[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

SOME ASPECTS OF THE REACTION OF SILVER CARBOXYLATES WITH BROMINE

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There has accumulated considerable evidence that the reaction of bromine with the silver salt of a carboxylic acid proceeds by a mechanism involving free radicals. Of this evidence, there may be cited, especially, failure of the neopentyl (1), *sec*-amyl (2), or cyclobutyl (3) systems to rearrange; formation of racemic halides from active 2-ethylhexanoic acid (4) and from active 2-methylbutanoic acid (5); and formation of products (2, 6) which would be expected from free radical intermediates. One of the few reports contraindicating the free radical mechanism is that of Kenyon and co-workers (7), who reported isolation of a partially active 1-phenylethyl bromide from reaction of bromine with active silver α-phenylpropionate. Persistent attempts in this laboratory[1] to repeat the experiments of Kenyon and co-workers have failed; in fact, we have been unable to isolate any 1-phenylethyl bromide from the reaction. Recently, Abbott and Arcus (8) have also reported inability to obtain 1-phenylethyl bromide from this reaction, while Arcus and Boyd (9) have reported racemization of active 1-phenylethyl bromide under conditions of the preparation (7) from the silver salt. Abbott and Arcus (8) have reported isolation of 3-bromoheptane with a small rotation (0.36°) from reaction of bromine with silver 2-ethylhexanoate of 93% optical purity; however, careful purification of the low yield of this bromide was not described, and this report would not appear to be substantial evidence against the free radical mechanism.

There have been numerous reports (5, 10) that in the silver salt and bromine reaction the carboxylic acid corresponding to the silver salt is a persistent by-product. We have observed this by-product even with rigorous exclusion of moisture and use of pure silver salt. The possibility that the intermediate complex of silver salt and bromine may rearrange in part to acyl bromide (rather than the acyl hypobromite) has been eliminated by work-up of the reaction under anhydrous conditions; no acyl bromide could be isolated. From reactions of silver caprylate with bromine in which excess of bromine was carefully avoided, there was isolated a mixture of dibromoheptanes, and the molar amount of parent acid isolated was somewhat in excess of dibromoheptanes. Thus, a plausible sequence of reactions leading to parent acid is as follows:

$$C_7H_{15}Br + Br\bullet \rightarrow \bullet C_7H_{14}Br + HBr$$
$$\bullet C_7H_{14}Br + Br_2 \rightarrow C_7H_{14}Br_2 + Br\bullet$$
$$C_7H_{15}CO_2Ag + HBr \rightarrow C_7H_{15}CO_2H + AgBr$$

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[1] The principal product obtained by us was 1-phenylethyl 2-phenylpropanoate. Details of our experiments are not reported, for a much more extensive investigation of this reaction has been carried out by Professor S. Winstein and co-workers at the University of California at Los Angeles.

Since some polybromination would result and traces of moisture would contribute some acid, the amount of acid should always be in excess of the dihalides isolated.

Since α-bromination of α-alkylalkanoic acids is rather sluggish, and there sometimes result by-products arising from loss of hydrogen bromide during the course of bromination (11), synthesis of α-bromo-α-alkyl esters by the silver salt and bromine reaction has been investigated. The required starting material is the half ester of a disubstituted malonic acid, a type of compound which appears not to have been subjected to the silver salt reaction. Mono-substituted half esters of malonic acid have been reported to give relatively low yields of α-bromoesters (12); however, there were used for these reactions the potassium salts which have been described (13) as inferior to the silver salts. Since α-bromo-α-alkyl esters are too unstable thermally to permit isolation by distillation, this product was dehydrohalogenated to give the α,β-unsaturated ester. By this procedure, it was possible to obtain a 73% over-all yield of ethyl 2-butyl-2-hexenoate with a four-degree boiling range; however, the ultraviolet spectrum revealed the presence of an impurity with a high extinction coefficient at a maximum slightly above 220 mμ. This impurity is neither conjugated dienoic ester (maximum at about 270 mμ) (11) nor allenic ester (infrared absorption at 1950 cm^{-1}) (14), and its identity has not been discovered. Separation of this impurity by fractional distillation has proved possible but so difficult as to defeat the usefulness of this synthesis of α-alkyl-α,β-unsaturated esters. Greater difficulties were encountered when the method was applied to synthesis of methyl 2-methyl-2-dodecenoate, for the intermediate silver salt was a low-melting solid.

It has been found possible to secure a high-yield conversion of diethyl di-*n*-butylmalonate to pure ethyl silver di-*n*-butylmalonate, which is moderately soluble in methanol and more soluble in carbon tetrachloride. Preparation of disilver di-*n*-butylmalonate is rendered impractical by the occurrence, during saponification of the malonate, of carbonate cleavage (15) of the intermediate half ester to give mono-acid. When saponification was continued until consumption of two molar-equivalents of alkali, the silver salt obtained from the product contained only 43.5% silver (theory for the disilver salt, 50.2%). Thus, application of the silver salt and bromine reaction to disubstituted malonic acids appears unpromising.

EXPERIMENTAL[2]

Silver caprylate. Commercial caprylic acid was purified by distillation, b.p. 123–125°/10 mm., n_D^{21} 1.4270. The acid in boiling aqueous suspension was neutralized with aqueous sodium hydroxide to a phenolphthalein end-point, and the hot solution was treated with

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[2] Unless otherwise specified, distillations are through a half-meter Podbielniak type column with simple tantalum wire spiral, heated jacket, and partial reflux head. Microanalyses are by the Microanalytical Division, Department of Chemistry, University of California. Ultraviolet spectra were determined with the Beckman Model DU quartz spectrophotometer in matched quartz cells with 95% ethanol as solvent. In a part of this experimental work, we were assisted by Richard J. Nagle and Mrs. Gloria B. Robbers.

one equivalent of aqueous silver nitrate. The precipitated silver salt was washed with water and methanol, then dried in a vacuum at 90–100° to constant weight in the dark; yield 99%.

Anal. Calc'd for $C_8H_{15}AgO_2$: Ag, 42.97. Found: Ag, 42.20.

By-products in preparation of n-heptyl bromide. The reaction flask containing the silver salt was dried in a vacuum at 100° overnight, and dryness was further assured by distilling from the reaction flask one-fourth of the dried carbon tetrachloride used as solvent. A dried solution of bromine in carbon tetrachloride was added, with stirring and cooling in an ice-bath, until a faint coloration from bromine persisted (addition time 15 min.), then stirring was continued for one hour as the mixture warmed to room temperature. At the end of this period, the bromine color remained. Evolution of carbon dioxide began within 1–5 min. after addition of bromine was begun. After silver bromide had been removed by filtration, distillation of a 0.2-mole run yielded 28.0 g. (79%) of *n*-heptyl bromide, b.p. 62–65°/12 mm., n_D^{21} 1.4496, 1.5 g. of an intermediate fraction, and 2.2 g. of a mixture of caprylic acid and dibromoheptanes, b.p. 122–129°/12 mm. In preparation of this primary bromide, no ester was encountered as a by-product.

The high-boiling fractions from four runs were extracted with sodium carbonate, which removed 2.15 g. (15 millimoles) of caprylic acid. Distillation of the neutral material at 10 mm. pressure yielded four fractions whose weight, b.p., and n_D^{21} were respectively: (a) 0.44 g., 70–101.5°, 1.4840; (b) 0.94 g., 101.5–106.5°, 1.4928; (c) 1.01 g., 106.5–111.5°, 1.4929; and (d) 0.75 g., 111.5–114.0°, 1.4969. The final three fractions are equivalent to 10.5 millimoles of dibromoheptanes. Analysis of these three fractions for bromine gave, respectively: 61.60, 59.98, 60.24 (Calc'd for $C_7H_{14}Br_2$, 61.95). The range of properties reported for dibromoheptanes is spanned by those for 1,1-dibromoheptane (16), b.p. 98–99°/11 mm., n_D^{15} 1.4959, and for 1,7-dibromoheptane (17), b.p. 124–125°/12 mm., n_D^{15} 1.5033.

Ethyl silver di-n-butylmalonate. Saponification was much more selective near room temperature than in boiling ethanol, and more homogeneous half ester was obtained when some di-ester was left unreacted. In one run carried out with 69 millimoles of diethyl di-*n*-butylmalonate according to the best procedure described below, the products of the reaction were assayed by decarboxylation and distillation of neutral and acidic fractions. Products obtained were: recovered di-ester, 20 mmoles; ethyl 2-butylhexanoate, 41 mmoles, and 2-butylhexanoic acid, 1.15 mmoles. Thus, the acidic fraction from the controlled saponification was about 97% half ester.

A solution of 20 g. of diethyl di-*n*-butylmalonate (redistilled, b.p. 124–126°/6 mm.) and 5.4 g. of 85% potassium hydroxide (1.1 molar equiv.) in 80 ml. of 95% ethanol was placed in a constant temperature bath at 28°. Course of the reaction was followed by titration of 1-ml. aliquots, and the mixture was worked up after 80 hours, at which time consumption of alkali was equivalent to 79% of the molar quantity of malonate used. Most of the alcohol was removed at reduced pressure and temperatures below 35°. After 100 ml. of water had been added to the residue, the mixture was brought to a phenolphthalein end-point with 6 *N* nitric acid. Extraction of this mixture with hexane yielded 4.1 g. of starting di-ester (98% recovery, based on alkali consumption). To the aqueous solution was added 1.1 equivalents (based on alkali consumed) of an aqueous solution of silver nitrate. After cooling in ice, the precipitated silver salt was collected, washed with ice-water, and dried in a vacuum at 90°; yield 20.8 g. (92%, based on alkali consumption).

Anal. Calc'd for $C_{13}H_{23}AgO_4$: Ag, 30.8. Found: Ag, 30.4.

Approximate solubilities of this salt at 20–25° were determined: 0.25 g./100 ml. in water, 2.0 g./100 ml. in methanol, *ca.* 10 g./100 ml. in carbon tetrachloride.

Ethyl 2-n-butyl-2-hexenoate. Ethyl silver di-*n*-butylmalonate (20 g.) was subjected to reaction with bromine as described for silver caprylate, but the reaction was worked up after addition of water as previously described (2). The crude bromoester, remaining after removal of solvent at reduced pressure, was heated with 5 equivs. of quinoline for 2 hours at 150–160°. The cooled mixture was shaken out with ether and dilute hydrochloric acid, and the quinoline was thoroughly extracted with dilute acid. After acid had been washed from the ether solution, the solvent was distilled and the product was rapidly distilled in a Claisen flask to remove a tarry residue. Fractionation yielded 0.3 g. of fore-run and 8.6 g. (74%) of crude ethyl 2-*n*-butyl-2-hexenoate, b.p. 100.5–104°/10 mm. This material, as obtained from several runs, contained small amounts of bromine (0.5–2.0%) and had λ_{max} 221–222 mμ, ϵ_{max} 14,000–19,000. The ultraviolet absorption is at too long a wavelength and has too high an extinction coefficient for a pure α,β-unsaturated ester (11).

For further purification, a 12-g. sample of the crude ester was fractionated through a 1.5-meter column at 4.5 mm. pressure and the distillate was received in eleven fractions. The highest concentration of the highly-absorbing impurity appeared in Frac. 5, wt. 0.5 g., b.p. 87–89°, n_D^{25} 1.4512, λ_{max} 224 mμ, ϵ_{max} 17,600. The unsymmetrical absorption curve, dropping steeply on the longer wavelength side and more gradually on the shorter wavelength side, indicates presence of considerable of the desired α,β-unsaturated ester in this fraction and, therefore, a considerably stronger maximum absorption for the impurity. A conjugated diene (hydrocarbon) would have such absorption characteristics, but a mechanism for its formation in significant amounts in the present reactions is not clear. Fracs. 7–10, weight 6 g., b.p. 90.0°, n_D^{25} 1.4443–1.4473, appeared to be reasonably homogeneous samples; however, the only fraction possessing the properties to be expected (11) of the pure α,β-unsaturated ester was Frac. 10, weight 1.0 g., n_D^{25} 1.4443, λ_{max} 219 mμ, ϵ_{max} 11,100 (symmetrical curve). This fraction was analyzed.

Anal. Calc'd for $C_{12}H_{22}O_2$: C, 72.73; H, 11.11.
Found: C, 72.35; H, 11.17.

SUMMARY

Attempts to repeat previously reported experiments contraindicating a free radical mechanism for the silver salt and bromine reaction have been unsuccessful.

Evidence has been obtained that the parent acid occurring as a by-product in the silver salt reaction arises from reaction of the silver salt with hydrogen bromide which, in turn, is generated by free-radical bromination of the alkane moiety of the alkyl bromide.

The silver salt reaction has been applied to half esters of disubstituted malonic acids. The resultant α-bromoester was dehydrohalogenated to the α,β-unsaturated ester. Although over-all conversion to the α-alkyl-α,β-unsaturated ester is satisfactory, properties of the silver salt and difficulty in purifying the product render the synthesis of little value.

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