A reaction similar to the one investigated herein was reported utilizing 4,5-epoxy-3-keto steroids, polyphosphoric acid, and either ethanedithio, β-mercaptoethanol, or ethyl mercaptan.[3] Tomoeda and coworkers observed no thioketalization with any of their systems.

### Experimental Section[4]

**4-Carbethoxycyclohexanone** (2) was prepared by the procedures described by Smissman, Lemke, and Creese.[5]

**2,6-Dibromo-4-carbethoxycyclohexanone** (3).—To a solution of 1.6 g (0.0094 mole) of ketone 2 dissolved in 25 ml of $CCl_4$ and maintained at 20° was added, while stirring, 3.2 g (0.02 mole) of $Br_2$ in 25 ml of $CCl_4$.[6] The addition took approximately 1.5 hr and was followed by an additional 0.75 hr of stirring. The $CCl_4$ solution was washed with a 10% solution of $NaHCO_3$ and dried ($Na_2SO_4$). Removal of the solvent left a residue of 3.17 g of a thick brown oil which by nmr appeared to be a mixture of isomers: nmr, 1.30 (3 H, triplet, $J$ = 7.0 cps), 1.35 (3 H, triplet, $J$ = 7.0 cps), 2.0–3.6 (10 H, broad multiplet), 4.20 (4 H, multiplet), 4.75 (1 H, broad triplet, $W_{1/2}$ = 9.0 cps), 5.40 (2 H, broad quartet, $W_{1/2}$ = 24 cps).

The dibromide was analyzed as the ethylene ketal.

*Anal.* Calcd for $C_{11}H_{16}O_4Br_2$: C, 35.51; H, 4.34. Found: C, 35.59; H, 4.22.

When the bromination was performed according to the procedure of Yanagita,[7] which consisted of using glacial acetic acid as the solvent, an impure oil was isolated which appeared to be a single isomer: nmr, 5.45 (1 H, doublet of doublets, $W_{1/2}$ = 22 cps), 4.73 (1 H, multiplet, $W_{1/2}$ = 7.0 cps), 4.18 (2 H, quartet, $J$ = 7.0 cps), 2.0–3.8 (5 H, broad band), 1.30 (3 H, triplet, $J$ = 7.5 cps).

**6-Carbethoxy-1,4-benzoxathian** (4).—To a flask containing 50 ml of dry benzene was added 0.60 g (0.0076 mole) of β-mercaptoethanol, 50 mg of $p$-toluenesulfonic acid, and 2.40 g (0.0073 mole) of 2,6-dibromo-4-carbethoxycyclohexanone (3). The mixture was heated under reflux for 5 hr and the water formed was collected in a Dean–Stark trap. The benzene was removed on a flash evaporator and the oil which remained (2.0 g) was chromatographed on 50 g of silica gel (Brinkmann) using petroleum ether (bp 63–68°)–$CHCl_3$ (3:1) as eluting solvent. The first six fractions (640 mg) were found to be the benzoxathian, 4 (40%): infrared, 5.84 (s), 6.25 (m), 6.73 μ (s); nmr, 1.34 (3 H, triplet, $J$ = 7.2 cps), 3.08 (2 H, multiplet), 4.31 (2 H, multiplet), 4.31 (2 H, triplet, $J$ = 7.0 cps), 6.91 (1 H, broad doublet of doublets), 7.50 (1 H, doublet of doublets), 7.70 (1 H, singlet); $\lambda_{max}^{CH_3OH}$ 237 mμ (ε 35,000), 268 (10,000), 3.12 (5000).

The oil was treated with 10 ml of 10% NaOH and heated at reflux temperature. Acidification of the basic layer resulted in precipitation of 6-carboxy-1,4-benzoxathian which after recrystallization from EtOH–$H_2O$ melted at 175–182°: infrared (KBr), 5.93 (s), 6.25 (s), 6.39 (w), and 6.7 μ (w); $\lambda_{max}^{CH_3OH}$ 218, 264, 272, 310 mμ.

*Anal.* Calcd for $C_9H_8O_3S$: C, 55.09; H, 4.11; S, 16.34. Found: C, 54.88; H, 3.93; S, 16.30.

To a flask containing 50 ml of benzene and two small scoops of freshly prepared Raney nickel (W-4) was added 196 mg of 6-carbethoxy-1,4-benzoxathian (4). The contents were stirred for 2 hr and the benzene was decanted. The Raney nickel was washed with benzene. The benzene layers were combined and the solvent removed leaving 140 mg of an oil: infrared, 5.82 (s), 6.21 (s), 6.6 μ (m); nmr, 1.35 (3 H, triplet, $J$ = 7.0 cps), 1.38 (3 H, triplet, $J$ = 7.0 cps), 4.02 (2 H, quartet, $J$ = 7.0 cps), 4.23 (2 H, quartet, $J$ = 7.0 cps), 7.35 (4 H, quartet, $J$ = 8 and 6.5 cps); $n^{25}D$ 1.5192 (lit.[8] $n^{25}D$ 1.5065). This material proved to be ethyl 4-ethoxybenzoate by comparison with an authentic sample.

**2,6-Dibromo-2-methylcyclohexanone** (6).—To a solution of 50 ml of $CHCl_3$ and 11.2 g (0.1 mole) of 2-methylcyclohexanone (5) cooled to 10° was added, while stirring, 32 g (0.2 mole) of $Br_2$ in 50 ml of $CHCl_3$. The addition took 1 hr; the mixture was then allowed to stand an additional 0.5 hr. Removal of the solvent *in vacuo* left a green solid which was recrystallized from 59% EtOH. A total of 17 g (63%) of white needles, mp 42°, was recovered (lit.[9] mp 42–43°).

**8-Methyl-14-benzoxathian** (8).—A solution of 50 ml of benzene, 1.56 g of (0.02 mole) of β-mercaptoethanol, and 5.10 g (0.019 mole) of bromo ketone, 6, was heated under reflux for 1.5 hr. Very little water was collected in the Dean–Stark trap and no hydrogen bromide could be detected. At this time 45 mg of $p$-toluenesulfonic acid was added to the reaction mixture and the system was again heated. An acidic gas was found to be evolved soon after the addition of the catalyst. The reaction was terminated after 3.5 hr. Removal of the solvent resulted in recovery of a thick oil which by glpc was shown to contain $o$-cresol (7) by rechromatography with a known added sample of this substance. The oil was chromatographed first on $Al_2O_3$ (Merck, reagent) using $CHCl_3$ as the eluting solvent, then on silica gel (Brinkmann) using petroleum ether (bp 63–68°)–benzene (6:1). The first oils collected contained a mixture of materials but later fractions contained pure 8. A yield of 1.15 g (37%) of the benzoxathian, 8, was obtained: infrared, 6.29 (s), 6.80 (s), 5.2 (w), 5.45 (w), and 5.65 μ (w); nmr, 2.12 (3 H, singlet), 2.99 (2 H, multiplet), 4.35 (2 H, multiplet), and 6.72 (3 H, broad singlet).

*Anal.* Calcd for $C_9H_{10}OS$: C, 65.02; H, 6.02; S, 19.29. Found: C, 65.27; H, 7.18; S, 19.30.

To a solution of 309 mg of the benzoxathian, 8, in 50 ml of dry benzene was added approximately 5 g of freshly prepared W-4 Raney nickel. The mixture was stirred for 2 hr at 25°. The benzene was decanted and the Raney nickel was washed with benzene. The benzene extracts were combined and the solvent was removed. The $o$-ethoxytoluene thus formed was treated with chlorosulfonic acid followed by aqueous ammonia to give 3-methyl-4-ethoxybenzenesulfonamide, mp 148–150° (lit.[10] mp 149°).

In another experiment a white solid was isolated from the silica gel column when the column was washed with benzene. The material was recrystallized from ethanol–water and was identified as the bisoxathian, 9: mp 112–114°; infrared (KBr), 6.97 (m), 7.73 (s), 8.40 (s), 8.66 (s), 9.17 (s), 9.52 μ (s); nmr, 3.90 (4 H, multiplet), 3.07 (3 H, multiplet), 0.97 (3 H, broad doublet), 1.1–2.6 (8 H, broad band).

*Anal.* Calcd for $C_{11}H_{18}O_2S_2$: C, 53.62; H, 7.36. Found: C, 53.62; H, 7.37.

**Registry No.**—**3**, 14789-67-4; **4**, 14789-68-5; free acid of **4**, 14789-69-6; **8**, 14789-70-9; **9**, 14789-71-0.

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(3) M. Tomoeda, T. Furuta, and T. Koga, *Chem. Pharm. Bull.* (Tokyo), **13**, 1078 (1965).

(4) Melting points were obtained on a Thomas–Hoover Unimelt and are corrected. Infrared data were recorded on Beckman IR-5, IR-8, and IR-10 spectrophotometers and the ultraviolet data were recorded on a Cary 14 spectrophotometer. Nmr data were obtained from a Varian Associates Model A-60 spectrometer utilizing $CCl_4$ as a solvent, unless otherwise stated, with tetramethylsilane as an internal standard, and reported in parts per million as δ values. Elemental analyses were performed by Huffman Microanalytical Laboratories, Wheatridge, Colo., and by Drs. G. Weiler and F. B. Strauss, Oxford, England.

(5) E. E. Smissman, T. L. Lemke, and M. W. Creese, to be published.

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(8) W. Emerson, J. Heyd, V. Lucas, E. Chapin, G. Owens, and R. Shortridge, *J. Am. Chem. Soc.*, **68**, 674 (1946).

(9) E. J. Corey, T. H. Topie, and W. A. Wozniak, *ibid.*, **77**, 5415 (1955).

(10) A. Vogel, "Practical Organic Chemistry," 3rd ed, Longmans, Green and Co. Ltd., London, 1956, p 673.

## A Deuterium Isotope Effect in a Nonaqueous Acid–Base System

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The purpose of this research was to determine if an isotope effect exists between hydrogen bromide and deuterium bromide in their interactions with the π-

electron systems of several aromatic hydrocarbons, a type of nonaqueous acid–base equilibrium which has received little attention.

Since solutions of hydrogen chloride in olefins have no appreciable conductivity and hydrogen chloride neither adds to nor isomerizes labile olefins at −78°, Brown and Brady[1] theorize that there exists an olefin–hydrogen chloride complex in which there is a weak interaction between the $\pi$ electrons and the hydrogen of the hydrogen chloride, as opposed to ionic species. The same type of interaction is suggested for both aromatic and olefinic complexes, *i.e.*, a $\pi$ complex is formed in both cases. The Henry's law constants


determined by Brown and Brady[1] for the relative basicity of olefins and aromatic hydrocarbons toward hydrogen chloride indicate that the difference in basicity between olefins and aromatic hydrocarbons is not too great to prevent analogies being drawn between the two systems. Further experiments by Brown and Melchiore[2] led them to the conclusion that hydrogen bromide forms analogous but weaker complexes with aromatic hydrocarbons.[3]

In general, the stability of the complex that is formed between the aromatic hydrocarbon and the hydrogen bromide or deuterium bromide is increased as electron-donating groups are added to the aromatic ring.[4] This has been amply verified by Brown's work.[1,2] The order of solubilities of hydrogen bromide and deuterium bromide in the solvents used in our work is in accord with this principle.

As Andrews[4] has pointed out many aromatic molecular complexes are so unstable that their presence must be determined by physical methods rather than by actual isolation. One of these physical methods cited was solubility measurements and this was the method used in this investigation. Using this type of procedure Brown[1,2] concluded from his investigations that the basic properties of aromatic nuclei may be measured by the solubility of hydrogen chloride or hydrogen bromide in them. Since the interaction of hydrogen chloride or hydrogen bromide with an aromatic is essentially the equilibrium of an acid–base system between the hydrogen halide and the $\pi$-electron system of the aromatic, a modification of Brown's[1] method was chosen as a means of searching for isotope effects in acid–base equilibria.

Since the prime purpose of this experiment was to determine whether any isotope effect could be observed the comparison of hydrogen bromide and deuterium bromide solubilites was carried out under as highly reproducible conditions as possible, but only over a relatively small range of pressures. As a consequence, the determination of the Henry's law constants was a secondary consideration, only being obtained to the extent necessary to show the validity of the experimental method (see Table I).

TABLE I

COMPARISON OF EXPERIMENTAL AND LITERATURE SOLUBILITY VALUES

| System | Temp, °C | $K_s \times 10^5$ Exptl | $K_s \times 10^5$ Lit. | Ref |
|---|---|---|---|---|
| HBr in $CCl_4$ | 25 | 4.49 | 5.03 | *a* |
| HBr in benzene | 30 | 8.64 | 8.45 | *b* |
| HBr in benzene | 25 | 9.53 | 9.89 | *c* |
| HBr in toluene | 25 | 11.16 | 11.48 | *c* |
| Krypton in benzene | 25 | ... | 0.36 | *d* |

[a] See ref 7. [b] A. F. Kapustinskii and V. A. Mal'tsev, *J. Phys. Chem. USSR*, **14**, 105 (1940). [c] See ref 5. $K_s$ was calculated from the solubility data in ref 5 and 8 footnote *b*. [d] J. H. Hildebrand and R. L. Scott, "Regular Solutions," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1962, p 162. $K_s$ was calculated from the solubility data in this reference. This value indicates the low order of solubility in the absence of acid–base interaction.

The solubilities of hydrogen bromide and deuterium bromide were compared in three aromatic solvents: benzene, toluene, and mesitylene. From Table II it can be seen that an isotope effect occurs in only one of the solvents, benzene, and that its magnitude is small, $K_H/K_D = 1.02$.

That the isotope effect should appear in the least basic solvent is somewhat surprising; however, a complete randomization of experiments precludes a systematic error. Toluene and mesitylene were originally included in the series because benzene represents so weak a base it was felt that, if no isotope effect were observed in benzene, these more basic aromatics might show one. It has been known for some time that hydrogen chloride and hydrogen bromide are more soluble in mesitylene than in toluene and in toluene than in benzene.[1,2,5] If it is assumed that the greater solubility is due to a higher degree of interaction of the hydrogen halide with the aromatic hydrocarbons, it would seem highly probable that the distortion of the hydrogen bromide or deuterium bromide bond would be greater in the more basic aromatics and thus the isotope effect, if any, should be most pronounced in the most basic sovent, mesitylene. The opposite result found can be rationalized if benzene is considered to exert less of a leveling effect on the difference in the solubilities of hydrogen bromide and deuterium bromide than does toluene or mesitylene. That is to say, the point of view can be taken that benzene will be inherently more discriminating because it is less reactive toward hydrogen bromide and deuterium bromide. Thus benzene should be more able to distinguish a difference between hydrogen bromide and deuterium bromide than either toluene or mesitylene.

This lack of appreciable isotope effect in $\pi$-complex formation bears on the kinetic isotope effects observed by Goering and Larsen[6] in the free-radical addition of mixtures of hydrogen bromide and deuterium bromide to olefins ($k_H/k_D = 2.4$). These authors suggested that one possible explanation for the observed *trans* stereochemistry of this reaction (using either HBr or DBr) might lie in complex formation between olefin and hydrogen bromide or deuterium bromide and the isotope effect reflects the different stabilities of hydrogen bromide–olefin *vs.* deuterium bromide–olefin

(1) H. C. Brown and J. D. Brady, *J. Am. Chem. Soc.*, **74**, 3570 (1952).
(2) H. C. Brown and J. J. Melchiore, *ibid.*, **87**, 5269 (1965).
(3) Brown and Melchiore attribute the stronger complexing of the hydrogen chloride with the aromatic hydrocarbons to the larger dipole moment of hydrogen chloride *vs.* hydrogen bromide.
(4) L. J. Andrews, *Chem. Rev.*, **54**, 713 (1954).
(5) S. J. O'Brien and E. G. Bobalek, *J. Am. Chem. Soc.*, **62**, 3227 (1940).
(6) H. L. Goering and D. W. Larsen, *ibid.*, **81**, 5937 (1959).

TABLE II
COMPARISON OF THE SOLUBILITY OF HYDROGEN BROMIDE AND DEUTERIUM BROMIDE IN BENZENE, TOLUENE, AND MESITYLENE AT 25°

| System | No. of detn[a] | $P_{HBr}$ range, mm | $K_s \times 10^5$ | Statistical significance[b] |
|---|---|---|---|---|
| Hydrogen bromide–benzene | (22) 20 | 153.0–209.0 | 9.53 ± 0.11 | Significant (at 99% level) |
| Deuterium bromide–benzene | (18) 16 | 164.5–172.8 | 9.61 ± 0.08 | |
| Hydrogen bromide–toluene | (11) 11 | 126.4–238.3 | 11.16 ± 0.22 | Not significant (even at 50% level) |
| Deuterium bromide–toluene | (17) 14 | 123.4–130.4 | 11.21 ± 0.17 | |
| Hydrogen bromide–mesitylene | (16) 11 | 257.1–268.5 | 13.52 ± 0.10 | Not significant (even at 50% level) |
| Deuterium bromide–mesitylene | (16) 15 | 151.5–266.6 | 13.54 ± 0.15 | |

[a] Values in parentheses are the total number of determinations; the other number represents the determinations statistically close enough to be included in the calculation of $K_1$ (see ref *b*). [b] t test: M. J. Moroney, "Facts from Figures," William Clowes and Sons Ltd, London, 1951, p 227.

complexes. It is now apparent that hydrogen bromide and deuterium bromide may be expected to form complexes of very nearly equal stability with olefins and the stereospecific nature of the reaction must be ascribed to other reasons, *e.g.*, "bridging" of the olefinic bond by bromine atoms.

### Experimental Section

**Materials.**—Mallinckrodt Analytical Reagent benzene, Baker and Adamson Reagent toluene, and Aldrich Puriss mesitylene were dried and stored over sodium ribbon; Mallinckrodt Analytical Reagent carbon tetrachloride was dried and stored over phosphorus pentoxide. Matheson anhydrous hydrogen bromide was purified as described below in the procedure for solubility determinations. Deuterium bromide was prepared by the reaction of deuterium oxide (Volk Radiochemical Co., 99.5% $D_2O$) with phosphorus tribromide (Matheson Coleman and Bell White Label). The apparatus for the production of deuterium bromide was thoroughly evacuated before the deuterium oxide and phosphorus tribromide were introduced. The deuterium bromide was purified by bulb-to-bulb distillation on a vacuum line. It was finally collected and stored in a thoroughly evacuated gas cylinder.

**Apparatus for Determination of the Solubility Values.**—The apparatus was a modification of that used by Howland,[7] *et al.* It consisted of storage vessels for aromatic hydrocarbon solvent and HBr, a mixing and equilibration chamber, and a sample-withdrawal system all incorporated into a vacuum line, with appropriate manometers, stopcocks, etc. Our apparatus was an all-glass system with the exceptions of Teflon needle valves and Teflon stopcocks incorporated into the apparatus at points where they would come into contact with solvent. The Teflon needle valves were fitted with mercury cups to prevent any leakage during the time that they were open. The solvent storage flask had a capacity of about 2000 ml. The absorption flask, where the hydrogen bromide or deuterium bromide came into contact with the solvent, had a capacity of about 500 ml. The absorption flask was submerged in a constant-temperature water bath so that all but short sections of capillary tubing extending from it were below the water level. The temperature of this bath could be maintained constant to within ±0.05°. Stirring of the contents of the absorption flask was accomplished by means of an air-driven magnetic stirrer, placed just below the flask, which propelled a Teflon-covered stirring bar. The apparatus could be maintained at pressures above or below atmospheric without significant change in the pressure for periods of several days under actual run conditions, as judged by the reading of a closed-end U-tube manometer.

**Procedure for Determination of the Solubility Values.**—The apparatus was thoroughly evacuated for at least 30 min. Solvent was then transferred from the storage flask to the absorption flask. Solvent was allowed to fill the absorption flask to approximately three-fourths of its volume.

The solvent was degassed by boiling under vacuum; to ensure complete degassing approximately 25% of the solvent was boiled off. The vapor pressure of the solvent was then read from the manometer. The absorption flask was then closed off from the rest of the system.

The hydrogen bromide storage flask was filled from the storage cylinder to a pressure of about 800 mm. The hydrogen bromide was dried over $P_2O_5$ and then degassed by freeze–pump–thaw cycles. Hydrogen bromide was allowed to enter the absorption flask until the desired total pressure was attained and remained unchanged for 1 hr. The hydrogen bromide storage flask was closed off from the rest of the system.

After equilibrium had been attained (no change in pressure over a 1-hr period), a sample was withdrawn from the absorption flask by means of a capillary into a sample flask containing approximately 25 ml of distilled water which had been evacuated to a pressure slightly less than that of the aromatic hydrocarbon plus HBr in the absorption flask. The first few milliliters of solvent–hydrogen bromide mixture were collected in a trap submerged in liquid nitrogen, thus assuring that any solvent that may not have been in equilibrium contact with the hydrogen bromide (*i.e.*, the small amount in the capillary withdrawal tube) was drawn into the trap and not into the sample flask. Then by turning the appropriate stopcocks the trap was isolated from the rest of the system and the solvent–hydrogen bromide mixture allowed to flow into the sample flask until the desired amount had been collected. The flask was then removed from the system, capped, and set aside for analysis. Several portions of the solvent–hydrogen bromide mixture were collected in this manner; sufficient time for equilibrium to be attained was always allowed before the next sample was withdrawn.

The flasks were weighed and the amount of solvent–hydrogen bromide mixture collected was determined. A correction for the small amount of water lost during the brief evacuation of the sample flask (0.03 g) was included in the weight determination.

Samples were titrated in the sample flasks (solvent not removed) with sodium hydroxide, using phenolphthalein as the indicator. The samples were stirred while being titrated with a small Teflon-covered stirring bar and a magnetic stirrer. Titrations were performed with an American Instrument Co. Meniscomatic buret. Titrations of three distilled water blanks were always performed both for sodium hydroxide standardization and sample titration. The normality of the sodium hydroxide was always determined just before the titration of the samples by titrating five dried and weighed portions of potassium acid phthalate dissolved in approximately 25 ml of distilled water.

A sample calculation of the solubility constant for HBr in benzene at 25° is given, where the weight of the benzene sample is 7.6245 g; the molecular weight of benzene is 78.11; $P_{total}$ 253.7 mm; $P_{benzene}$ 95.5 mm; NaOH 2.8296 ml; NaOH 0.5238 *N*; molecular weight of hydrogen bromide 80.92.

$$b = \frac{(2.8296\text{ ml})(0.5238\ N)}{1000}(80.92\text{ g/mole}) = 0.1199\text{ g}$$

$$N_{HBr} = \frac{\dfrac{(2.8296\text{ ml})(0.5238\ N)}{1000}}{\dfrac{7.6245\text{ g} - 0.1199\text{ g}}{78.11} + \dfrac{(2.8296\text{ ml})(0.5238\ N)}{1000}} = 0.0152$$

$$P_{HBr} = 253.7\text{ mm} - 95.5\text{ mm}\ (1 - 0.0152) = 159.7\text{ mm}$$

$$K_s = \frac{0.0152}{159.7} = 0.00009518 = 9.518 \times 10^{-5}$$

**Treatment of Data.**—The calculation of the solubility constants, $K_s$, in Tables I and II is substantially the same as that used by Howland,[7] *et al.*, with the exception that the factor used in calculations to correct for the moles of hydrogen bromide gas

(7) J. J. Howland, Jr., D. R. Miller, and J. E. Willard, *J. Am. Chem. Soc.*, **63**, 2807 (1941).

in the capillary withdrawal tube on the absorption flask was not included. This factor was included in Howland's calculations since the capillary withdrawal tube contained some hydrogen bromide gas which was pushed over with the sample into the sample flask. It can, however, be justifiably omitted from our calculations since the first few milliliters of sample and any hydrogen bromide gas in the tube were collected in a trap and did not enter the sample flask.

$$K_s = \frac{N_{HBr}}{P_{HBr}}$$

$$N_{HBr} = \frac{\frac{ml \times N}{1000}}{\frac{\text{wt of sample} - b}{\text{mol wt of solvent}} + \frac{ml \times N}{1000}}$$

$$P_{HBr} = P_{total} - P_{solvent}(1 - N_{HBr})$$

where $N_{HBr}$ = mole fraction of HBr in each sample, $P_{HBr}$ = partial pressure of HBr in the gas phase, $K_s$ = solubility constant, ml = milliliters of NaOH solution used for titration, $N$ = normality of NaOH, $b$ = weight in grams of gas in sample, $P_{total}$ = total pressure in millimeters, $P_{solvent}$ = vapor pressure of pure solvent in millimeters.

**Registry No.**—Hydrogen bromide, 10035-10-6; deuterium bromide, 13536-59-9.

## Direct Synthesis of 1,1,4,4-Tetraethylpiperazinium Dichloride

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The formation of 1,1,4,4-tetraethylpiperazinium dichloride has been reported[2-6] on a number of occasions where the hydrochloride of β-chloroethyldiethylamine was treated in alkaline media. The unstable chloroamine cyclodimerizes to the title product through the aziridine intermediate.[5] Cope[7] has reported formation of the tetraalkylpiperazinium salts under acidic conditions. We wish to report a facile single-step process which gives practically quantitative yields of the tetraalkylpiperazinium dichloride when β-chloroethyldiethylamine hydrochloride is added to an epoxide, which acts as an acid scavenger and is converted into the chlorohydrin.

### Experimental Section

To 17.0 g (0.099 mole) of β-chloroethyldiethylamine hydrochloride, reagent grade recrystallized from absolute ethanol, in 50 ml of absolute ethanol was added 10 g (0.108 mole) of 1,2-epoxy-3-chloropropane (epichlorohydrin). The mixture became homogeneous when heated to approximately 60°. Crystals of the product formed within 30 min; the reaction mixture was maintained at 60° for an additional 1.5 hr and then cooled to −10° to give 13.3 g (97%) of white crystalline product (dec. 270°). The presence of 1,3-dichloropropanol in the alcoholic mother liquor was shown by glpc. The DTA curve showed an initial rapid endotherm at 270° which continued to 342°. The infrared spectrum contained no peaks due to unsaturation or $NH^+$.

*Anal.* Calcd for $C_6H_{14}NCl$: C, 53.14; N, 10.33; H, 10.33; total Cl, 26.20; ionic Cl, 26.20. Found: C, 53.13; N, 10.33; H, 10.32; total Cl, 26.25; ionic Cl, 25.91.

The reaction can be run neat, using epichlorohydrin as the solvent and the acid scavenger, to give a 95% yield. Epoxides other than epichlorohydrin can be used. For example, 1,2-epoxybutane at a 1:1 mole ratio in absolute ethanol gave a 95% yield of the piperazinium dichloride product.

**Registry No.**—1,1,4,4-Tetraethylpiperazinium dichloride, 5449-19-4.

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) G. A. C. Gough and H. King, *J. Chem. Soc.*, 2426 (1928).

(3) R. R. Burtner, *J. Am. Chem. Soc.*, **71**, 2578 (1949).

(4) J. Cadogan, *J. Chem. Soc.*, 2971 (1955); 4154 (1957).

(5) P. D. Bartlett, S. D. Ross, and C. G. Swain, *J. Am. Chem. Soc.*, **71**, 1415 (1949).

(6) N. J. Leonard, *Rec. Chem. Progr.*, **26**, 211 (1965).

(7) A. C. Cope and M. Burg, *J. Am. Chem. Soc.*, **74**, 611 (1952).

## Preparation of 2-Carbethoxycyclopentane-1,3-dione

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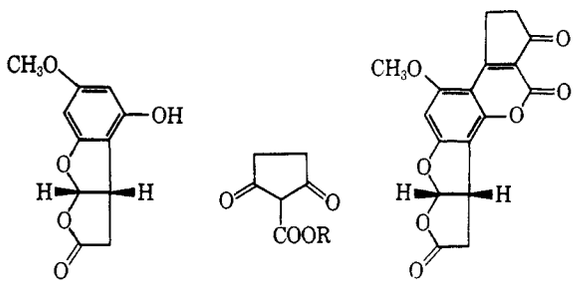
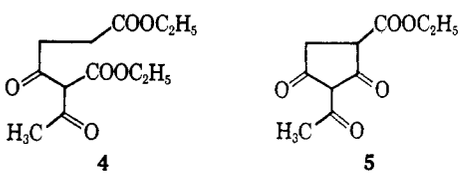
Condensation of phenol **1** with a 2-carbalkoxycyclopentane-1,3-dione (**2**) appeared to be an expeditious method for the preparation of the pentacyclic coumarin **3** which is an intermediate in the synthesis of aflatoxin $B_1$.[2] Syntheses of 2-carbethoxycyclopentane-1,3-dione (**12**) have been claimed in the literature but none could be verified.[3] The most direct approach




1 2 3

involving a Dieckmann cyclization of methyl ethyl β-ketoadipate could never be reduced to practice[3] but the successful cyclization of 1,4-dicarbethoxyhexane-3,5-dione (**4**) to 2-acetyl-4-carbethoxycyclopentane-1,3-dione (**5**)[4] led us to investigate the cyclization of




4 5

the corresponding malonic ester **6**. This intermediate has now been synthesized as follows.

The mixed anhydride prepared from ethyl chloroformate and *t*-butyl hydrogen succinate in the presence of triethylamine was condensed with diethyl ethoxymagnesiomalonate to give diethyl 3-carbo-*t*-butoxy-

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