

THE CONVERSION OF ESTERS TO PHENYL THIOESTERS BY BORON THIOPHENOXIDE
AND ALUMINUM THIOPHENOXIDE

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Thioesters have attracted a great deal of recent attention as active acylating agents, particularly in the preparation of macrocyclic lactones.¹ Masamune² has brilliantly exploited the activation of phenyl thioesters by transition metal ions in the preparation of such lactones. A number of methods have recently become available for the preparation of thioesters from carboxylic acids via replacement of the carboxylic proton with a group Y, which causes OY to become a good leaving group, followed by treatment of the active intermediate with a thiol or its salt.¹⁻⁴ In contrast, there is only one method presently available for the direct conversion of esters to thioesters; this involves treatment of the ester with the reagent R_2AlSR' in which R is an alkyl group and R' is alkyl,^{5,6} aryl⁵ or vinyl⁷. Only in the very recent report by Hatch and Weinreb,⁶ in which R' = *t*-butyl, were enough examples provided to demonstrate the generality of the conversion and it is this paper which prompts us to report at this time the results of our study of the reaction of boron thiophenoxide and its aluminum analogue with esters.

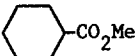
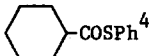
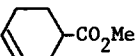
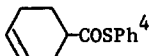
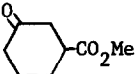
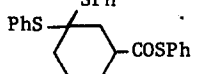
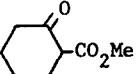
The former was recently introduced as a reagent for converting enones in one step to 1,3-bis(phenylthio)alkenes.⁸ It has now been found that this reagent is capable of converting esters, including α,β -unsaturated esters, to phenyl thioesters in good yield, but the temperature (140°C) of refluxing xylene is required.

In seeking a reagent which would perform the desired conversion at lower temperatures, we turned to the analogous aluminum thiophenoxide. It was found that this material is indeed capable of converting simple esters into phenyl thioesters at 25°C during one hour or at 5°C

during 4 hours (Table)¹⁰. In all cases the yields are quantitative and the thioesters are pure by ¹H NMR spectroscopy as isolated; since the aluminum salts are soluble in the alkaline wash used in the work-up, no chromatography is required. Most of the methods proceeding from the acid require chromatographic purification or reagents which are expensive or poisonous.²⁻⁴

The products from α, β -unsaturated esters are contaminated with 3-(phenylthio)thioesters; an analogous problem was reported⁶ when dimethylaluminum *t*-butylthiolate was used. Since the boron reagent was found not to be subject to this limitation (Table), it nicely complements the aluminum reagent for the conversion of esters into thioesters.

Table. Treatment of Esters with Aluminum Thiophenoxide (A) in Benzene and Boron Thiophenoxide (B) in Xylene

| Ester | Reagent | Conditions ^a | Product | Mp, °C | Yield, % |
|---|----------------|-------------------------|---|--------|------------------|
| Me ₂ CHCO ₂ Me | A | 25°, 1 hr or 5°, 4 hr | Me ₂ CHCOSPh | oil | 100 ^b |
| PhCO ₂ Et | A | 25°, 1 hr or 5°, 4 hr | PhCOSPh ^{4,5} | 56-57 | 100 ^b |
|  | A | 25°, 1 hr or 5°, 4 hr |  | 38-39 | 100 ^b |
|  | A | 25°, 1 hr or 5°, 4 hr |  | oil | 100 ^b |
|  | A ^c | 25°, 1 hr |  | 81-82 | 65 |
|  | A | 25°, 1 hr | Reactant recovered | - | 0 |
| (E)-MeCH=CHCO ₂ Me | B | 140°, 17 hr | (E)-MeCH=CHCOSPh ² | oil | 71 ^d |
| Me ₂ C=CHCO ₂ Me | B | 140°, 17 hr | Me ₂ C=CHCOSPh | oil | 90 ^d |
| (E)-PhCH=CHCO ₂ Me | B | 140°, 12 hr | (E)-PhCH=CHCOSPh ² | 92-93 | 75 ^e |

^aOne mole of metal reagent per mole of ester, unless otherwise stated. ^bPure by ¹H NMR spectroscopy as isolated. ^c2.5 Moles of Al(SPh)₃ per mole of ester. ^dAfter silica chromatography.

^eAfter recrystallization.

A keto group at the 3-position inhibits the reaction while such a group at the 4-position leads to production of the thioketal of the thioester. Reducing the molar ratio of aluminum reagent to 4-ketoester from 2.5 to 0.71 does not prevent attack on the keto group, but it leads instead to production of a thiolactol ether. Production of the thioketal should not be a major drawback in most cases as the thioketal could be converted to a ketone¹¹ at a later stage.

All experiments are conducted under an argon atmosphere. If several runs are to be performed, it is convenient to use aluminum thiophenoxide from a stock supply prepared as follows. To a solution containing 250 mL of dry, deoxygenated, xylene and 29 mL of 2.35 M hexane solution of $\text{Al}(\text{Me})_3$ (0.068 mol) is added dropwise during 5 min 20 mL of thiophenol. The solution is stirred at 25° for 10 min and heated at reflux for 48 hr.¹² The flask is transferred to a glove bag and the white solid is removed by filtration, washed with benzene, transferred to vials and dried over night in a vacuum desiccator. For individual runs, the reagent can be prepared as above and used directly as a suspension in xylene; of course, the latter is more difficult to remove from the thioester than the benzene that can be used in the case of preformed reagent.

A mixture of 1.56 g (4.4 mmol) of aluminum thiophenoxide and 4.4 mmol of the ester in 50 ml of benzene is stirred at 25°C for one hr or at 5°C for 4 hr. While vigorous stirring is maintained, 10% aqueous sodium hydroxide solution (10 mL) is added at the reaction temperature. The mixture is equilibrated between ether and 10% aqueous sodium hydroxide and the organic layer is washed twice with aqueous base, dried (MgSO_4) and evaporated to produce a light yellow liquid which, in most cases, is spectroscopically pure thioester.

In order to produce an α,β -unsaturated thioester, the unsaturated ester (6.6 mmol) is added with stirring at 25° to a solution of 3.2 g (9.5 mmol) of $\text{B}(\text{SPh})_3$ ⁸ in 100 mL of xylene and the solution is heated at reflux for 17 hr. Work-up as above provides a yellow oil which is very largely the thioester (¹H NMR), and which is readily purified by chromatography on silica gel using ethyl acetate (1% + 5%) in hexane as eluent.

There is only a single example in the literature of the conversion of an ester to a phenyl thioester (75% yield) and the reagent used was dimethylaluminum phenylthiolate.⁵ Even if that

method proves to be general, the procedure described here offers a yield advantage and our reagent contains no rather basic methyl groups which could cause trouble with certain functional groups. The boron reagent should also find some use, particularly for the conversion of α,β -unsaturated esters to thioesters; it is the only reagent now available for performing such a transformation.

We have found that aluminum thiophenoxide has other interesting uses in organic chemistry and we will report these in due course.

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10. All products were characterized by their infrared, 1H NMR, and mass spectra; satisfactory exact masses were obtained for those which are new compounds.
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12. If the temperature of refluxing benzene is used instead, it appears by NMR analysis and by methane evolution from the reagent upon acidification that only two methyl groups are displaced. The resulting reagent appears to be slightly less reactive than aluminum thiophenoxide but has given good yields of thioester from several simple esters.

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