[Contribution from the Department of Chemistry, State University of Iowa]

THE BROMOHYDRINS OF STYRENE[1]

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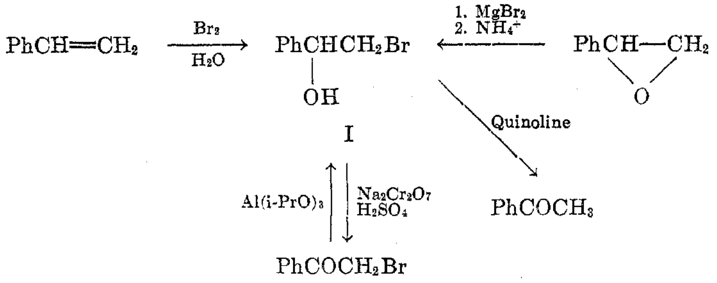
Received May 15, 1953

The previously reported (1) synthesis of styrene bromohydrin by the addition of bromine to styrene in hot aqueous potassium bromide gave a 96% yield of a product which proved to be α-bromomethylbenzyl alcohol (I) as predicted by Markovnikov's rule. This bromohydrin had not been adequately characterized before, so its 3,5-dinitrobenzoate, m.p. 92–93° has been prepared. This derivative was used for the identification of α-bromomethylbenzyl alcohol from the various preparations.

This same bromohydrin was also the product of the acid-catalyzed reaction of N-bromoacetamide with styrene in aqueous dioxane. With only the amount of water necessary to form the bromohydrin, N-bromoacetamide reacted with styrene to give a 64% yield of the dibromide by what appeared to be a free radical reaction such as that observed (2) for the reactions in chloroform, carbon tetrachloride, or excess styrene.

The opening of the ring of styrene oxide by magnesium bromide in ether followed by hydrolysis of the product gave a low yield (20%) of α-bromomethylbenzyl alcohol, the same isomer as obtained by addition of the elements of hypobromous acid to styrene. This reaction had been reported (3) as giving the other isomer, β-bromophenethyl alcohol (II), but none of this compound could be isolated. Similarly with lithium bromide, only a low yield (12%) of the α-bromomethylbenzyl alcohol could be isolated. With hydrogen bromide directly styrene oxide yielded only polymeric products in amounts large enough to isolate.



Reduction of α-bromoacetophenone by aluminum isopropoxide in isopropyl alcohol to α-bromomethylbenzyl alcohol was possible in 63% yield if the modified method (4) of short heating developed for the synthesis of halohydrins was used rather than the conventional distillation of acetone from the reaction mixture. Although this conventional reduction was reported (5) to give 80% yields of α-bromomethylbenzyl alcohol the only product which could be isolated was a small amount of phenethyl alcohol, which presumably arose from styrene oxide

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[1] Abstracted from the Ph.D. thesis of John E. Maurer.

as an intermediate. Even when the method (6) of gentle heating for several hours was tried the product was phenethyl alcohol. Similar results have been reported by others (4, 7–10) for the Meerwein-Pondorf reduction of halohydrins. The bromohydrin, itself, was oxidized in 52% yield to α-bromoacetophenone, so that its structural relationship to the ketone is completely established. The reduction of α-bromoacetophenone by sodium borohydride to give α-bromomethylbenzyl alcohol has also been reported (11).

The photobromination of phenethyl formate followed by methanolysis of the brominated ester gave rise to a 56% yield of β-bromophenethyl alcohol which was probably contaminated by phenethyl alcohol. Presumably bromination yielded some phenethyl bromoformate along with the β-bromophenethyl formate. The bromoformate would be expected to undergo methanolysis to yield the unbrominated alcohol. Such a halogenation of the formyl group has been reported (12) in the photochlorination of methyl formate. Bromination of phenethyl 3,5-dinitrobenzoate gave β-bromophenethyl 3,5-dinitrobenzoate, m.p. 112–113°, which was identical with that prepared from the impure preparations of the bromohydrin. A m.p. of 103° had been reported (3) for a sample of this ester prepared from the bromohydrin product of the reaction of magnesium bromide with styrene oxide. This m.p. is one which is characteristic of a mixture of the 3,5-dinitrobenzoates of the styrene bromohydrins.

The action of bromine on phenethyl alcohol led to phenylacetaldehyde and α-bromophenylacetaldehyde as the major products. Bromine first acted as an oxidizing agent and then as a brominating agent.

$$\begin{tikzcd}
\mathrm{PhCH_2CH_2OH} \arrow[r, "\mathrm{HCOOH}"] \arrow[d, "\mathrm{Br_2}(h\nu)"] & \mathrm{HCOOCH_2CH_2Ph} \arrow[r, "\mathrm{Br_2}", "h\nu"'] & \mathrm{HCOOCH_2CHBrPh} \arrow[d, "\mathrm{MeOH}(\mathrm{H^+})"] \\
\mathrm{PhCH_2CHO} & & \mathrm{PhCHBrCH_2OH} \arrow[ll, "\mathrm{Quinoline}"'] \\
 & & \mathrm{II}
\end{tikzcd}$$

The photobrominations of several other 3,5-dinitrobenzoates were carried out. The esters of α-methylbenzyl alcohol and benzyl alcohol yielded unstable solids which on standing gave acetophenone in the former case and benzaldehyde in the latter case. Bromination presumably took place at the carbon atom *alpha* to the benzene ring in each case. The esters of ethyl alcohol and methanol were recovered contaminated by only slight amounts of brominated products after extensive ultraviolet illumination in the presence of bromine.

Both styrene bromohydrins were dehydrohalogenated by quinoline without migration of the oxygen atom. That is, the dehydrohalogenation did not take place by way of a common intermediate such as styrene oxide. α-Bromomethylbenzyl alcohol gave acetophenone while β-bromophenethyl alcohol gave phenylacetaldehyde.

EXPERIMENTAL

All melting points were corrected.

Addition of the elements of hypobromous acid to styrene. A total of 25 g. (0.24 mole) of styrene was added portionwise to 500 ml. of hot water into which enough aqueous solution, 7% bromine and 10% potassium bromide, was rapidly stirred until a slightly yellow color prevailed. This method (1) gave 46.1 g. (96%) of α-bromomethylbenzyl alcohol of b.p. 96–97° (1 mm.), 109–110° (2 mm.).

The addition of 13.8 g. (0.10 mole) of N-bromoacetamide to a solution of 50 ml. of pure dioxane in 50 ml. of water containing a crystal of *p*-toluenesulfonic acid led to a yellow solution. To this solution 10.4 g. (0.10 mole) of styrene was added dropwise. The solution was colorless within 15 minutes after the addition. Isolation of the product by extraction with ether followed by distillation yielded 16.6 g. (83%) of α-bromomethylbenzyl alcohol of b.p. 110–114° (4 mm.).

When an experiment such as the one described above was carried out in a solution of 1.8 g. (0.10 mole) of water in 120 ml. of dioxane containing a little *p*-toluenesulfonic acid it was necessary to heat the reaction mixture under reflux in order to complete the reaction. Filtration of the reaction mixture removed the crystalline acetamide. Distillation of the filtrate yielded a solid, b.p. 97–103° (6 mm.), which was crystallized from 80% ethyl alcohol to give 8.4 g. (64% based on N-bromoacetamide) of styrene dibromide, m.p. 71–73°.

Addition of the elements of hydrogen bromide to styrene oxide. A mixture of 4.9 g. (0.20 g.-atom) of magnesium and 120 ml. of anhydrous ether was cooled as 32.3 g. (0.20 mole) of bromine was slowly added. A solution of 24.2 g. (0.20 mole) of styrene oxide in 30 ml. of ether was slowly added to the mixture. After the addition the reaction mixture was heated under reflux for an hour. A solution of 20 g. of ammonium chloride in 75 ml. of water containing 10 g. of ice was thoroughly mixed with ether solution. Distillation of the ether layer gave 8.0 g. (20%) of α-bromomethylbenzyl alcohol, b.p. 113.5–114° (4 mm.). Similar experiments in which the ether was replaced by benzene or dioxane after the reaction with bromine gave about the same results.

A mixture of 17.5 g. (0.20 mole) of lithium bromide and 120 ml. of anhydrous ether was boiled under reflux as 24 g. (0.20 mole) of styrene oxide was slowly added. After the addition was complete the solution was boiled under reflux for four hours. A solution of 20 g. of ammonium chloride in 100 ml. of ice-water was mixed with the ether layer. Distillation yielded 5 g. (12%) of α-bromomethylbenzyl alcohol, b.p. 116–120° (6 mm.). The use of dioxane as a solvent led to essentially the same results.

All reactions carried out between styrene oxide and hydrogen bromide in various anhydrous solvents led to polymeric products as the only ones isolated.

Reduction of α-bromoacetophenone. To the aluminum isopropoxide prepared from 15 g. (0.56 g.-atom) of aluminum and 300 ml. of anhydrous isopropyl alcohol in the presence of 0.5 g. of mercuric chloride was added a solution of 20 g. (0.10 mole) of α-bromoacetophenone in 10 ml. of isopropyl alcohol. The reaction mixture was boiled under reflux for 20 minutes. The solvent was distilled rapidly at reduced pressure and 45 ml. of concentrated hydrochloric acid in 200 ml. of water was added. Extraction with ether followed by distillation yielded 1.0 g. (8%) of phenethyl alcohol, b.p. 82° (3 mm.), and 12.6 g. (63%) of α-bromomethylbenzyl alcohol, b.p. 106–108° (3 mm.). This method using a short reduction time has been used (4) before for α-haloketones.

The usual procedure (5) for the reduction of α-bromoacetophenone which involved distillation of the reaction mixture until all of the acetone had been removed (about 20 hours) yielded a small amount of phenethyl alcohol as the only product isolated. Shorter heating for three hours gave the same result.

Synthesis of β-bromophenethyl alcohol. A mixture of 40 g. (0.33 mole) of phenethyl alcohol and 220 g. of 98% formic acid was heated under reflux for seven hours. Distillation yielded 46 g. (94%) of phenethyl formate, b.p. 73–75° (3 mm.).

A solution of 22.5 g. (0.15 mole) of phenethyl formate in 300 ml. of carbon tetrachloride was illuminated in a Pyrex flask with an ultraviolet lamp while a solution of 24 g. (0.15 mole) of bromine in 100 ml. of carbon tetrachloride was added over a period of one hour. Distillation of the solution yielded 23.1 g. (67%) of a monobromoester, b.p. 116.5–117° (3.5 mm.), n_D^{20} 1.5562, d_D^{20} 1.497. This bromo ester did not keep well and was used immediately.

Anal. Calc'd for $C_9H_9BrO_2$: C, 47.2; H, 3.96; Br, 34.9.

Found: C, 47.7; H, 3.93; Br, 35.5.

A solution of 16.2 g. (0.071 mole) of the monobromoester in 45 ml. of methanol containing a drop of sulfuric acid was boiled under a partial take-off reflux condenser filled with ether until 4.5 ml. of methyl formate was distilled. Most of the solvent was then distilled, and 100 ml. of water was added. Ether extraction followed by distillation yielded 8.9 g. (62%) of impure β-bromophenethyl alcohol, b.p. 102–104 (5 mm.), with a bromine analysis which was considerably lower than the calculated value.

Several preparations of β-bromophenethyl alcohol carried out by the method outlined above gave similar results in that analyses for bromine were low and those for carbon and hydrogen were high. On the basis that the monobromoester was β-bromophenethyl formate contaminated by some of the isomeric phenethyl bromoformate the bromohydrin obtained by methanolysis would be expected to contain phenethyl alcohol as the chief impurity. The best sample of β-bromophenethyl alcohol was obtained following the above procedure except that the carbon tetrachloride solution of the monobromoester was washed with cold, dilute, aqueous sodium bicarbonate in order to remove the phenethyl bromoformate before the solution was distilled. Methanolysis of this bromo ester product gave an over-all yield of 56% (based on phenethyl formate) of β-bromophenethyl alcohol, b.p. 96–130° (2 mm.).

Anal. Calc'd for C_8H_9BrO: Br, 39.7. Found: Br, 35.5.

Preparation of 3,5-dinitrobenzoates of the styrene bromohydrins. The method using anhydrous pyridine as a solvent for ester formation was completely unsatisfactory. Actually α-bromomethylbenzyl alcohol with pyridine has been reported (13) as giving a quantitative yield of 2-phenyl-2-hydroxyethylpyridinium bromide.

A mixture of 2 ml. of α-bromomethylbenzyl alcohol and the 3,5-dinitrobenzoyl chloride, prepared (14) from 1 g. of the acid, in 50 ml. of chloroform was heated under reflux until all the acid chloride dissolved (about six hours). The solution was washed with 10 ml. of 5% aqueous sodium bicarbonate and then concentrated by evaporation. When 5 ml. of solution was left a solid precipitated. Crystallization from 95% ethyl alcohol followed by "Skellysolve B" gave α-bromomethylbenzyl 3,5-dinitrobenzoate, m.p. 92–93°. This ester could be prepared from each of the samples of the bromohydrin from the various sources.

Anal. Calc'd for $C_{15}H_{11}BrN_2O_6$: C, 45.6; H, 2.81.
Found: C, 45.1; H, 3.29.

β-Bromophenethyl 3,5-dinitrobenzoate was prepared from various samples of the bromohydrin—even though impure—by the method described above for its isomer except that no solvent was used and the reaction was completed in 15 minutes. After crystallization from 95% ethyl alcohol, "Skellysolve B," and finally methanol a product of m.p. 111.5–112°, which was identical with that obtained by the bromination of phenethyl 3,5-dinitrobenzoate, was obtained.

Mixtures of the two bromohydrin 3,5-dinitrobenzoates softened noticeably at 86–90° but did not melt completely until 102–103°.

Preparation of 3,5-dinitrobenzoates of unbrominated alcohols. 3,5-Dinitrobenzoyl chloride, freshly prepared (14) from the acid and thionyl chloride, was used for all ester preparations. The esters were all prepared by about the same procedure as that for phenethyl alcohol. A solution of 71.7 g. (0.59 mole) of phenethyl alcohol and 3,5-dinitrobenzoyl chloride from 43 g. (0.20 mole) of the acid, in 65 ml. of anhydrous pyridine was heated on a steam-bath for 45 minutes. After treatment with 250 ml. of 5% sodium bicarbonate solution the solid was filtered and was crystallized twice from 95% ethyl alcohol to give 47.5 g. (75% based on 3,5-dinitrobenzoic acid) of phenethyl 3,5-dinitrobenzoate, m.p. 107–108°. The 3,5-dinitrobenzoates of the following alcohols were prepared by this method (yields are based on 3,5-dinitrobenzoic acid): α-methylbenzyl alcohol (75%), m.p. 94–95°; benzyl alcohol (48%), m.p. 113–113.5°; ethyl alcohol (50%), m.p. 92.3–93°; methanol (56%), m.p. 106.8–107.4°.

Bromination of phenethyl 3,5-dinitrobenzoate. A solution of 45 g. (0.14 mole) of phenethyl 3,5-dinitrobenzoate in 500 ml. of carbon tetrachloride in a Pyrex flask was illuminated by an ultraviolet lamp as 24 g. (0.15 mole) of bromine in 100 ml. of carbon tetrachloride was added dropwise with stirring. When the addition was completed and the bromine color had disappeared the solution was distilled, and the residue was crystallized from 95% ethyl alcohol and then "Skellysolve B" to yield 27.7 g. (50%) of β-bromophenethyl 3,5-dinitrobenzoate, m.p. 112–113°.

Anal. Calc'd for $C_{15}H_{11}BrN_2O_6$: C, 45.6; H, 2.81; Br, 20.2.

Found: C, 45.9; H, 2.84; Br, 20.7.

Bromination of other 3,5-dinitrobenzoates. A solution of 15.2 g. of α-methylbenzyl 3,5-dinitrobenzoate in 175 ml. of carbon tetrachloride was treated with 8 g. of bromine in 35 ml. of carbon tetrachloride as described for the bromination of phenethyl 3,5-dinitrobenzoate. Crystallization of the product yielded an unstable solid of m.p. 92–176°. On standing, the solid yielded an oil and some of the unbrominated ester. The oil gave a *phenylhydrazone* of m.p. 102–104° which was identified by mixture m.p. as that of acetophenone.

In a completely analogous experiment benzyl 3,5-dinitrobenzoate yielded an unstable solid of m.p. 172–197° which on standing yielded a little benzoic acid, m.p. 120–121°, 3,5-dinitrobenzoic acid, m.p. 200–203°, and an oil whose *methone* derivative, m.p. 194–197°, was identified as that of benzaldehyde by mixed m.p.

Similar experiments with the ethyl and methyl 3,5-dinitrobenzoates in which the bromination solutions were illuminated nine or ten days gave only ester products which gave weak qualitative tests for halogen and were shown after crystallization to be identical with the unbrominated esters.

Bromination of phenethyl alcohol. To a stirred solution of 24 g. (0.20 mole) of phenethyl alcohol in 230 ml. of carbon tetrachloride 32 g. (0.20 mole) of bromine in 100 ml. of carbon tetrachloride was added over a period of 60 hours while the mixture was illuminated by an ultraviolet lamp. Distillation gave 8.2 g. (34%) of phenylacetaldehyde, b.p. 76–79° (6 mm.), *2,4-dinitrophenylhydrazone,* m.p. 121–122°; and 4.6 g. (12%) of α-bromo-α-phenylacetaldehyde, b.p. 88–89° (2 mm.), 2,4-*dinitrophenylhydrazone,* m.p. 140–142° (15).

Oxidation of α-bromomethylbenzyl alcohol. A mixture of 20 g. (0.10 mole) of α-bromomethylbenzyl alcohol, 10 g. of potassium dichromate, 15 ml. of concentrated sulfuric acid, and 19 ml. of water was cooled in an ice-bath. When thoroughly cold the mixture was extracted with ether. After distillation of the ether the residue was solidified and then was crystallized from methanol to yield 10.3 g. (52%) of α-bromoacetophenone, m.p. 48–50°, which gave no lowering of the m.p. when mixed with an authentic sample.

Dehydrobromination of the styrene bromohydrins. A solution of 3 g. of the bromohydrin in 5 ml. of quinoline was heated so that the volatile products distilled slowly into 15 ml. of 95% ethyl alcohol. The alcoholic solutions of the distillates were used directly to prepare the 2,4-dinitrophenylhydrazones. That from α-bromomethylbenzyl alcohol was acetophenone 2,3-dinitrophenyl hydrazone, m.p. 248–250°, and that from β-bromophenethyl alcohol was phenylacetaldehyde 2,4-dinitrophenylhydrazone, m.p. 119–121°.

SUMMARY

1. α-Bromomethylbenzyl alcohol was characterized by its 3,5-dinitrobenzoate. This bromohydrin was prepared by the addition of the elements of hypobromous acid to styrene, by the addition of the elements of hydrogen bromide to styrene oxide, and by the reduction of α-bromoacetophenone. Oxidation of the bromohydrin yielded α-bromoacetophenone.

2. β-Bromophenethyl alcohol was synthesized by the photobromination of phenethyl formate followed by methanolysis. This bromohydrin was characterized by its 3,5-dinitrobenzoate which was also prepared by the bromination of phenethyl 3,5-dinitrobenzoate.

3. Both bromohydrins were dehydrohalogenated without migration of the oxygen atom.

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