-phenyl-3-methylglycidamide. There was no keto amide formed.

The reaction of cyclohexanone with *N,N*-diethyl-α-chloroacetamide with sodium hydride in hexane was performed at 50°. Ethyl chloroacetate under these conditions gave a 90% yield of the epoxy ester. The rate of hydrogen evolution at 50° was almost as fast as when the chloroacetate was used at 30°. Thus, the chloroamide reacts more slowly with sodium hydride in the formation of its enolate than does chloroacetate. The evolution of hydrogen, however, abruptly stopped at 69% conversion due undoubtedly to the coating of sodium hydride by the precipitated sodium chloride. The carbonyl containing fraction amounted to 79% after accounting for the unreacted cyclohexanone and chloroacetamide. However, the infrared spectrum of this material showed the same bands as the methoxide and ethoxide reactions.

Acetone and *N,N*-diethyl-α-chloroacetamide, in the presence of sodium hydride gave essentially the same mixture of carbonyl containing products as in the methoxide experiments.

Thus, whereas ethyl chloroacetate reacted with either acetone or cyclohexane to give high yields of the epoxy ester (Id and IIc) regardless of the basic condensing agent used, *N,N*-diethyl-α-chloroacetamide with these ketones gave mixture of products regardless of the base used.

All major fractions in the alkoxide and sodium hydride experiments showed infrared absorption at 5.81–5.85 μ and at 10–11 μ. The carbonyl component appeared to be the major product by infrared analysis. The identity of the carbonyl containing component was necessary to ascertain whether α-keto amides (III) were formed by rearrangement of the epoxy amide as reported in the Darzens condensation with halo esters[8] or whether the γ-keto amides (IV and V) were produced by alkylation of the enolate of the ketone by the chloroamide. Authentic samples of the epoxy amides were also required to

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(3) A. J. Speziale and R. C. Freeman, *J. Org. Chem.*, **23**, 1883 (1958).

(4) W. S. Johnson, J. S. Belew, L. J. Chinn, and R. H. Hunt, *J. Am. Chem. Soc.*, **75**, 4995 (1953).

(5) After this work was completed, G. Vasiliu and L. Gertler [*Chem. Abstr.*, **52**, 1944 (1958); *Chem. Abstr.*, **53**, 19921 (1959)] reported that cyclohexanone with *N*-methyl-*N*-phenyl-α-chloroacetamide gave 64% and 27–56% yields of the epoxy amide with potassium *t*-butoxide or sodium in ethyl or butyl ethers respectively. *N*-Ethyl-*N*-phenyl-α-chloroacetamide behaved similarly in that 57 and 47% yields were obtained. The epoxy amides derived from acetone and methyl ethyl ketone with *N*-(2-thiazoyl)chloroacetamide were also reported.

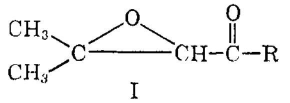
(6) Recently α-chloroacetonitrile has been used successfully in the Darzens condensation with aliphatic and alicyclic ketones in the formation of epoxy nitriles. G. Stork, W. S. Worrall, and J. J. Pappas, *J. Am. Chem. Soc.*, **82**, 4315 (1960). See also N. V. Phillips, British Patent **735,990**. V. F. Martynov and A. V. Shchelkunov, *J. Gen. Chem.* (*U.S.S.R.*), 1271 (1956) and F. F. Blicke and J. A. Faust, *J. Am. Chem. Soc.*, **76**, 3156 (1956).

(7) *Sodium Hydride Dispersed in Oil*, Metal Hydrides Inc., Beverly, Mass. Revised 4/58, p. 13–14.

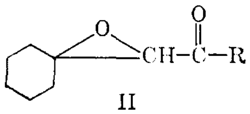
(8) Reference 1a, pp. 420–421, 423.

determine their infrared spectra and whether they would undergo rearrangement to the α-keto amides. Infrared absorption in the hydroxyl region could be due to diols formed by the opening of the oxirane ring. The enols of the α-keto amides were excluded since the products gave a negative ferric chloride test.[8]

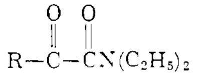
Authentic samples of the epoxy amides (Ib and IIa) were prepared by treatment of the sodium salts of the respective glycidic acids (Ic and IIb) with oxalyl chloride. The epoxy acid chlorides, without isolation, were converted to the amides at −35° by reaction with diethylamine. Under these conditions, the epoxy group remained essentially intact. The α-keto amides (IIIa,b) were prepared by the action of isopropylmagnesium bromide and cyclohexylmagnesium chloride on ethyl diethyloxamate. The γ-keto amides (IV and V) were prepared from levulinyl chloride and diethylamine and by the alkylation of *N*-(1-cyclohexenyl)pyrrolidine with *N*,*N*-diethyl-α-chloroacetamide respectively. The four keto amides were converted to their 2,4-dinitrophenylhydrazones. A comparison of these with the 2,4-dinitrophenylhydrazones prepared from the epoxy fractions of the Darzens condensation showed the γ-keto amides (IV and V) to be the carbonyl containing component. The infrared spectra of the four keto amides and the authentic epoxy amides were also compared with Darzens condensation reaction products. This comparison confirmed the presence of epoxy amides and that the γ-keto amides were the only carbonyl components present. There was no evidence either by infrared analysis or from the 2,4-dinitrophenylhydrazones for the presence of α-keto amides in the Darzens condensation of acetone and cyclohexanone with *N*,*N*-diethyl-α-chloroacetamide.[9]


I

a. R = NH_2
b. R = $N(C_2H_5)_2$
c. R = ONa
d. R = OC_2H_5

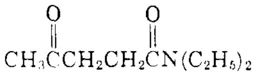

II

a. R = $N(C_2H_5)_2$
b. R = ONa
c. R = OC_2H_5



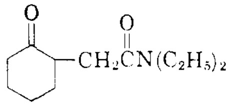
$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}N(C_2H_5)_2}$

IIIa. R = *i*-C_3H_7
b. R = C_6H_{11}



$\mathrm{CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}N(C_2H_5)_2}$

IV


V

In an attempt to effect the Darzens condensation of chloral with *N*,*N*-diethyl-α-chloroacetamide in the presence of *t*-butoxide, 80% of the amide was recovered unchanged. However, almost one equivalent of chloride ion was produced. This indicated that chloral had undergone reaction and that dichlorocarbene might have been formed in a manner analogous to action of base on trichloroacetate esters.[10] This supposition proved correct. When chloral and cyclohexene were treated with potassium *t*-butoxide, a 40% yield of 1,1-dichloronorcarane was isolated. These experiments clearly demonstrated the preference for carbene formation over the abstraction of a proton from the amide.

The infrared spectrum of epoxy compounds with respect to assignment of bands specific to the oxirane ring has been studied. In general, bands for the epoxide group appear at 8.0 μ and 10.5–12.3 μ.[11] The bands in 11 and 12 μ regions are believed to be the most characteristic for *trans*- and *cis*-1,2-epoxy alkanes, respectively.[12] In glycidic esters, bands attributable to the epoxy group were observed at 8.0, 8.25, 11.25, 11.75–12.0, and 12.0–12.25 μ. Assignment of bands to *cis*- and *trans*-epoxy esters were not made. These absorptions show there is no significant effect of conjugation between the epoxy and ester groups.[13] Various investigators have noted a splitting of the ester carbonyl group in epoxy esters and House[14] has offered a rationale for this

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(9) The Darzens condensation of acetone and cyclohexanone with ethyl chloroacetate (ref. 1a and Johnson ref. 4), chloroacetonitrile (Stork ref. 6) and *N*,*N*-diethyl-α-chloroacetamide (present investigation) clearly demonstrates the relative acidity of the α-hydrogen atoms of the halocarbonyl component as it affects the course of the Darzens condensation. An aldol type mechanism for the Darzens condensation has been demonstrated. [M. Ballester and D. Perez-Blanco, *J. Org. Chem.*, **23**, 652 (1958) and H. E. Zimmerman and L. Ahramjian, *J. Am. Chem. Soc.*, **82**, 5459 (1960)]. The success of the Darzens condensation rests on the fact that the enolate of the chloro carbonyl compound is formed in preference to that of the ketone or aldehyde (when the ketone or aldehyde are present as substrates). The α-hydrogen atom in ethyl chloroacetate and chloroacetonitrile will be more acidic than those in acetone or cyclohexanone due to the inductive effect of the α-chlorine atom and the electromeric effect of the carbonyl and the nitrile groups. However, the greater resonance stabilization of amides as compared to esters by contribution of resonance forms $\mathrm{O{=}\underset{|}{C}{-}NR_2 \longleftrightarrow \overset{\ominus}{O}{-}\underset{|}{C}{=}\overset{\oplus}{N}R_2}$, would predict that chloroacetamides would be less acidic than chloroacetates. This decrease in acidity would account for the alkylation of acetone and cyclohexanone, and for the displacement of the α-chlorine atom by methoxide and ethoxide in the case of α-chloroactamides. The order of acidity or ease of carbanion formation of the reactants in the Darzens condensation can be formulated as chloroacetonitrile > ethyl chloroacetate > acetone ≈ cyclohexanone > *N*,*N*-diethyl-α-chloroacetamide. The introduction of an aromatic group on the nitrogen atom of the amide would increase the acidity of the α-hydrogen atom and the amide would thereby compete favorably in the Darzens condensation. [See Vasiliu and Gertler (ref. 5)].

(10) W. E. Parham and F. C. Loew, *J. Org. Chem.*, **23**, 1705 (1958).

(11) J. Bomstein, *Anal. Chem.*, **30**, 544 (1958).

(12) O. D. Shreve, M. R. Heether, H. B. Knight, and D. Swern, *Anal. Chem.*, **23**, 277 (1951).

(13) E. D. Bergmann, S. Yaroslavsky, and H. Weiler-Feilchenfeld, *J. Am. Chem. Soc.*, **81**, 2775 (1959).

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

TABLE I

INFRARED SPECTRA[a] OF SOME GLYCIDIC ACID DERIVATIVES

Compound	Frequencies in Microns				
	Carbonyl	Epoxide			
Ethyl 3,3-pentamethyleneglycidate (IIc)[e]	5.70 5.79[b]	7.83	10.81 11.11	11.50	12.00
Ethyl 3,3-dimethylglycidate (Id)[e]	5.69 5.78[b]	7.81 8.00	10.81	11.75 11.85	
Sodium 3,3-pentamethyleneglycidate (IIb)[f]	6.18	7.98 8.07	11.00 11.08	11.79	12.06
Sodium 3,3-dimethylglycidate (Ic)[f]	6.17	8.04	11.19		11.90
N,N-Diethyl-3,3-pentamethyleneglycidamide (IIa)[c]	6.11	7.83 7.91	10.85 11.13	11.58	12.00
N,N-Diethyl-3,3-dimethylglycidamide (Ib)[c]	6.10	7.81 8.03	10.91		
3,3-Dimethylglycidamide (Ia)[d,g]	5.99	7.73 8.06	10.98		12.31
N,N-Diethyl-3-methyl-3-phenylglycidamide					
A[e]	6.07	7.89 8.21	10.95 11.17	11.50	12.10
B[e]	6.07	7.78 8.05	10.99 11.16		12.11
C[d]	6.07	7.93	10.95	11.50	11.95

[a] Taken in 0.2 mm. sodium chloride cell using a Perkin-Elmer Model 21 instrument. [b] See reference 14. [c] 3% carbon tetrachloride solution. [d] 3% chloroform solution. [e] Capillary film 0.01 mm. [f] 40% Nujol mull. [g] NH_2 absorption at 2.87, 2.94, 3.05, 3.15, and 6.34 μ.

behavior. Schaer[15] has found that the epoxy bands in α,β-epoxy aldehydes appear at 8.0 μ and 11.25 μ. The infrared spectrum of 3-(p-methoxyphenyl)-glycidamide is reported[16] and the epoxide absorption appears at 11.0 μ.

Our infrared data are presented in Table I and assignments for the oxirane ring correspond to those previously given for α,β-epoxy esters. For diagnostic purposes, the bands in the 10.5–11.5 μ were more reliable than those in 8.0 μ region.

EXPERIMENTAL[17]

Ethyl 3,3-pentamethyleneglycidate (IIc). The procedure as given by Metal Hydrides[7] was followed except that methanol was omitted and hexane was used as solvent. To a flask previously swept with nitrogen, there was added 49.0 g. (0.5 mole) of cyclohexanone, 67.3 g. (0.55 mole) of ethyl chloroacetate, and 125 ml. of hexane. The mixture was cooled to 0–5°, under nitrogen, and a suspension of 12.0 g. (0.5 mole) of sodium hydride (actual charge 24.6 g. sodium hydride in oil, 50% assay, 97.5% purity) in hexane was added in 1 hr. at 5–10°. At this time only 36.4% of the theoretical amount of hydrogen was evolved. The mixture was allowed, to warm to room temperature and stirring continued for 17.5 hr., at which time the theoretical amount of hydrogen had been evolved. The mixture was filtered and the filter cake was dissolved in water and titrated potentiometrically for chloride ion (0.525 mole). The hexane mother liquors were concentrated and the epoxy ester[4] distilled: wt. 86.6 g. (93.6% yield); b.p. 91° (2.4 mm.) n_D^{25} 1.4578–1.4580.

At 50–52°, the reaction time was 6.5 hr. and a yield of 90.4% was obtained.

Equimolar amounts of cyclohexanone and sodium hydride in hexane at 0–25° liberated less than 1% of the theoretical amount of hydrogen in 3 hr. One equivalent of ethyl chloroacetate was then added and reaction continued as indicated above. The epoxy ester was isolated in 88.4%. This indicates that the enolate of the ketone is not formed to an appreciable extent and that reaction of sodium hydride with chloroester in the *presence of cyclohexanone* is direct.

Equimolar amounts of ethyl chloroacetate and sodium hydride in hexane gave rise to 85% of the theoretical amount of hydrogen in 3 hr. at 0–5°. The additional 15% hydrogen was liberated on addition of 1 equivalent of cyclohexanone at 0–5° in 2 hr. Epoxy ester was not isolated in this instance but rather a 29.4% recovery of cyclohexanone, and nondistillable, nonidentified residue. Evidently, the enolate of the chloro ester underwent acetoacetic ester condensation.

Ethyl 3,3-dimethylglycidate (Id). The procedure of Johnson[4] was used with some modification. A solution of potassium *t*-butoxide (prepared from 16 g. (0.41 g-atom) of potassium and 400 ml. of *t*-butyl alcohol dried by distilling from sodium; assay (99.95%) was added to a mixture of 23.2 g. (0.4 mole) of acetone and 49 g. (0.4 mole) of ethyl chloroacetate over a period of 2 hr. at 10–15° and held at this temperature for an additional 2 hr. The reaction was run under an atmosphere of nitrogen. The *t*-butyl alcohol was removed *in vacuo* to a maximum pot temperature of 50°. Ether was added to the residue and the mixture quenched with the minimum amount of water and separated. The ether was dried with magnesium sulfate and evaporated to dryness. Distillation of the residue afforded 43.1 g. (74.8% yield) of ethyl 3,3-dimethylglycidate; b.p. 65–67° (7.0 ml.); n_D^{25} 1.4192. Johnson[4] reported a 66% yield; b.p. 87–89.5° (30 mm.); n_D^{25} 1.4181.

Sodium 3,3-pentamethyleneglycidate (IIb). To a solution of sodium ethoxide in ethanol (7.48 g., 0.33 g.-atom of sodium and 145 ml. of ethanol) at 0–5°, 60 g. (0.33 mole) of ethyl 3,3-pentamethyleneglycidate was added in 0.5 hr. The clear yellow solution was treated dropwise with 6.0 g. (0.33 mole) of water at 0–5°. The solid precipitated immediately. The mixture was allowed to warm to room temperature and stirred overnight. The solid was filtered, washed with ether and dried; wt. 57.5 g. (99% yield).

Sodium 3,3-dimethylglycidate (Ic). This was prepared according to the procedure for the cyclohexyl derivative from 4.4 g. (0.19 g.-atom) of sodium, 100 ml. of ethanol, 27.4 g. (0.19 mole) of ethyl 3,3-dimethylglycidate, and 3.4 g. (0.19 mole) of water. The yield was 24 g., 91.6%.

N,N-Diethyl-3,3-pentamethyleneglycidamide (IIa). A suspension of 41 g. (0.23 mole) of sodium 3,3-pentamethylene

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(15) C. Schaer, *Helv. Chim. Acta*, **75**, 674 (1958).

(16) V. F. Martynov and G. Olman, *J. Gen. Chem. (U.S.S.R.)*, **27**, 1944 (1957).

(17) Melting points and boiling points are uncorrected. Microanalyses by Du-Good Laboratories, St. Louis, Mo. We are indebted to Dr. B. Katlafsky and Mr. O. Kinast for the infrared spectra.

glycidate in 200 ml. of dry benzene was cooled to 0–5° and treated with 10 drops of dry pyridine followed by 44.5 g. (0.35 mole) of freshly distilled oxalyl chloride.[18] The addition of oxalyl chloride required 1 hr. and was controlled by the rate of evolution of carbon monoxide and carbon dioxide. The mixture was held at 0–5° for 0.5 hr., then evaporated to dryness *in vacuo* below 15°. A fresh 150-ml. portion of dry benzene was added. This was distilled *in vacuo* below 15° and the crude epoxy acid chloride was dissolved in ether and cooled to −25 to −30°. A solution of 33.6 g. (0.46 mole) of diethylamine in 100 ml. of ether was added at this temperature during 2 hr. The mixture was held at −20° for 0.5 hr., warmed to −10° and treated with 50 ml. of water. The ether layer was separated and, while drying with magnesium sulfate, the solvent was removed *in vacuo*. The epoxy amide was distilled, b.p. 123° (1.5 mm.) n_D^{25} 1.4831, wt. 34.8 g., 71.6% yield. Redistilled material boiled at 90° (0.15 mm.) n_D^{25} 1.4828–1.4832.

Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21, H, 10.02, N, 6.63. Found: C, 68.10, H, 10.01, N, 6.67.

N,N-Diethyl-3,3-dimethylglycidamide (Ib). The compound was prepared by the method given for *N,N*-diethyl-3,3-pentamethyleneglycidamide from 20 g. (0.145 mole) of sodium 3,3-dimethyl glycidate, 27.9 g. (0.22 mole) of oxalyl chloride, and 21.4 g. (0.29 mole) of diethylamine. The epoxy amide was distilled at 79° (0.15 mm.); n_D^{25} 1.4540; wt. 7.8 g.; 31.5% yield.

Anal. Calcd. for $C_9H_{17}NO_2$: C, 63.18; H, 10.01; N, 8.18. Found: C, 63.28; H, 10.20; N, 8.22.

1-(Diethylcarbamoylmethyl)cyclohexanone (V). *N*-(1-Cyclohexenyl)pyrrolidine[19] was prepared in 93% yield [b.p. 62° (0.35 mm.)] from 196 g. (2.0 moles) of cyclohexanone and 497 g. (7.0 mole) of pyrrolidine in 1.5 l. of benzene. A modification of the method of Stork[20] was used for the alkylation of the enamine. A mixture of 45.3 g. (0.3 mole) of *N*-(1-cyclohexenyl)pyrrolidine, 49.5 g. (0.33 mole) of *N,N*-diethyl-α-chloroacetamide, 1.67 g. (0.01 mole) of potassium iodide, and 500 ml. of dry methanol was heated under a nitrogen atmosphere at reflux (66°) for 17 hr. Titration of an aliquot with silver nitrate showed that 92% of the theoretical amount of chloride ion was formed. Fifty milliliters of water was added, the mixture heated under reflux for 1 hr. at 70°, and the excess methanol removed *in vacuo*. The residue was treated with 150 ml. of water and 10 ml. of 10% sulfuric acid (*p*H 1.0) and extracted with ether. Evaporation of the ether left 49 g. (78.6%) of light, yellow oil. Distillation of this material gave 25.2 g. (40.5% yield) of desired product; b.p. 120° (0.6 mm.) n_D^{25} 1.4830. Infrared: 5.85 μ (carbonyl), 6.10 μ (amide): 8.00, 8.78, 8.88 μ.

Anal. Calcd. for $C_{12}H_{21}NO_2$: C, 68.21: H, 10.02; N, 6.63. Found: C, 67.95: H, 10.18: N, 6.71.

The *2,4-Dinitrophenylhydrazone* was prepared by treating 3.7 g. of V with 100 ml. of 2,4-dinitrophenylhydrazine–phosphoric acid reagent[21] on the steam bath for 0.5 hr. The mixture was cooled, poured into 500 ml. of water, and extracted with chloroform. Evaporation of the solvent and recrystallization of the residue from ethyl acetate–hexane mixture gave 5 g. (73%) of the phenylhydrazone as orange needles m.p. 158–159°. The melting point was raised to 162–163° after two additional recrystallizations from ethyl acetate–hexane. A mixture melting point with the 2,4-dinitrophenylhydrazone prepared from the cyclohexanone–chloroacetamide Darzens reaction product was not depressed: m.p. 161–163°.

Anal. Calcd. for $C_{18}H_{25}N_5O_5$: C, 55.23; H, 6.44; N, 17.84. Found: C, 55.32; H, 6.19; N, 17.51.

N,N-Diethylcyclohexylglyoxylamide (IIIb). Ethyl *N,N*-diethyloxamate[22] was prepared in 78% yield [b.p. 118–120°, (8.5 mm.) n_D^{25} 1.4416] from ethyl oxalate and diethylamine.

The glyoxylamide was prepared according to the procedure of Barre.[22] Cyclohexylmagnesium bromide, prepared from 106 g. (0.625 mole) of cyclohexyl bromide and 15.5 g. (0.64 g.-atom) of magnesium in 225 ml. of ether, was treated with 86.6 g. (0.5 mole) of ethyl *N,N*-diethyloxamate at −15 to −20° in 80 min. The mixture was held at −15° for 0.5 hr., allowed to warm to 0° and then treated with 60 ml. of acetic acid in 200 ml. of water. The ether layer was separated and combined with the ether extract of the aqueous layer. After removal of the ether, a solid remained in the liquid residue. This was filtered (10 g.) and recrystallized from absolute ethanol to give 8.3 g. of the *tert*-carbinol, 2,2-dicyclohexyl-2-hydroxy-*N,N*-diethylacetamide, m.p. 181–181.5°; infrared: 3.02 μ (hydroxyl); 6.23 μ (amide).

Anal Calcd. for $C_{18}H_{23}NO_2$: C, 73.17; H, 11.26; N, 4.74. Found: C, 72.84; H, 11.25; N, 4.80.

The liquid residue was distilled to give 17.6 g. (20.7% recovery) of unchanged ethyl *N,N*-diethyloxamate and 42.3 g. (50% yield) of *N,N*-diethylcyclohexylglyoxylamide; b.p. 91–92° (0.25 mm.) n_D^{25} 1.4760. Infrared: 5.86 μ (carbonyl), 6.11 μ (amide), 9.44 μ and 10.22 μ.

Anal. Calcd. for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 67.81; H, 10.24; N, 6.81.

The *2,4-dinitrophenylhydrazone* prepared as described above was obtained after one recrystallization from ethyl acetate–hexane in 74% yield as yellow needles, m.p. 118–119°. The analytical sample melted at 119–120°.

Anal. Calcd. for $C_{18}H_{25}N_5O_5$: C, 55.23; H, 6.44; N, 17.84. Found: C, 55.23; H, 6.22; N, 17.67.

N,N-Diethyllevulinamide (IV). This α-keto amide, prepared by the procedure of Haskelberg,[23] was obtained in a 27.6% yield: b.p. 80° (0.30 mm.) n_D^{25} 1.4576. Haskelberg reported a yield of 60%; n_D^{25} 1.457. The infrared absorption spectrum showed the carbonyl band at 5.83 μ and amide band at 6.1 μ.

The preparation from levulinyl chloride[24] gave somewhat higher yields. A solution of 58 g. (0.5 mole) of levulinic acid in 61 g. (0.51 mole) of thionyl chloride in 150 ml. of dry benzene was heated at reflux for 1.75 hr. The solvent was removed *in vacuo*. The crude acid chloride was dissolved in 150 ml. of ether and treated with 74 g. (1.0 mole) of diethylamine at 10–15° during 1 hr. The amine hydrochloride was filtered and the levulinamide recovered by distillation: wt. 56.1 g. (65.6% yield) b.p. 87–104° (0.45 mm.) n_D^{25} 1.4563. Redistillation gave pure material in 43.5%, b.p. 90–91° (0.85 mm.) n_D^{25} 1.4570. Infrared: 5.83 μ (carbonyl), 6.10 μ (amide), 7.95, 8.62, and 8.82 μ.

Anal. Calcd. for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 63.39; H, 10.19; N, 8.18.

The *2,4-dinitrophenylhydrazone*, prepared as described above, was formed in 95% yield after recrystallization from ethyl acetate–hexane. The yellow-orange plates melted at 188°. After a second recrystallization, the melting point was raised to 121–122°. A mixture melting point with the 2,4-dinitrophenylhydrazone of the product from acetone and *N,N*-diethyl-α-chloroacetamide was not depressed (m.p. 120–121°).

Anal. Calcd. for $C_{15}H_{21}N_5O_5$: C, 51.27; H, 6.03; N, 19.93. Found: C, 51.46; H, 6.17; N, 19.63.

N,N-Diethylisopropylglyoxylamide (IIIa). This compound was prepared from 60 g. (0.49 mole) of isopropyl bromide 14.6 g. (0.6 g.-atom) of magnesium, and 69.3 g. (0.40 mole) of ethyl *N,N*-diethyloxamate according to the procedure for the cyclohexyl analog. On distillation of the

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[19] G. Stork and H. K. Langesman, *J. Am. Chem. Soc.*, **78**, 5128 (1956).

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[21] L. F. Fieser, *Experiments in Organic Chemistry*, D. C. Heath and Co., Boston, Mass., 1957, p. 316.

[22] R. Barre, *Ann. Chim.*, **9**, 204 (1928).

[23] L. Haskelberg, *J. Am. Chem. Soc.*, **70**, 2830 (1948).

[24] N. L. Drake and C. M. Eaker, U. S. Patent **2,581,842**.

crude material, there was obtained 34.2 g. (50% yield) of glyoxylamide, b.p. 106–115° (11.5 mm.) n_{D}^{25} 1.4438–1.4450 and 17.4 g. [b.p. 115–125° (11.5 mm.) n_{D}^{25} 1.4456–1.4458] of a mixture of unchanged oxamate and *tert*-carbinolamide (infrared analysis). Redistillation of the glyoxylamide fraction gave pure material; wt. 29.8 g. (43.5% yield) b.p. 106–110° (11.5 mm.) n_{D}^{25} 1.4435. Infrared: 5.80 μ (carbonyl), 6.12 μ (amide), and 9.62 μ.

Anal. Calcd. for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 63.57; H, 10.07; N, 7.90.

The *2,4-dinitrophenylhydrazone* prepared as described above, was isolated in 83% yield, m.p. 60–62°. Three recrystallizations from hexane raised the m.p. to 74–75°.

Anal. Calcd. for $C_{15}H_{21}N_5O_5$: C, 51.27; H, 6.03; N, 19.93. Found: C, 51.38; H, 6.10; N, 19.60.

3,3-Dimethylglycidamide (Ia). To a suspension of 28 g. (0.3 mole) of chloroacetamide and 220 ml. (3.0 mole) of acetone, there was added a solution of potassium *t*-butoxide in *t*-butyl alcohol (prepared from 12 g. (0.315 g.-atom) of potassium and 300 ml. of dry *t*-butyl alcohol distilled from sodium) under nitrogen at 5–10° in 2 hr. The mixture was stirred 1 hr. at 10–15° and then the acetone-*t*-butyl alcohol was removed *in vacuo* at 40 mm. The residue was treated with 500 ml. of acetone and filtered. The filter cake was dissolved in water and was shown to contain 0.3 mole of chloride ion. The acetone mother liquors were concentrated *in vacuo* to give 59.5 g. oil which was digested with hexane. The hexane insoluble portion weighed 23.0 g. (m.p. 80–100°) and the soluble portion weighed 29.0 g. The latter material showed no absorption in the infrared for amide group and was discarded. Repeated attempts at purification of the hexane insoluble solid finally afforded 4 g. (11.6% yield) of 3,3-dimethylglycidamide; m.p. 124–125°.

Anal. Calcd. for $C_5H_9NO_2$: C, 52.16; H, 7.68; N, 24.38. Found: C, 52.17; H, 7.93; N, 24.46.

The infrared spectra of the crude material and fractions isolated from it were very similar but not identical with the spectrum of 3,3-dimethylglycidamide. All fractions contained epoxy bands in the 10-11 μ region. These by-products could arise *via* the Darzens condensation of chloroacetamide with the acetone self-condensation products. A 1:1 and 3:3-1 ratio of acetone to amide gave essentially the same results.

Fourneau[2a] and von Schickh[2b] reported m.p. 85–87° and 121° respectively for this compound.

Reaction of cyclohexanone with N,N-diethyl-α-chloroacetamide. 1. A solution of 49.0 g. (0.5 mole) of cyclohexanone, 82 g. (0.55 mole) of *N*,*N*-diethyl-α-chloroacetamide, and 125 ml. of hexane was cooled to 0–5° and treated with a suspension of 24.6 g. (0.5 mole) of sodium hydride (50% dispersion in oil) during 45 min. The off-gas hydrogen was passed through a Wet Test Meter. About 2% of the hydrogen was evolved during this period. The mixture was heated to 50° in 2 hr. (5% hydrogen total). Rate of hydrogen evolution increased and continued to 69% of theory in 8 hr. No additional hydrogen was evolved during the next 4 hr. and even when the temperature was raised to 70–72°. The mixture was filtered and the filter cake, after thorough washing with hexane, was cautiously added to absolute ethanol. After the excess sodium hydride had reacted, water was added and aliquots were titrated for chloride and hydroxide ions. These titrations indicated that 66% of the amide and 64% of hydride had undergone reaction. The solvent was evaporated from the hexane solution and the products distilled. There was recovered 27.5% of cyclohexanone and 24.4% of the chloroamide. The main fraction was collected at 73–113° (0.14 mm.); n_{D}^{25} 1.4730–1.4800; wt. 60.2 g. (57.4% yield on cyclohexanone charged, or 79.0% yield on cyclohexanone consumed). Redistillation of this fraction afforded: I) b.p. 92–96° (0.17 mm.) n_{D}^{25} 1.4800; 3.2 g., II) b.p. 100–102° (0.17 mm.) n_{D}^{25} 1.4820; 20.0 g., III) b.p. 109–112° (0.27 mm.) n_{D}^{25} 1.4820: 23.5 g., IV) b.p. 112° (0.27 mm.) n_{D}^{25} 1.4800; 2.7 g.

The infrared spectra of these four fractions were compared with those of authentic samples of 1-(diethylcarbamoylmethyl)cyclohexanone, *N*,*N*-diethylcyclohexylglyoxylamide, and *N*,*N*-diethyl 3,3-pentamethylene glycidamide. None of the glyoxylamide was present. These fractions were assayed by using the band at 8.88 μ for the γ-keto amide and the band at 11.13 μ for the epoxy amide. All fractions contained a mixture of the γ-keto amide and epoxy amide. The per cents of keto amide increased and the epoxy amide decreased from fractions I–IV.

These fractions averaged 57% of keto amide and 33% of epoxy amide. The over-all yield by infrared analysis based on cyclohexanone consumed was 27% γ-keto amide and 21% of epoxy amide.

The *2,4-dinitrophenylhydrazone* of fraction III (infrared assay 76% γ-keto amide) prepared as described previously, was isolated in 74.2% yield. The orange needles melted at 163–164° and the melting was not depressed on mixing with an authentic sample of the 2,4-dinitrophenylhydrazone of 1-(diethylcarbamoylmethylcyclohexanone) m.p. 161–163°.

Anal. Calcd. for $C_{18}H_{25}N_5O_5$: C, 55.23; H, 6.44; N, 17.89. Found: C, 54.60; H, 6.33; N, 17.89.

The *semicarbazone* of fraction III isolated in 21.8% yield was recrystallized from hot water, m.p. 179–180°.

Anal. Calcd. for $C_{13}H_{24}N_4O_2$: C, 58.18; H, 9.01; N, 20.88. Found: C, 58.67; H, 8.97; N, 20.83.

In a second experiment, sodium hydride was added at 50°. The temperature was gradually raised to reflux (73°). Hydrogen evolution completely stopped after 16 hr. at 46% of theory. There remained 61% of unchanged sodium hydride. A 48% recovery of cyclohexanone and 56.4% recovery of chloroamide were also made. The infrared spectrum of the crude product was no different from fractions I and II above and contained bands at 5.85 and 8.88 μ (carbonyl) and at 10.85 μ, 11.13 μ, and 12.00 μ (epoxide). Infrared analysis of the crude gave 42% γ-keto amide and 17% epoxy amide. The yields were therefore 21% keto amide and 9% epoxy amide.

Methanol did not catalyze the condensation of cyclohexanone with *N*,*N*-diethyl-α-chloroacetamide as noted by Metal hydrides[7] for the analogous reaction with ethyl chloroacetate.

2. To a mixture of 29.4 g. (0.3 mole) of cyclohexanone and 45 g. (0.3 mole) of *N*,*N*-diethyl-α-chloroacetamide, under nitrogen, a solution of potassium *t*-butoxide in *t*-butyl alcohol (prepared from 12.0 g. (0.31 g.-atom) of potassium and 300 ml. of dry *t*-butyl alcohol) was added at 10–15° in 1.75 hr. The mixture was stirred overnight at 10–15°, the *t*-butyl alcohol was removed *in vacuo* and the residue treated with ether and water. The water layer was separated and shown to contain (0.3 mole of chloride ion). The ether solution was dried and distilled. There was obtained 34.5 g. (54.5%) yield of material; b.p. 99–114° (0.25 mm.). A residue of 20 g. was not distillable up to 195° (0.25 mm.). The infrared spectrum of the product showed no ether bands (therefore no α-*t*-butoxyamide) but only bands which were characteristic for the epoxy amide at 6.10, 10.85, 11.13, and 12.0 μ and bands at 5.85 and 8.88 μ for a ketone carbonyl. The intensities of the bands indicated that the product consisted of 40% epoxy amide and 60% γ-keto amide.

3. When the above reaction was repeated with 29.4 g. (0.3 mole) cyclohexanone, 74.8 g. (0.5 mole)of *N*,*N*-diethyl-α-chloroacetamide and 28.3 g. (0.5 mole) of sodium methoxide[1a] in 125 ml. of ether, there was isolated 45% of unchanged cyclohexanone, 19.3% *N*,*N*-diethyl-α-methoxyacetamide [b.p. 108° (25 mm.); n_{D}^{25} 1.4450; Infrared: amide, 6.1 μ, and ether, 9.0 μ] and 25.9% of material, b.p. 90–115°/0.25 mm. n_{D}^{25} 1.4850. On redistillation of the last fraction, three fractions were obtained in 18.7% yield: I, b.p. 83–87° (0.11 mm.) n_{D}^{25} 1.4925, 2.3 g.; II, b.p. 88–91° (0.11 mm.) n_{D}^{25} 1.4850, 4.0 g.; III, b.p. 97° (0.14 mm.) n_{D}^{25} 1.4850, 4.5 g. The infrared spectra of these fractions were not significantly different from the sodium hydride reaction.

With sodium ethoxide in toluene,[1a] essentially the same results were obtained. Cyclohexanone (56%), *N*,*N*-diethyl-α-ethoxyacetamide [41%; b.p. 51° (0.3 mm.) n_{D}^{25} 1.4432. *Anal.* Calcd. N = 8.80. Found N = 8.75. infrared: amide, 6.1 μ and ether, 9.0 μ] and carbonyl fraction (26.0% yield) b.p. 74–120° (0.8 mm.) n_{D}^{25} 1.4800–1.4832 were isolated. The infrared spectrum of the last fraction did not differ from that of the previous experiment.

Another experiment was performed under the usual Darzens conditions.[1a] Dry sodium ethoxide 27.4 g. (0.40 mole) was added to a mixture of 35.5 g. (0.36 mole) of cyclohexanone and 59.0 g. (0.40 mole) of *N*,*N*-diethyl-α-chloroacetamide at 0–5° in 70 min. under nitrogen. The mixture was allowed to warm to room temperature and stand overnight. It was then heated to 90° for 2 hr. cooled and poured into ice water and acidified with a few milliliters of glacial acetic acd. This was extracted with ether and the ether solution dried and the solvent evaporated. The residue was distilled to give 51.8% of cyclohexanone, 60% of *N*,*N*-diethylethoxyacetamide [b.p. 50°/0.3 mm. *Anal.* Calcd. N = 8.80. Found N = 9.03] and 26% of material, b.p. 102–117° (0.15 mm.) n_{D}^{25} 1.4820–1.4832. The last fraction, collected into three fractions of about 5° boiling range, was not significantly different by infrared analysis from the sodium hydride reaction.

Reaction of acetone with N,N-diethyl-α-chloroacetamide. 1. The procedure of von Schickh[2b] was followed as closely as possible except that sodium methoxide was used in place of sodium amide. Von Schickh did not give the yield of *N*,*N*-diethyl-3,3-dimethylglycidamide but reported its boiling point at 122–124° (0.3 mm.).

A solution of 4.50 g. (0.3 mole) of *N*,*N*-diethyl-α-chloroacetamide in 450 ml. of acetone was treated with 16.2 g. (0.3 mole) of sodium methoxide over 80 min. at 0–5°. The mixture was held at this temperature for 2 hr., allowed to warm to 23–25° in 5 hr. and held for 10 hr. The salts were filtered (95.4% of chloride ion), acetone was removed and the residue distilled. There was obtained a low boiling material [b.p. 54–80° (53–26 mm.)] which was not identified, a 30% yield of *N*,*N*-diethyl-α-methoxyacetamide (b.p. 79–80° n_{D}^{25} 1.4480), and 34.5% of material, b.p. 112–130° (13 mm.) n_{D}^{25} 1.4573. The last fraction was redistilled and five cuts were taken; b.p. 91–120° (5.4 mm.) n_{D}^{25} 1.4505–1.4585. Infrared spectra were not significantly different from sodium hydride reaction (below).

2. A solution of 17.4 g. (0.3 mole) of acetone, 45.0 g. (0.3 mole) of *N*,*N*-diethyl-α-chloroacetamide, and 125 ml. of hexane was treated with 14.4 g. (0.3 mole) sodium hydride, (50% dispersion in oil) in 75 ml. of hexane in 1 hr. at 5°. The mixture was stirred 19 hr. at 25° at which time only 36% of the theoretical amount of hydrogen was liberated. An additional 39.5 g. (0.68 mole) of acetone was added at 25° and the remainder of the hydrogen (64%) was liberated in 40 min. The mixture was filtered and an aliquot of an aqueous solution of the filter cake showed that the theoretical amount of chloride ion was formed and that all the sodium hydride had reacted. The solvent was removed and the liquid residue distilled; b.p. 72–85° (0.25 mm.) n_{D}^{25} 1.4538–1.4570; wt. 41.2 g. (78.8% yield). Redistillation gave two fractions in 64% yield. I: b.p. 65–70° (0.25 mm.) n_{D}^{25} 1.4540 at 24.8 g. II: b.p. 70–79° (0.25 mm.) n_{D}^{25} 1.4562 at 9.6 g. Infrared spectra of Fractions I and II were almost identical (intensities varied) and were compared with those of authentic samples of *N*,*N*-diethyllevulinamide, *N*,*N*-diethylisopropylglyoxylamide, and *N*,*N*-diethyl-3,3-dimethylglycidamide. Both fractions consisted of a mixture of the γ-keto amide and epoxy amide (none of the glyoxylamide was present in these fractions or in the crude material) and were assayed by using the band at 8.82 μ for the γ-keto amide and the band at 10.91 μ for the epoxy amide. These fractions contained 36% of the γ-keto amide and 64% of the epoxy amide. The over-all yield by infrared analysis was 33 and 41% respectively.

The *2,4-dinitrophenylhydrazone* of Fraction II (infrared assay 73% γ-keto amide) was prepared as described above in 61% yield, m.p. 122°. A mixture melting point with authentic *N*,*N*-diethyllevulinamide-2,4-dinitrophenylhydrazone (m.p. 121–122°) was not depressed (m.p. 121°).

3. A solution of 23.2 g. (0.40 mole) of acetone and 59.8 g. (0.4 mole) of *N*,*N*-diethyl-α-chloroacetamide was treated with potassium *t*-butoxide in *t*-butyl alcohol [16.0 g. (0.41 g.-atom) of potassium and 400 ml. of *t*-butyl alcohol] under nitrogen at 10° during the course of 2 hr. The mixture was allowed to stir 1 hr. at 10° and the solvent removed *in vacuo*. Ether and water were added to the residue and the layers separated. The aqueous layer contained 0.43 mole of chloride ion. The ether layer was dried and evaporated to give 61.9 g. (90.4%) of oil. On distillation three fractions were obtained: I: b.p. 60–70° (1.0 ml.); n_{D}^{25} 1.4540; 23.0 g.; II: 70–80° (1.0 mm.) n_{D}^{25} 1.4569, 12.3 g.; III: 145–160° (1.0 mm.) n_{D}^{25} 1.4802 (10.8 g.). Fraction III (no epoxide, infrared) was discarded. Fractions I and II were almost identical in their infrared spectra: 5.78 μ (carbonyl), 6.13 μ (amide), and 10.91 μ (epoxide). The intensity of the bands indicated that fraction I contained more epoxide than II. No evidence for the α-*t*-butoxy amide was found. Fractions I and II, obtained in 51.4% yield, assayed 38% for γ-keto amide and 62% for epoxy amide.

N,N-Diethyl-3-methyl-3-phenylglycidamide. This compound was prepared by the *t*-butoxide method as described for ethyl 3,3-dimethyl glycidate from 24 g. (0.2 mole) of acetophenone, 29.9 g. (0.2 mole) of *N*,*N*-diethyl-α-chloroacetamide, 8.0 g. (0.2 g.-atom) of potassium, and 250 ml. of *t*-butyl alcohol. There was obtained 47.6 g. of crude oil which by infrared analyses showed no absorption in the 5.8 μ region. The oil was distilled; A: b.p. 119–126° (0.25 mm.); 25.7 g., 60% yield. The distilled glycidamide partially solidified on standing. The infrared spectrum of the semisolid mass was not different from the crude. A portion was recrystallized from hexane to give pure material; B; m.p. 94–95°. The hexane mother liquors were evaporated to give an oil (C).

Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: (A) C, 71.89; H, 8.10; N, 5.92. (B) C, 71.96; H, 8.56; N, 6.52.

The infrared spectra of A, B, and C were run in 3% chloroform. All showed aromatic bands at 13.1 and 14.3 μ. (A) 6.05 μ (amide); 7.89, 11.16, 12.1 μ (epoxide). (B) 6.05 μ (amide); 7.89, 11.16, 12.1 μ (epoxide). (C) 6.05 μ (amide); 7.92, 11.16, 11.95 μ (epoxide).

Fractions B and C are the diastereoisomeric glycidamides. There were distinct differences in the intensities of the bands in the 10.5–12.0 μ region. The band at 12.1 μ present in fraction B was absent in the spectrum of fraction C and 11.95 μ band in fraction C was a shoulder on the 12.1 μ band in A.

Reaction of chloral with N,N-diethyl-α-chloroacetamide. A solution of potassium *t*-butoxide (7.8 g.; 0.2 g.-atom) of potassium and 250 ml. of *t*-butyl alcohol was added to a mixture 29.5 g. (0.2 mole) of chloral and 29.9 g. (0.2 mole) of *N*,*N*-diethyl-α-chloroacetamide at 10–15° over 2 hr. This was allowed to stir for 2 hr. at 10–15° and the *t*-butyl alcohol removed under pressure. Ether was added and the mixture quenched with water. An analysis of the aqueous layer showed that 92.5% of chloride ion had been produced. The ether layer was evaporated to an oil (29.5 g.) which on distillation gave 24 g. (80.2% yield) of starting amide; b.p. 60–61° (0.58 mm.). The infrared spectrum was superimposable with that of the starting material.

1,1-Dichloronorcarane.[25] To a suspension of potassium *t*-butoxide (0.2 mole) and cyclohexene (16.4 g., 0.2 mole) in pentane (200 ml.), chloral (29.5 g., 0.2 mole) was added

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[25] We are indebted to Dr. K. W. Ratts for this experiment.

[26] W. von E. Doering and A. K. Hoffman, *J. Am. Chem. Soc.*, **76**, 6162 (1954), W. von E. Doering and W. A. Henderson, *J. Am. Chem. Soc.*, **80**, 5276 (1958).

over 45 min. while maintaining the temperature below 10°. After standing overnight, the mixture was filtered and the filter cake washed with pentane. The pentane filtrate was stripped to an amber liquid which was distilled to give 1,1-dichloronorcarane[26]; 9.3 g., 40% yield; b.p. 80–81° (16 mm.) n_D^{21} 1.4990.

St. Louis 66, Mo.

[Contribution from Department of Chemistry, Duke University]

Conjugate Addition of Disodiophenylacetate to Ethyl Cinnamate to Form *erythro*- and *threo*-4-Carbethoxy-2,3-diphenylbutyric Acids

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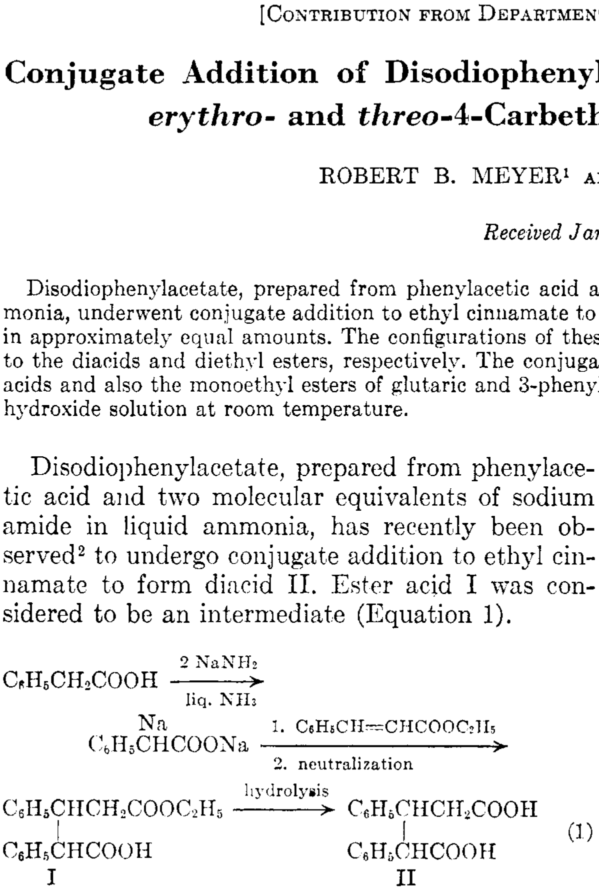
Disodiophenylacetate, prepared from phenylacetic acid and two molecular equivalents of sodium amide in liquid ammonia, underwent conjugate addition to ethyl cinnamate to form *erythro*- and *threo*-4-carbethoxy-2,3-diphenylbutyric acids in approximately equal amounts. The configurations of these isomers were established by hydrolysis and by esterification to the diacids and diethyl esters, respectively. The conjugate addition appeared to occur nonstereospecifically. The ester acids and also the monoethyl esters of glutaric and 3-phenylglutaric acids underwent rapid hydrolysis with excess sodium hydroxide solution at room temperature.

Disodiophenylacetate, prepared from phenylacetic acid and two molecular equivalents of sodium amide in liquid ammonia, has recently been observed[2] to undergo conjugate addition to ethyl cinnamate to form diacid II. Ester acid I was considered to be an intermediate (Equation 1).

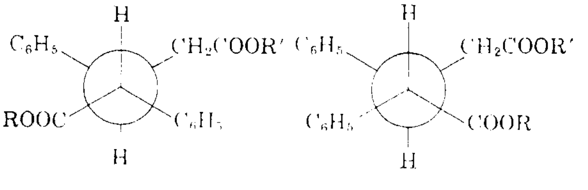


$$C_6H_5CH_2COOH \xrightarrow[\text{liq. NH}_3]{2\ NaNH_2} \overset{Na}{C_6H_5CHCOONa} \xrightarrow[\text{2. neutralization}]{\text{1. } C_6H_5CH{=}CHCOOC_2H_5} \underset{\text{I}}{\begin{matrix} C_6H_5CHCH_2COOC_2H_5 \\ | \\ C_6H_5CHCOOH \end{matrix}} \xrightarrow{\text{hydrolysis}} \underset{\text{II}}{\begin{matrix} C_6H_5CHCH_2COOH \\ | \\ C_6H_5CHCOOH \end{matrix}} \qquad (1)$$

The stereochemistry of this reaction has not been studied. Neutralization of the reaction mixture in liquid ammonia with ammonium chloride afforded a 96% yield of a mixture of the diastereomers of ester acid I. The higher melting isomer of I was isolated in 49% yield and the lower melting isomer in 32% yield; most of the remaining 15% of the product was probably the latter isomer (see Experimental). Each of these isomers gave satisfactory analyses not only for carbon and hydrogen but also for the ethoxy group; moreover they gave acceptable neutralization equivalents. Their infrared spectra showed sharp peaks at 5.82 and 5.90 μ,[3] whereas the spectrum of each of the diastereomers of diacid II exhibited a single carbonyl peak at 5.88 μ.[3]

When the condensation was performed using potassium amide or lithium amide, similar results were obtained. However, in the latter case the yields were somewhat lower.

The configurations of each isomer of ester-acid I were determined by hydrolysis by means of dilute hydrochloric acid to form the diastereoisomers of diacid II, the configurations of which have been well established.[4,5] Thus, the higher melting ester-acid was assigned the *erythro* configuration Ia and the lower melting isomer the *threo* configuration Ib, since they gave the *erythro*- and *threo*-diacids IIa and IIb in yields of 99 and 79%, respectively. Furthermore, the higher and lower melting isomers of ester-acid I were esterified with ethanol to form the *erythro*- and *threo*-diethyl esters IIIa and IIIb in yields of 97 and 46%, respectively. Authentic samples of these diesters were prepared by esterification of the corresponding diacids.



erythro	*threo*
Ia. R = H, R′ = C_2H_5 (M.p. 189.5–190°)	Ib. R = H, R′ = C_2H_5 (M.p. 104–105°)
IIa. R = R′ = H (M.p. 230–231°)	IIb. R = R′ = H (M.p. 212–213°)
IIIa. R = R′ = C_2H_5 (M.p. 92.5–93°)	IIIb. R = R′ = C_2H_5 (M.p. 76–76.5°)
IVa. R = R′ = CH_3 (M.p. 142–142.5°)	IVb. R = R′ = CH_3 (M.p. 85–86°)

Although the acid-catalyzed hydrolyses and esterifications mentioned above involved refluxing aqueous or ethanolic solutions or suspensions for several hours, little if any epimerization appeared to occur. Certainly complete epimerization in each reaction, which would have to be assumed if the

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[1] American Cyanamid Co. Fellow, 1959–1960.

[2] C. R. Hauser and M. T. Tetenbaum, *J. Org. Chem.*, **23**, 1146 (1958).

[3] See L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2nd ed., Wiley, New York, 1958, pp. 161, 178.

[4] S. Avery and W. D. Maclay, *J. Am. Chem. Soc.*, **51**, 2833 (1929).

[5] D. Lednicer and C. R. Hauser, *J. Am. Chem. Soc.*, **80**, 6364 (1958).