Observations on the Bromination of Phenylmercaptoacetic Acid

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In view of the preparation of 4-bromophenyl methyl sulfide by bromination of phenyl methyl sulfide in yields of greater than 90%,[1,2] it was surprising that 4-bromophenylmercaptoacetic acid could be obtained in yields of only about 60% by bromination of phenylmercaptoacetic acid in acetic acid. During the search for other possible products, 2-bromophenylmercaptoacetic acid, 3-bromophenylmercaptoacetic acid, 4-bromophenylmercaptoacetic acid, bis(2-bromophenyl) disulfide, bis(3-bromophenyl) disulfide and bis(4-bromophenyl) disulfide were prepared for comparison. It was found that 4-bromophenylmercaptoacetic acid was the only solid, nonvolatile, bromine-containing acid produced by bromination of phenylmercaptoacetic acid and that water in the reaction mixture led to the production of disulfides.

As the reaction proceeded, water was introduced as (a) water vapor in the air used to evaporate the reaction mixture, which contained unreacted bromine, and (b) water into which the acetic acid solution of the residue was poured. In order to determine the effect of water introduced while bromine was still present, the reaction was conducted in a solvent mixture, acetic acid and water. The solid product obtained was diphenyl disulfide. To illustrate the same effect, a solution of glacial acetic acid, 4-bromophenylmercaptoacetic acid and bromine was not evaporated but was poured into water and allowed to stand for an hour; bis(4-bromophenyl) disulfide was isolated from the insoluble solid. The negligible effect of water in the absence of bromine was demonstrated by the observation that phenylmercaptoacetic acid could be recrystallized from water with good recovery.

A possible reaction pathway, which will account for products found, is outlined below. We have not attempted to isolate bromoacetic acid from the reaction mixture.

(a) $H_2O + Br_2 \longrightarrow HBr + HOBr$

(b) $ArSCH_2CO_2H + HBr \longrightarrow ArSH + BrCH_2CO_2H$

(c) $2\ ArSH + HOBr \longrightarrow ArSSAr + H_2O + HBr$
or
$2\ ArSH + Br_2 \longrightarrow ArSSAr + 2\ HBr$

The mild conditions for the cleavage of this particular carbon - sulfur bond may be compared with conditions required for cleavage of aryl alkyl sulfides.[3] Such a facile room temperature cleavage as this might explain the low herbicidal activity of arylmercaptoacetic acids.[4-6]

EXPERIMENTAL

Materials. Phenylmercaptoacetic acid was obtained from Evans Chemetics, Inc. 2-, 3-, and 4-Bromoanilines were purchased from Distillation Products Industries. These compounds were purified by recrystallization or by distillation before use. Acetic acid was purified by repeatedly discarding eutectic compositions from partially melted commercial glacial acetic acid.

Bromination of phenylmercaptoacetic acid. To a solution of 4.00 g. (0.024 mole) of phenylmercaptoacetic acid and 100 ml. of glacial acetic acid in a flask protected by a drying tube was added 4.8 g. (0.030 mole) of bromine. The solution was allowed to remain out of direct sunlight for 5 days. Volatile constituents were removed from the orange solution by passing a gentle stream of air over the surface at ambient temperature; evaporation was continued until a dry residue remained. The dry, colorless, solid residue was dissolved in 25 ml. of hot acetic acid. The hot solution was poured into 100 ml. of cold water. The colorless precipitate was removed by filtration and dried *in vacuo.* The weight of the dried solid was 4.89 g.

The solid was recrystallized from water and then from an ethanol-water mixture. There was obtained 3.66 g. (62%) of 4-bromophenylmercaptoacetic acid.

The filtrates from the recrystallizations were extracted with ether. The extracts were combined, dried, and evaporated to dryness. The solid residue (melting range 90–113°) was analyzed with the infrared spectrophotometer.[7] Its spectrum consisted of contributions by phenylmercaptoacetic acid and 4-bromophenylmercaptoacetic acid.

The reaction was repeated several times. In the spectrum of one residue a very weak absorption at 14.05 μ indicated the presence of 2-bromophenylmercaptoacetic acid. However, attempts to estimate its concentration by infrared analysis were fruitless.

Bromophenylmercaptoacetic acids. 2-, 3-, and 4-Bromophenylmercaptoacetic acids were prepared from the corresponding bromoanilines. The bromoanilines were converted to the bromobenzenethiols by the method of Schwarzenbach and Egli.[8] The thiols were subsequently treated with sodium hydroxide and chloroacetic acid in a manner similar to that employed by Gabriel[9] for the synthesis of phenylmercaptoacetic acid. The bromophenylmercaptoacetic acids were recrystallized from ethanol-water mixtures. Physical constants of the previously known bromobenzenethiols and 4-bromophenylmercaptoacetic acid were comparable with literature values.[10,11]

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(1) T. Van Hove, *Bull. sci. acad. roy. Belg.*, (5) **12**, 929 (1926); *Chem. Abstr.*, **21**, 2256 (1927).

(2) M. P. Balfe, R. E. Dabby, and J. Kenyon, *J. Chem. Soc.*, 382 (1951).

(3) Summarized by D. S. Tarbell and D. P. Harnish, *Chem. Revs.*, **49**, 1 (1951).

(4) H. E. Thompson, C. P. Swanson, and A. G. Norman, *Botan. Gaz.*, **107**, 476 (1946).

(5) J. Ashmore, *The Synthesis and Testing of Differential Herbicides*, M.S. thesis, North Texas State College, 1948.

(6) M. Sugii and A. Sugii, *Bull. Inst. Chem. Research, Kyoto Univ.*, **31**, No. 1, 27 (1953); *Chem. Abstr.*, **47**, 7610 (1953).

(7) Infrared spectra of solids were of potassium bromide disks and the spectrum of bis(3-bromophenyl) disulfide was of the pure liquid film between potassium bromide plates; all were recorded with a Perkin-Elmer Model 21 spectrophotometer.

(8) G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, **17**, 1176 (1934).

(9) S. Gabriel, *Ber.*, **12**, 1639 (1879).

(10) R. Pummerer, *Ber.*, **42**, 2275 (1909).

(11) H. F. Wilson and D. S. Tarbell, *J. Am. Chem. Soc.*, **72**, 5200 (1950).

2-Bromophenylmercaptoacetic acid crystallized as colorless platelets from an ethanol-water mixture, m.p. 117–118°.

Anal. Calcd. for $C_8H_7O_2BrS$: Br, 32.34; neut. equiv., 247. Found: Br, 32.52; neut. equiv., 247.

3-Bromophenylmercaptoacetic acid crystallized from an ethanol-water mixture as colorless needles, m.p. 85–86°.

Anal. Calcd. for $C_8H_7O_2BrS$: Br, 32.34; neut. equiv., 247. Found: Br, 32.63; neut. equiv., 247.

Disulfides. Diphenyl disulfide, bis(2-bromophenyl) disulfide, bis(3-bromophenyl) disulfide, and bis(4-bromophenyl) disulfide were prepared by oxidation of the corresponding sodium thiophenoxides with air. The disulfides, recrystallized from ethanol or distilled, exhibited physical properties consistent with values reported in the literature.[11,12]

Infrared spectra. Infrared spectra of phenylmercaptoacetic acid, the bromophenylmercaptoacetic acids, and the disulfides were recorded. Prominent absorption bands in the region of out-of-plane CH deformations, which were used in analysis of residues obtained from recrystallization filtrates, are listed. Wave lengths are in microns and the most prominent band(s) in each spectrum is in italics. Phenylmercaptoacetic acid, 12.35, *13.55*, 14.3, 14.58; 2-bromophenylmercaptoacetic acid, 12.4, *13.3*, 14.05; 3-bromophenylmercaptoacetic acid, *12.9*, *13.3;* 4-bromophenylmercaptoacetic acid, *12.45;* diphenyl disulfide, *13.5*, *13.6*, 14.58; bis(2-bromophenyl) disulfide, *13.44*, 14.19; bis(3-bromophenyl) disulfide, 12.35, *12.95*, *13.44;* bis(4-bromophenyl) disulfide, *12.32*, 13.84.

Bromination in acetic acid-water mixture. To a solution of 4.00 g. of phenylmercaptoacetic acid, 75 ml. of glacial acetic acid, and 25 ml. of distilled water was added 4.8 g. of bromine. Conditions and isolation procedure were the same as described for the reaction in acetic acid. The crystalline product obtained after recrystallization consisted of 1.53 g. (67%) of diphenyl disulfide. No pure chemical individual could be isolated from extracts of the filtrates.

Cleavage of 4-bromophenylmercaptoacetic acid. A solution of 2.96 g. of 4-bromophenylmercaptoacetic acid, 100 ml. of glacial acetic acid, and 2.4 g. of bromine in a flask equipped with a drying tube was kept in the dark for 5 days. The reaction mixture was poured into 500 ml. of cold water, this resulting in formation of a colorless precipitate. After an hour the precipitate was removed by filtration. The dried solid weighed 1.45 g. and exhibited a melting range of 85–105°. Acidic and neutral fractions were separated. By recrystallization of these fractions there were obtained 1.02 g. (34% recovery) of 4-bromophenylmercaptoacetic acid and 0.11 g. (6.7% yield) of bis(4-bromophenyl) disulfide.

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[12] H. Hubner and J. Alsberg, *Ann.*, **156**, 308 (1870).

Acid-Catalyzed Rearrangement of Diethyl Ketone and Diisopropyl Ketone[1]

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Acid-catalyzed ketone rearrangements have received considerable attention in the past few years[2–4] and the mechanism of the reaction appears to be well established.[2] The ketone conjugate acid rearranges to an isomeric carbonium ion by an alkyl or aryl group shift, which in turn reverts to the original ketone conjugate acid or rearranges to the conjugate acid of the isomeric ketone by a second alkyl or aryl group shift. All mechanisms involving oxygen function migration (oxide conjugate acid formation, hydroxide shift or reversible pinacol formation) are excluded by the work of Barton and Porter[5] and the observation[6] that 3,3-dimethyl-2-butanone-1-2-C^{14} does not rearrange to 3,3-dimethyl-2-butanone-3-C^{14} under conditions where 3,3-dimethyl-2-butanone-1-C^{14} rearranges to an equilibrium mixture with 3,3-dimethyl-2-butanone-4-C^{14}.

Barton and Porter[5] and Zook, Smith, and Greene[7] studied the acid-catalyzed rearrangements of a number of aliphatic ketones, including in both cases, diisopropyl ketone, for which no rearrangement was observed.[8] Barton and Porter conclude that only those ketones whose carbonyl groups are attached to at least one quaternary carbon can rearrange. In terms of the established mechanism, the conclusion could be stated that rearrangement would take place only when a tertiary carbonium ion can be formed in the migration of an alkyl group to the carbonyl carbon.

The results of the present research demonstrate that ketone rearrangements do occur, not only where such tertiary carbonium ions would be formed, but also where secondary and primary carbonium ions would be required, assuming the same rearrangement mechanism.

Upon treatment with perchloric or sulfuric acid at 90° for three hours diisopropyl ketone rearranges to the extent of 70% to 3,4-dimethyl-2-pentanone. No other rearrangement products could be detected by gas chromatography. The rearranged ketone was identified by gas chromatographic and chemical comparison with an authentic sample of 3,4-dimethyl-2-pentanone.

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[1] This research was supported by the Atomic Energy Commission.

[2] T. S. Rothrock and A. Fry, *J. Am. Chem. Soc.*, **80**, 4349 (1958), and references mentioned there.

[3] A. Fry, W. L. Carrick, and C. T. Adams, *J. Am. Chem. Soc.*, **80**, 4743 (1958).

[4] Z. N. Parnes, S. V. Vitt, and D. N. Kursanov, *Zhur. Obshchei Khim.*, **28**, 410 (1958).

[5] S. Barton and C. R. Porter, *J. Chem. Soc.*, 2483 (1956).

[6] C. T. Davis and A. Fry, *Chem. & Ind. (London)*, 277 (1906).

[7] H. D. Zook, W. E. Smith, and J. L. Greene, *J. Am. Chem. Soc.*, **79**, 4436 (1957).

[8] The conditions used by both groups of workers were much less conducive to rearrangement than those used in most cases in the work reported here, and the small amount of rearrangement which does occur under conditions used by Zook, Smith, and Greene[7] might well have gone undetected, since it is within the limits of accuracy claimed for their analytical method. Barton and Porter state that they did not look for minor rearrangement products.