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# A Convenient Procedure for the Conversion of Carboxylic Acids to α-Bromo Thiolesters

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### A CONVENIENT PROCEDURE FOR THE CONVERSION OF CARBOXYLIC ACIDS TO α-BROMO THIOLESTERS

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**Abstract**: Carboxylic acids can be conveniently transformed to the corresponding  $\alpha$ -bromo thiolesters by a one-pot procedure involving Hell-Volhard-Zelinsky reaction and trapping the  $\alpha$ -bromo acyl bromide intermediate with mercaptans.

In connection with an investigation on the synthetic utility of glycidic thiolesters, it was necessary to prepare a variety of  $\alpha$ -bromo thiolesters.  $\alpha$ -Halothiolesters can be conveniently synthesized from mercaptans and  $\alpha$ -halo carboxylic acids or their halides.<sup>1-4</sup> A classical method for the preparation of the latter two types of compounds is by the use of Hell-Volhard-Zelinsky reaction.<sup>8</sup> In the presence of a catalytic amount of phosphorus tribromide, carboxylic acids possessing one or more  $\alpha$ -hydrogens are converted to the corresponding  $\alpha$ -bromo carboxylic acids with bromine. When more than one equivalent of

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phosphorus tribromide is applied, the reaction gives rise to  $\alpha$ -bromo acyl bromide as the product. It is conceivable that the latter compound, which is unstable and difficult to handle, can be trapped with an appropriate thiol to facilitate the formation of  $\alpha$ -bromo thiolesters. On the basis of this consideration, a practical one-pot procedure has been developed for the transformation of carboxylic acids to  $\alpha$ -bromo thiolesters.

The feasibility of the method was first demonstrated by the formation of S-tert-butyl 2-bromoethanethioate (1) from acetic acid. In an early experiment, a mixture of acetic acid and 0.3 molar equivalent of phosphorus tribromide was heated in an oil bath maintained at 110°C while a small excess of bromine (1.2 equivalents) was added dropwise. The resulting brown residue was then dissolved in methylene chloride and treated with *tert*-butyl mercaptan at room temperature. The <sup>1</sup>H nmr spectrum of the colorless liquid thus obtained showed three singlets at  $\delta$ 3.98 (2H, CH<sub>2</sub>), 1.52 (9H, C(CH<sub>3</sub>)<sub>3</sub>) and 1.0. The last signal varied in intensity for products obtained from different runs and was apparently due to the presence of an impurity which was latter recognized to be ditert-butyl disulfide (3). As shown in Scheme 1, this by-product could have arisen from the reaction of tert-butyl mercaptan and tert-butylsulfinyl The latter, in turn, could have been produced by bromide (2). bromination of tert-butyl mercaptan with the excess bromine present. To suppress the formation of disulfide 3, the reaction apparatus was flushed, prior to the addition of tert-butyl mercaptan, with a moderate flow of argon to remove the excess of bromine. Using this procedure, pure  $\alpha$ -bromo thiolester 1 was obtained in 89% yield.

To confirm the amount of phosphorus tribromide required in the transformation, an experiment was carried out under similar conditions



but using only 0.1 molar equivalent of the reagent. As a result, only 25% yield of compound 1 was obtained. Clearly, a quantitative amount of phosphorus tribromide is required in order to obtain high yields of  $\alpha$ -bromo thiolesters. In the subsequent experiments, 0.3-0.4 molar equivalent of the reagent was used and, in all the cases examined, desired products were obtained in high yields (>80%). Results are summarized in Table 1.

As described above, a convenient and apparently general one-pot method for converting carboxylic acids to  $\alpha$ -bromo thiolesters has been developed. A typical experimental procedure is illustrated below with *S*phenyl 2-bromopropanethioate (4).

A mixture of propionic acid (3.70 g, 50 mmol) and phosphorus tribromide (3.24 g, 20 mmol) was placed in a three-neck flask equipped with a dropping funnel, a magnetic stirrer and condenser connected to a hydrogen bromide gas absorption bottle containing aqueous sodium hydroxide solution. While the mixture was heated by an oil-bath maintained at 100-120°C, liquid bromine (3.1 mL, 60 mmol) was added dropwise over a period of 1.5 h. The completion of the reaction was indicated by the retention of the brown color of bromine. The system was



Table 1. Conversion of Carboxylic Acids to  $\alpha\mbox{-Bromo}$  Thiolesters

then flushed with a moderate flow of argon to remove excess bromine (ca. 0.5 h). When the color of the reaction mixture turned to light yellow, the oil bath was removed and methylene chloride (20 mL) was introduced. After the reaction mixture was cooled to room temperature, a solution of thiophenol (5.78 g, 52.5 mmol) in methylene chloride (20 mL) was slowly added. After stirring for 16 h, the mixture was washed with saturated aqueous sodium bicarbonate solution and the aqueous layer was extracted with methylene chloride (2 x 20 mL). The organic solutions were washed with aqueous saturated sodium chloride solution, combined, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated. Vacuum distillation (108-112°C/0.1 mmHg) of the residue gave compound 4 (10.4 g, 42 mmol, 85% yield): <sup>1</sup>H nmr (CDCl<sub>3</sub>)  $\delta$  1.90 (d, 3H, J = 7 Hz, -CH<sub>3</sub>), 4.62 (q, 1H, J = 7 Hz, -CHBr-), and 7.45 (s, 5H, ArH); ir 1705 cm<sup>-1</sup> (C=O); ms M+ 245.9531 and 243.9552 (calcd. for C9H9BrOS: 245.9537 and 243.9558). Anal. Calcd. for C<sub>9</sub>H<sub>9</sub>BrOS: C, 44.10; H, 3.70; S, 13.08. Found: C, 44.42; H, 3.67; S, 13.32.

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