A mixture of 3.6 g. of sodium hydroxide, 5.0 g. of VIIIc, and 30 ml. of dry dimethyl sulfoxide was stirred for 19 hr. at 80–85°. The mixture was cooled, and 100 ml. of ether and 100 ml. of water were added in that order. The phases were separated, and the organic layer was washed successively with 100 ml. of water and 30 ml. of 6 *N* sodium chloride. The ether solution was distilled, and 3.3 g. of VIIIc was collected. The residue, which was mainly VIIIc, weighed 0.8 g.

Glycidyl Ether Reactions with Urethanes and Ureas. A New Synthetic Method for 2-Oxazolidones

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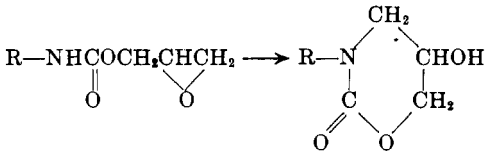
Tertiary amines and quarternary ammonium salts have been found to be efficient catalysts for the intermolecular addition reaction between urethane linkages and epoxy rings. Addition products of urethanes and epoxides undergo an intramolecular exchange of alcohols to give the oxazolidone derivatives in good yields.

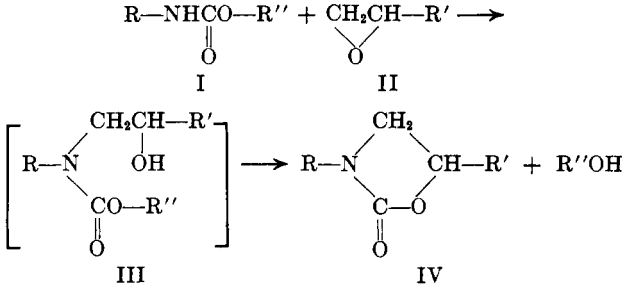
Epoxy compounds are known to produce ring-opened addition products with nucleophilic reagents,[1-4] but up to this time there has been no report about the reaction between epoxy compounds and the imide group of urethane linkages. Imide groups of urethane linkages are not reactive enough nucleophiles to react with epoxy rings without catalysts.

As we reported previously,[5] glycidyl urethanes are isomerized by heating to give N-substituted 5-hydroxytetrahydro-1,3-oxazin-2-ones. We attempted to extend these intramolecular reactions to intermolecular



addition reaction between urethanes and epoxides using catalysts.

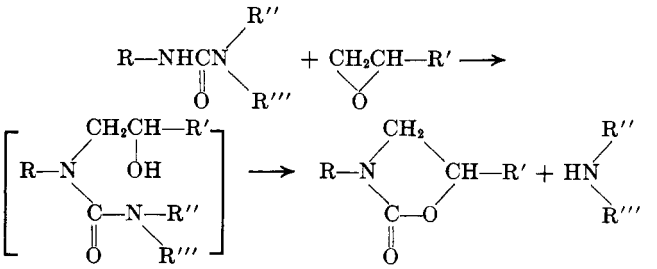
Tertiary amines and quarternary ammonium salts are useful catalysts to accelerate the intermolecular nucleophilic addition reactions between imide groups of urethane linkages and epoxy compounds, and, since



the reaction products (III) obtained by this addition split off alcohols rather rapidly to give the oxazolidone derivatives (IV), we can only isolate the oxazolidone derivatives as the final products in the intermolecular addition reactions between urethanes and epoxides.

As explained in detail in a later section, there is sufficient evidence that these reactions giving oxazolidone derivatives do not proceed *via* dissociation of urethanes to isocyanates and alcohols. According to Homeyer,[6] alkali-catalyzed reaction of α-amino alcohols and diethyl carbonate gives oxazolidones. From our experiments, it was found that condensation reactions of α-amino alcohols and ethyl chlorocarbonate also gave oxazolidones even at room temperature. These two results give support to reaction mechanisms involving nucleophilic addition and intramolecular exchange of alcohols as indicated by the previous formula.

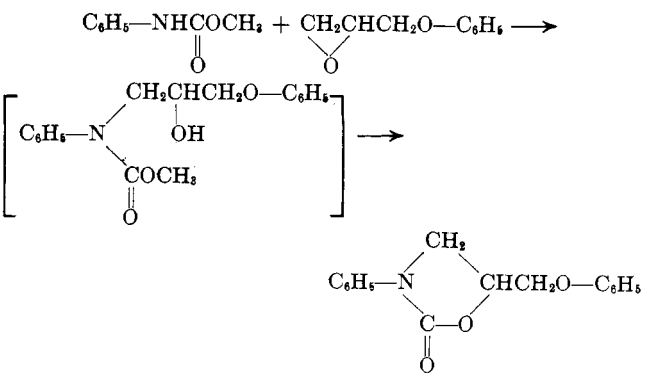
From the analogy of the mechanism of this reaction, we expect that ureas also would give the oxazolidones. In fact the intermolecular addition reaction between di- and trisubstituted ureas and epoxy



compounds gave the oxazolidone derivatives. In this case, the primary or secondary amines which are produced react with other epoxy compounds quickly; thus it is necessary that two or three molar equivalents of epoxy compounds be added.

Results and Discussion

Reaction between Urethanes and Epoxides.—To investigate the ability of intermolecular addition reaction of urethane linkages and epoxy rings, the reaction of N-phenylmethylurethane with phenyl glycidyl ether was examined expecting the following reaction. On



(1) L. Shechter, J. Wynstra and R. P. Kurkjy, *Ind. Eng. Chem.*, **48**, 86 (1956).
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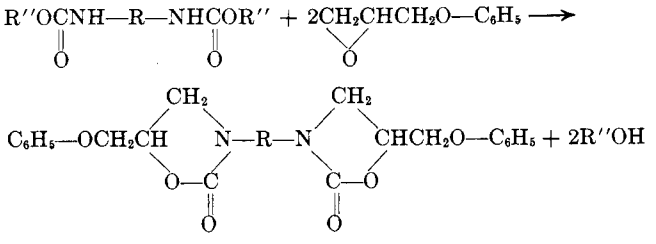
(3) R. M. Laird and R. E. Parker, *J. Am. Chem. Soc.*, **83**, 4277 (1961).
(4) R. E. Parker, *et al.*, *J. Chem. Soc.*, 1708 (1961).
(5) Y. Iwakura and Y. Taneda, *J. Org. Chem.*, **24**, 1992 (1959).
(6) A. H. Homeyer, U. S. Patent 2,399,118 (April 23, 1946).

heating without catalyst these two compounds did not show any changes at all in the temperature range from room temperature to 200°, and at high temperature there was observed only self-polymerization of epoxides. It was observed that tertiary amines and quarternary ammonium salts were effective catalysts for the intermolecular addition reaction between urethane linkages and epoxy rings and that these were also effective catalysts for isomerization of glycidyl carbamates. For example, at 25° using triethylamine, phenylmethylurethane and phenyl glycidyl ether gave 3-phenyl-5-phenoxymethyl-2-oxazolidone quantitatively in only two hours. The reaction using these catalysts was accompanied by no side reactions at all up to 140°, and the higher the reaction temperature used, the faster the reaction rate observed. At 140° in two or three minutes the reaction was almost completely finished. Attempted other catalysts, such as NaOH, $NaOCH_3$, BF_3OEt_2, and Lewis acids, were not effective in this reaction.

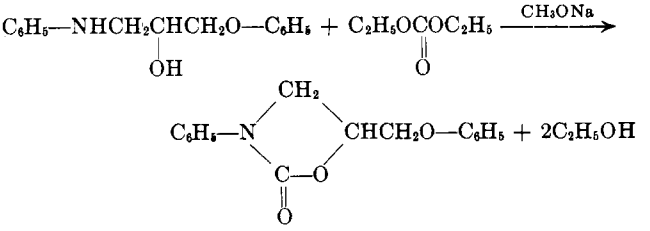
The reaction also proceeds in solvent with obviously decreased rate. The product obtained later was only an oxazolidone derivative. Solvents used were ethanol. benzene, toluene, chloroform, and dimethylformamide.

Reactivities of the urethanes having substituents (R) on nitrogen and substituents (R′) on oxygen to phenyl glycidyl ether were observed in order to investigate the effects of these substituents. The results are listed in Table I. The reactions were carried out without solvent, using triethylamine as catalyst, at 90° for one hour; an oxazolidone derivative was obtained quantitatively in the reaction between phenylmethylurethane and phenyl glycidyl ether. In the case of N-arylurethanes it was observed that the reaction products with phenyl glycidyl ether were quantitatively oxazolidone derivatives. In the case of N,N′-bifunctional arylurethanes which were synthesized from diisocyanates and alcohols, bisoxazolidone derivatives also were obtained quantitatively. N-Alkylurethanes, however, did not react with phenyl glycidyl ether under these conditions and the infrared spectra of reaction mixture showed little change before and after treatment.



The effects of substituents on the oxygen atom of urethane linkages were studied using N-phenylurethanes obtained from phenyl isocyanate and various hydroxy compounds. It was shown that the product of each reaction between these urethanes and phenyl glycidyl ether was 3-phenyl-5-phenoxymethyl-2-oxazolidone. The kind of substituent on the oxygen atom has no influence on the reaction mechanism, though we can not say anything quantitatively about the reaction rate.

As mentioned previously, the reactions between urethanes and phenyl glycidyl ether were generated by tertiary amines and quarternary ammonium salts in the case of N-arylurethane derivatives to give oxazolidone derivatives. 3-Phenyl-5-phenoxymethyl-2-oxazolidone obtained through this reaction route was identical with an authentic sample synthesized from N-phenyl-3-phenoxy-2-hydroxypropylamine and diethyl carbonate by Homeyer's method.[6]



The reaction of N-phenyl-3-phenoxy-2-hydroxypropylamine and ethyl chlorocarbonate at room temperature also gave 3-phenyl-5-phenoxymethyl-2-oxazoli-

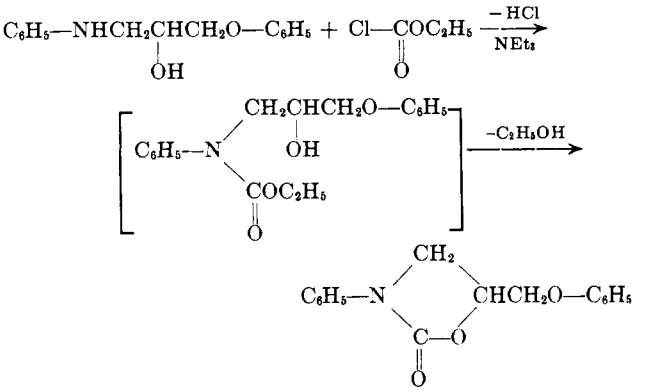


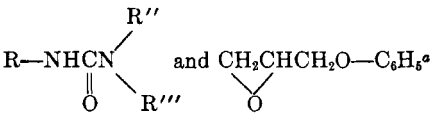
TABLE I

$R—NHCO—R''$ and $CH_2CHCH_2O—C_6H_5$ (O)

No.	R	R″	Results
1	C_6H_5–	–CH_3	Oxazolidone[b]
2	p-NO_2–C_6H_4–	–C_2H_5	Oxazolidone[c]
3	p-Cl–C_6H_4–	–C_2H_5	Oxazolidone[d]
4	p-C_2H_5O–C_6H_4	–C_2H_5	Oxazolidone[e]
5	p-CH_3–C_6H_4–	–C_2H_5	Oxazolidone[f]
6	2-C_5H_4N–	–C_2H_5	Oxazolidone[g]
11	C_2H_5–	–C_3H_7	No reaction[h]
12	C_2H_5–	–C_6H_5	No reaction[h]
13	C_4H_9–	–C_2H_5	No reaction[h]
14	C_5H_{11}–	–C_3H_7	No reaction[h]
21	C_6H_5–	–C_2H_5	Oxazolidone[b]
22	C_6H_5–	–C_3H_7	Oxazolidone[b]
23	C_6H_5–	–C_6H_5	Oxazolidone[b]

[a] Reaction conditions: without solvent, NEt_3 catalyst, 90°, 1 hr. [b] 3-Phenyl-5-phenoxymethyl-2-oxazolidone was obtained quantitatively. [c] 3-p-Nitrophenyl-5-phenoxymethyl-2-oxazolidone was recrystallized from acetone, m.p. 162–163°. *Anal.* Calcd. for $C_{16}H_{14}O_5N_2$: C, 61.14; H, 4.49; N, 8.91. Found: C, 61.03; H, 4.56; N, 8.83. [d] 3-p-Chlorophenyl-5-phenoxymethyl-2-oxazolidone was recrystallized from acetone, m.p. 158–160°. *Anal.* Calcd. for $C_{17}H_{16}O_3NCl$: C, 63.25; H, 4.64; N, 4.61. Found: C, 63.12; H, 4.76; N, 4.63. [e] 3-p-Ethoxyphenyl-5-phenoxymethyl-2-oxazolidone was recrystallized from acetone, m.p. 131–133°. *Anal.* Calcd. for $C_{18}H_{19}O_4N$: C, 68.99; H, 6.11; N, 4.47. Found: C, 69.11; H, 6.07; N, 4.71. [f] 3-p-Tolyl-5-phenoxymethyl-2-oxazolidone was recrystallized from acetone, m.p. 149–151°. *Anal.* Calcd. for $C_{17}H_{17}O_3N$: C, 72.06; H, 6.05; N, 4.94. Found: C, 71.71; H, 6.14; N, 5.03. [g] 3-(2-Pyridyl)-5-phenoxymethyl-2-oxazolidone was recrystallized from ethanol, m.p. 115–116°. *Anal.* Calcd. for $C_{15}H_{14}O_3N_2$: C, 66.67; H, 5.19; N, 10.37. Found: C, 66.81; H, 5.25; N, 10.29. [h] Infrared spectra of reaction mixture showed little change before and after treatment.

TABLE II

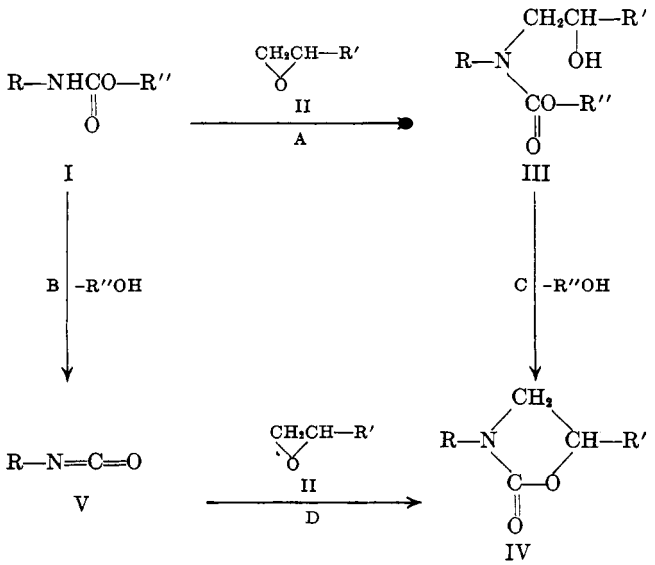


No.	R	R''	R'''	Epoxide (mole) / urea (mole)	Time, hr.	Results
1	C_6H_5–	C_2H_5–	C_2H_5–	1	1	Oxazolidone[b]
2	C_6H_5–	C_2H_5–	C_2H_5–	2	1	Oxazolidone[c]
3	C_6H_5–	C_4H_9–	C_4H_9–	2	1	Oxazolidone[c]
4	C_6H_5–	CH_3–	C_6H_5–	1	1	Oxazolidone[b]
5	C_6H_5–	CH_3–	C_6H_5–	2	1	Oxazolidone[c]
11	C_2H_5–	CH_3–	C_6H_5–	2	2	No reaction[d]
12	C_5H_{11}–	CH_3–	C_6H_5–	2	5	No reaction[d]
21	C_6H_5–	H–	C_6H_5–	2	1	Oxazolidone[b]
22	C_6H_5–	H–	C_6H_5–	3	1	Oxazolidone[c]
23	C_6H_5–	H–	C_4H_9–	3	1	Oxazolidone[c]

[a] Reaction conditions: without solvent, NEt_3 catalyst, 90°. [b] The infrared spectra of the reaction mixture indicated the presence of an unchanged urea derivative. [c] 3-Phenyl-5-phenoxymethyl-2-oxazolidone was isolated and the major part of the residue was an adduct of amine and epoxide. [d] The infrared spectrum of reaction mixture showed little change before and after treatment.

done; thus it was considered that it might be impossible to obtain the addition intermediate (III) in our case.

The reaction mechanism of oxazolidone formation from urethanes and epoxides is shown by process A and C in the reaction scheme. Thermal dissociation



of urethanes to isocyanates and alcohols has been reported in many cases.[7,8] In this reaction, however, processes B and D including dissociation of urethanes were completely eliminated by the observation that urethanes did not dissociate into isocyanates and alcohols under the conditions used as was demonstrated in an infrared heating cell. It is known that isocyanates (V) and epoxides (II) on heating with tertiary amines give an isocyanate trimer, and we observed that under these conditions oxazolidone derivatives were not isolated. Therefore, process D did not occur. Further, by the addition of alcohols to an isocyanates–epoxide–tertiary amine system, oxazolidone derivatives were obtained. This fact indicates that isocyanates and alcohols gave urethanes (I) by the reverse reaction of process B and that urethanes and epoxides gave oxazolidones (IV) by the processes A and C.

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(8) T. Mukaiyama and T. Akiba, *Bull. Chem. Soc. Japan*, **33**, 1707 (1960).

Reaction between Ureas and Epoxides.—From the consideration of the fact that the epoxy ring of phenyl glycidyl ether can react with urethanes catalyzed by tertiary amines and quarternary ammonium salts and that ureas and urethanes have the same imide group, the reactivity of the epoxy ring with urea linkages was studied. The reaction conditions used were the most suitable for the case of urethanes: 90° without solvent with triethylamine as catalyst.

The reactions between ureas and phenyl glycidyl ether were slightly complex compared with the urethanes. The intermolecular addition reaction between N-aryl-N′,N′-disubstituted ureas and phenyl glycidyl ether was accomplished easily under these conditions, and intramolecular substitution of newly produced secondary alcohols and urea linkages happened rather rapidly to give oxazolidone derivatives. It was impossible to obtain the addition intermediate in this case. Using these intramolecular reactions, amines were produced simultaneously and they reacted with the epoxy ring faster than the ureas did. Using 2 moles of phenyl glycidyl ether to 1 of urea the reaction occurred quantitatively to give 3-phenyl-5-phenoxymethyl-2-oxazolidone and N,N-disubstituted 3-phenoxy-2-hydroxypropylamine. In these reactions a difference in the effect of substituents on the nitrogen atom containing active hydrogen was obviously observed; *i.e.*, the reactivity of ureas with aryl groups was different from those with alkyl groups. N-Alkyl-N′,N′-disubstituted urea derivatives were almost ineffective to the ring-opening reaction of phenyl glycidyl ether. In the case of N,N′-disubstituted urea derivatives where R′′ was a hydrogen atom, by variation of R and R′′′ groups, various reaction products were produced. It was observed generally that the imide groups substituted by an aryl group reacted with the epoxy ring of phenyl glycidyl ether, and in this case 3 moles of epoxide were needed for 1 mole of urea. For example, N-phenyl-N′-*n*-butylurea reacted with 3 moles of phenyl glycidyl ether to give 80% or more of crystalline 3-phenyl-5-phenoxymethyl-2-oxazolidone and N,N-bis(3-phenoxy-2-hydroxypropyl)-*n*-butylamine as a viscous liquid which was confirmed by its infrared spectrum. These results are listed in Table II.

Experimental[9]

Phenyl Glycidyl Ether.—To a mixture of 84 g. (1.0 mole) of phenol and 370 g. (4 moles) of epichlorohydrin was added dropwise with stirring during 1 hr. at room temperature 54 g. (1.0 mole) of sodium methylate in 400 ml. of methanol, and the mixture was stirred for an additional 1 hr. After removal of epichlorohydrin, the residue was distilled under reduced pressure to obtain 115 g. (77%) of phenyl glycidyl ether, b.p. 102° (5 mm.).

Urethanes.—Urethanes were prepared by two methods: (A) an addition reaction of the corresponding isocyanates and alcohols, and (B) a condensation reaction of the corresponding amines and ethyl chlorocarbonate. Examples follow.

N-Phenylmethylurethane (Methyl Phenylcarbamate).—To a solution of 32.0 g. (1.0 mole) of methanol and 0.1 g. of triethylamine in 100 ml. of benzene was added dropwise with stirring during 1 hr. at 50° 59.5 g. (0.5 mole) of phenyl isocyanate in 300 ml. of benzene; the mixture was heated for an additional hour. After removal of benzene, the residue was recrystallized from ether–petroleum ether (b.p. 30–60°) to give 68.5 g. (90%) of phenylmethylurethane, m.p. 48–49°.

N-*p*-Chlorophenylethylurethane.—To a solution of 21.7 g. (0.2 mole) of ethyl chlorocarbonate in 150 ml. of benzene was added with stirring at 10° 25.5 g. (0.2 mole) of *p*-chloroamiline and 20.2 g. (0.2 mole) of triethylamine in 200 ml. of benzene, and the mixture was allowed to stand for 3 hr. After filtering the triethylamine hydrochloride and removal of the benzene, the crystalline solid was recrystallized from cyclohexane to give 30.5 g. (76%) of *p*-chlorophenylethylurethane, m.p. 67–69°.

(9) Melting points and boiling points are uncorrected. Microanalyses were performed in the Laboratory of Organic Chemistry, Tokyo Institute of Technology.

Ureas.—Ureas were prepared by addition reactions of corresponding isocyanates and primary or secondary amines.

N-Phenyl-N′,N′-diethylurea.—To a boiling solution of 23.9 g. (0.2 mole) of phenyl isocyanate in 100 ml. of benzene was added dropwise with stirring 14.6 g. (0.2 mole) of diethylamine in 100 ml. of benzene; this was heated under reflux for an additional hour. After removal of benzene, the residue was recrystallized from ether to give 30.2 g. (79%) of N-phenyl-N′,N′-diethyl urea, m.p. 86–88°.

3-Phenyl-5-phenoxymethyl-2-oxazolidone. A. From Phenylmethylurethane and Phenyl Glycidyl Ether.—A mixture of 15.1 g. (0.1 mole) of phenylmethylurethane, 15.0 g. (0.1 mole) of phenyl glycidyl ether, and 0.1 g. of triethylamine was heated at 90° for 15 min. After cooling, the adduct was recrystallized from acetone to give 24.5 g. (91%) of 3-phenyl-5-phenoxymethyl-2-oxazolidone, m.p. 139–140°. A mixture melting point with an authentic sample showed no depression. In the infrared spectrum there was found an absorption band at 1740 cm.$^{-1}$ for C=O and no absorption band arising from N—H, O—H, and an epoxy group was recognized.

Anal. Calcd. for $C_{16}H_{15}O_3N$: C, 71.38; H, 5.58; N, 5.20; mol. wt., 269. Found: C, 71.34; H, 5.54; N, 5.47; mol. wt., 258.

B. From N-phenyl-N′,N′-diethylurea and Phenyl Glycidyl Ether.—A mixture of 9.6 g. (0.05 mole) of N-phenyl-N′,N′-diethylurea, 15.0 g. (0.1 mole) of phenyl glycidyl ether, and 0.1 g. of triethylamine was heated at 90° for 1 hr. The resulting oily viscous substance was recrystallized from acetone to give 11.0 g. (81%) of 3-phenyl-5-phenoxymethyl-2-oxazolidone. After removal of acetone from the filtrate, the viscous oily residue was a mixture of 3-phenyl-5-phenoxymethyl-2-oxazolidone and N,N-diethyl-2-hydroxy-3-phenoxypropylamine, the infrared spectra of which was identical with that of an authentic sample.

Reactions of 2-Bromo-2-(α-halogenobenzyl)-1-indanones

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Reactions of 2-bromo-2-(α-bromobenzyl)-1-indanone (I) and 2-bromo-2-(α-chlorobenzyl)-1-indanone (IV) have been investigated. With nucleophilic reagents, three types of reaction have now been established. The *cis* and *trans* isomers of 2-(α-chlorobenzal)-1-indanone (III) have been prepared and separated. Structural assignments have been strengthened by an examination of the proton magnetic resonance spectra of deuterated derivatives.

It has long been known that 2-bromo-2-(α-bromobenzyl)-1-indanone (I) is readily debrominated to give 2-benzal-1-indanone (II).[2a] Suitable reagents are, for example, ethanolic solutions of sodium hydroxide, sodium acetate, or potassium iodide. More recently conditions have been found which lead, in addition to II, to substantial yields of 2-benzal-1-indanones substituted in the 3-position; these products are formed by endocyclic dehydrobromination followed by an allylic substitution.[2b,3]

Further reactions of I have been investigated. In most instances II has been found as the favored product. In one instance a third type of product, involving replacement of the bromine β to the carbonyl group accompanied by exocyclic dehydrobromination, is formed in good yield.

Reaction of I with piperidine in benzene is known[2b,3] to lead to a good yield of 3-piperidino-2-benzal-1-indanone. Reaction with piperidine in acetonitrile leads to a product no part of which can be extracted by acid and which on recrystallization gives a 50% yield of II. Reaction of I with N-methylpiperidine in benzene proceeds with precipitation of N-methylpiperidine hydrobromide and on work-up a good yield of 2-benzal-1-indanone is obtained.

Reaction of I with tetraethylammonium bromide in acetonitrile at 75° leads to a 95% yield of the debromination product, II. Reaction of I with excess tetraethylammonium chloride in acetonitrile at 90° differs markedly from the bromide ion-promoted reaction in that it leads to an 80% yield of a mixture of *cis*- and *trans*-2-(α-chlorobenzal)-1-indanone (81% IIIa and 19% IIIb). Reaction for a longer period of time and with a reduced chloride ion concentration leads to some tar formation and to some accompanying 2-benzal-1-indanone (II).

The addition of bromine chloride to α,β-unsaturated carbonyl compounds is established[4] as proceeding *via* 1,4-addition with chlorine entering the 4-position. In this way 2-bromo-2-(α-chlorobenzyl)-1-indanone (IV)

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(2) (a) F. S. Kipping, *J. Chem. Soc.*, **65**, 499 (1894); (b) N. H. Cromwell and R. P. Ayer, *J. Am. Chem. Soc.*, **82**, 133 (1960).

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