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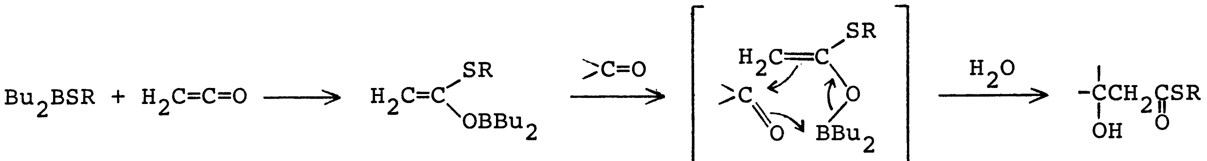
A CONVENIENT METHOD FOR THE PREPARATION OF β-HYDROXY THIOLESTERS AND ESTERS

Katsuhiko INOMATA, Tatsuo KAWAHARA, and Teruaki MUKAIYAMA
Laboratory of Organic Chemistry, Tokyo Institute of Technology
Ookayama, Meguro-ku, Tokyo 152

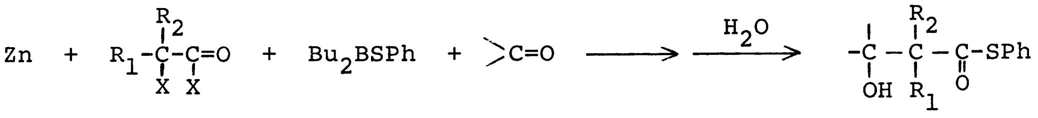
It was found that thioboronite reacted with substituted ketene (produced from α-haloacyl halide and zinc dust) and carbonyl compounds to give the corresponding α-substituted β-hydroxyalkanethioates in good yields. Also, it was established that β-hydroxyalkanoates were obtained in good yields by utilizing aluminum alkoxide in place of thioboronite in the above reaction.

We recently reported a convenient method for the preparation of β-hydroxyalkanethioates (IV) by the reaction of thioboronite (I) and carbonyl compounds with ketene (II) and it was confirmed that the reaction proceeded through an intermediate, vinyloxyborane (III), formed from thioboronite and ketene, as sketched in the following scheme.1)~3)



I II III IV

On the other hand, it is well known4a,b) that substituted ketenes can be prepared by dehalogenation of α-haloacyl halides (V) with zinc dust. Based on the facts, a method for the preparation of α-substituted β-hydroxyalkanethioates by utilizing substituted ketenes in place of free ketene (II) in the above equation was investigated.



$$\mathrm{Zn} + \underset{\mathrm{V}}{R_1\text{-}\overset{R_2}{\underset{X}{C}}\text{-}\underset{X}{C}{=}O} + Bu_2BSPh + {>}C{=}O \longrightarrow \xrightarrow{H_2O} \underset{\mathrm{VI}}{\text{-}\underset{OH}{C}\text{-}\overset{R_2}{\underset{R_1}{C}}\text{-}\underset{O}{\overset{}{C}}\text{-}SPh}$$

It was found that various β-hydroxyalkanethioates were obtained in good yields as shown in Table I. A typical reaction procedure is shown in the following; a mixture of zinc dust (0.325 g, 5.0 mmol), 2,2-dichloroacetyl chloride (0.265 g, 1.8 mmol), phenyl di-n-butylthioboronite (0.281 g, 1.2 mmol) and benzaldehyde (0.106 g, 1.0 mmol) in 20 ml dry ether was refluxed for 2 hr under argon. The mixture was then cooled to room temperature and the remaining zinc was separated by filtration. After removal of ether, an oily substance was treated with 1 ml of 30% H_2O_2 in methanol (20 ml) at 0°C. The solution was allowed to stand overnight at room temperature and methanol was evaporated in vacuo. The resulting mixture was extracted with ether and the ether layer was washed with 5% solution of sodium bicarbonate and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was chromatographed over silica gel to obtain 0.233 g (82%) of S-phenyl α-chloro-β-hydroxyhydrocinnamethioate (m.p. 70-71°).

Table I. Yields of α-substituted β-hydroxyalkanethioates (VI)

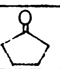
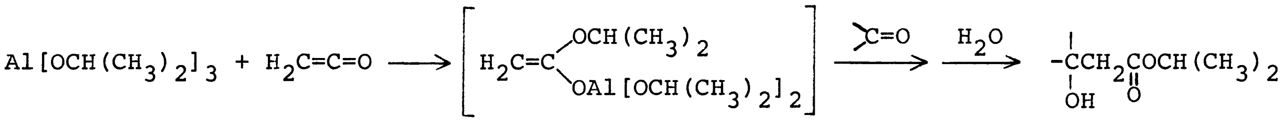
Carbonyl Compounds / Acyl halides	Isolated yield[a],%	
	PhCHO	
$BrCH_2COBr$	80	90
$CH_3CHBrCOBr$	85	82
$(CH_3)_2CBrCOBr$	82	67
$Cl_2CHCOCl$	82	80
Cl_3CCOCl	81	84

Table II. Yields of β-hydroxy alkanoates (IX)

Carbonyl Compounds	Yield[a],%
PhCHO	83
PhCH=CHCHO	81
$PhCH_2CH_2CHO$	80
$CH_3(CH_2)_5CHO$	57

a) The thioates and the alkanoates were confirmed by IR and PMR spectra.

Next, analogous reactions by using aluminum alkoxide in place of thioboronite in the above reaction were tried with the expectation that the intermediate (VIII), probably formed by the reaction of aluminum alkoxide with ketene, would exhibit the same reactivity toward carbonyl compounds. It was established that β-hydroxy alkanoates are prepared in good yields by the reaction of aluminum isopropoxide[5], ketene and carbonyl compounds, as expected. Aluminum isopropoxide (2.0 mmol in hexane solution) and benzaldehyde (0.213 g, 2.0 mmol) in 20 ml dry ether were treated with ketene at 0°C for 20 min. After stirring for 30 min at 0°C, 6 ml of 1 N HCl solution was added and then extracted with ether. The ether layer was dried over anhydrous sodium sulfate. Ether was evaporated and the residue was chromatographed over silica gel to obtain 0.347 g (83%) of isopropyl β-hydroxyhydrocinnamate. The results are listed in Table II.



$$\mathrm{Al[OCH(CH_3)_2]_3} + \mathrm{H_2C{=}C{=}O} \longrightarrow \left[\mathrm{H_2C{=}C}\begin{matrix}\diagup\mathrm{OCH(CH_3)_2}\\ \diagdown\mathrm{OAl[OCH(CH_3)_2]_2}\end{matrix}\right] \xrightarrow{\rangle\mathrm{C{=}O}} \xrightarrow{\mathrm{H_2O}} -\underset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}\mathrm{CH_2}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{OCH(CH_3)_2}$$

VII VIII IX

REFERENCES

1) T. Mukaiyama and K. Inomata, Bull. Chem. Soc. Japan, 44, 3215 (1971).
2) T. Mukaiyama, K. Inomata, and M. Muraki, J. Amer. Chem. Soc., 95, 967 (1973).
3) K. Inomata, M. Muraki, and T. Mukaiyama, Bull. Chem. Soc. Japan, 46, 1807 (1973).
4) a) W. T. Brady, H. G. Liddell, and W. L. Vaughn, J. Org. Chem., 31, 626 (1966).
b) Staudinger and Klerrer, Ber., 39, 968 (1906).
5) No alcohols derived from the aldehydes were isolated. The result suggests that the formation of vinyloxyaluminum took place much faster than the reduction of the aldehyde.

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