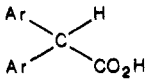
C. This is the basis of a highly versatile method for carboxylic acid homologation.[7]

Studies on alkylation of crowded enolates of carboxylic acid derivatives are not as prevalent as those of aldehydes and ketones, probably due to the difficulty in enolizing esters of di-*tert*-alkylacetic acids. The α-proton in these compounds is not removed by standard bases—again revealing the increase in strain energy that occurs on enolate formation. Dubois and McPhee[8] have studied the alkylation of enolates of α-isopropyl-*tert*-butylacetate esters and found them to undergo C-alkylation (except in the case of α-isopropyl-α-*tert*-butylacetate ester where predominant O-alkylation was observed).

We now wish to report exclusive O-alkylation of enolates of esters of diarylcarboxylic acids such as **1a,b**. These are among the most hindered diarylacetic acids synthesized to date because of the "buttressing effect" of the meta substituents in each ring.



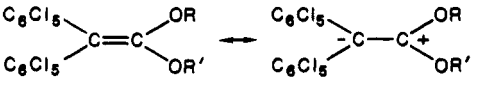
1a, Ar = C_6Me_5
b, Ar = C_6Cl_5

Enolates of esters of **1b** are easily formed due to the electron-withdrawing effect of the pentachlorophenyl groups. Thus treatment of the isopropyl ester **2** with sodium hydride in THF gives a yellow-orange air-stable solution of the sodium enolate **3**. This is not alkylated by methyl iodide or sulfate but is rapidly alkylated by methyl triflate at −5 °C. Quenching the solution followed by chromatography on silica affords (in 70% yield) bis(pentachlorophenyl)ketene methyl isopropyl acetal (**4**)[9] (Scheme II). No C-alkylated product was formed.

Enolates of esters of **1a** are more difficult to form but can be obtained in two ways. Reaction of bis(pentamethylphenyl)ketene (**5**) with lithium alkoxide in THF at 0 °C affords quantitative yields of the lithium ester enolates. Also treatment of esters of **1a** with 3 equiv of *n*-butyllithium in THF at ambient temperature affords the enolates. These anions are highly air-sensitive, and on exposure to oxygen, solutions change immediately from yellow to purple because of their oxidation to (α-alkoxycarbonyl) bis(pentamethylphenyl)methyl radicals.[10]

Thus, treatment of bis(pentamethylphenyl)ketene (**5**) with 1 equiv of lithium methoxide in THF at 0 °C, followed by addition of excess methyl sulfate, afforded 16% yields of bis(pentamethylphenyl)ketene dimethyl acetal (**7**)[9] after chromatography and recrystallization. The main product in this reaction was methyl bis(pentamethylphenyl)acetate. Again no C-alkylation was detected.

The two ketene acetals **4** and **7** show strong ν(C=C) absorptions in their IR spectra at 1610 and 1635 cm^{-1} and have characteristic UVs [308 (log ε = 3.92) and 260 nm (log ε = 4.17)]. The chloro compound **4** is considerably more polar than its precursor, isopropyl bis(pentachlorophenyl)acetate (**2**), while **7** is considerably *less* polar than its precursor methyl bis(pentamethylphenyl)acetate (**8**) (as judged from TLC). This is probably due to dipolar resonance **9** which is important in **4** but not in **7**.



9

The hydrolysis of **7** was surprisingly slow and followed in mixtures of concentrated aqueous HCl and methanol ranging in stoichiometric HCl concentrations from 1.96 to 3.92 M (Table I). The ketene acetal **4** could not be hydrolyzed at all, remaining unchanged in 6.23 M TFA in methanol (50% TFA) over 24 h at 25 °C.

Table I. Acid-Catalyzed Hydrolysis of Bis(pentamethylphenyl)ketene Dimethyl Acetal (7)[a]

[HCl], M[b]	$10^4 k_{obsd}$, s^{-1}	$t_{1/2}$, s
3.92	59.8	116
2.94	15.6	444
1.96	2.4	2900

[a] At 25 °C in methanol–water; the reactions were followed by UV spectroscopy. [b] In 1:1 MeOH–H_2O.

The extreme acid-resistance of these ketene acetals (many orders of magnitude less reactive than the previously least reactive species)[11] is ascribed to resistance to proton transfer from above or below the plane of the double bond by this very bulky aryl groups.

In summary, we have shown that introduction of pentasubstituted aryl groups into the α-carbon of an ester leads to exclusive O-alkylation of the ester enolate and that the resulting ketene acetals are highly acid-resistant. Studies are in hand at present with the novel pentamethylphenyl and pentachlorophenyl groups to determine stabilization of otherwise reactive species.

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(9) Both **4** and **7** give correct elemental analyses and the expected ^1H NMR spectra. The NMR spectrum of the methylated compound **7** is temperature dependent and shows coalescence below 0 °C, due to restricted rotation of the aryl groups. Also formed with **4** in this reaction was bis(pentachlorophenyl)ketene isopropyl 4-methoxybutyl acetal (formed by prior methylation of the solvent THF); starting material was also recovered in both cases.
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A Novel Method for Direct Conversion of Carboxylic Acids to 1,3-Dithianes by 1,3,2-Dithiaborinane–Dimethyl Sulfide and Stannous Chloride

Summary: Reaction of carboxylic acids with 1,3,2-dithiaborinane–dimethyl sulfide in the presence of stannous chloride in tetrahydrofuran affords the corresponding 1,3-dithianes in high yields.

Sir: We wish to report the direct conversion of carboxylic acids into synthetically useful 1,3-dithianes[1] in high yields under mild conditions. The method for this facile conversion consists of a sequence of two steps, partial reduction of carboxylic acids into the aldehyde stage[2] and

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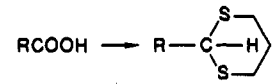
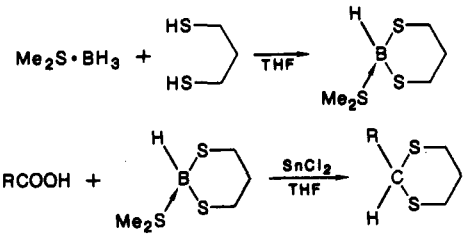
Table I. Direct Conversion of Carboxylic Acids to 1,3-Dithianes by 1,3,2-Dithiaborinane–Dimethyl Sulfide and Stannous Chloride[a,b]



cmpd	R	time, h	isolated yield of 1,3-dithianes, %	bp, °C (mmHg) [mp, °C]	lit. bp, °C (mmHg) [mp, °C]
1	$C_6H_5CH_2$	5	84	133–138 (2.0)	112–115 (0.25)[11]
2	$CH_3(CH_2)_6$	3.5	90	154–159 (4.0)	98–100 (0.07)[12]
3	$(CH_3)_2CH$	5	81	58–63 (1.1)[13]	
4	cyclohexyl	3.5	82	[49–50]	[51.5–52.5][14]
5	1-adamantanyl	6	80	[68–69]	
6	C_6H_5	20	77	[71–72]	[74][15]
7	p-ClC_6H_4	20	71	[86–87]	
8	p-$CH_3OC_6H_4$	20	75	[114–115]	[115–116][12]
9	$Br(CH_2)_{10}$	9	82	151–156 (2.7)	
10	$MeOOC(CH_2)_4$	12	83	123–127 (3.5)	
11	$Et_2NCO(CH_2)_4$	9	59	155–160 (2.0)	
12	$CH_2{=}CH(CH_2)_8$	10	72	155–160 (3.0)	
13	$CH_2{=}CHCH_2$	18	75	61–65 (4.7)	

[a] Reacted with 1.7 equiv of the reagent for aliphatic carboxylic acids and 2.0 equiv for aromatic carboxylic acids in the presence of 1.0 equiv of stannous chloride in tetrahydrofuran at room temperature. [b] See ref 16 for ^1H NMR spectral data of new compounds.

subsequent protection as 1,3-dithianes.[3] As far as we are aware, this is the first example among various partial reductions using complex hydride reducing agents where partial reduction and subsequent protection are cleanly achieved by an one-step procedure.



The reagent, 1,3,2-dithiaborinane–dimethyl sulfide, is readily prepared by treating borane–dimethyl sulfide complex with 1 equiv of 1,3-propanedithiol in tetrahydrofuran and subsequent stirring at room temperature for a week.[4,5] Reaction of phenylacetic acid with 2 equiv of the reagent in tetrahydrofuran at room temperature for 3 h gave a 60:25 mixture of 2-benzyl-1,3-dithiane and phenethyl alcohol along with a small amount of several unidentified byproducts.[6] Encouraged by this result, we investigated the present reaction in detail.

After much experimentation to find out optimum conditions, several important observations have been made. First, the addition of stannous chloride is very effective for clean conversion of carboxylic acids into 1,3-dithianes without accompanying alcohols.[7] Secondly, even more important is the observation that carboxylic acids can be selectively converted into 1,3-dithianes in the presence of alkenes by using stannous chloride as an additive. Thirdly, 2 equiv of the reagent is not essential for this facile conversion.[8,9] The best conditions found for maximum yield and functional group selectivity are to employ 1.7 equiv of 1,3,2-dithiaborinane–dimethyl sulfide and 1.0 equiv of stannous chloride for each mole of aliphatic carboxylic acid in tetrahydrofuran at room temperature. In the case of aromatic carboxylic acids, the use of 2 equiv of the reagent is recommended to obtain better yields without accompanying byproducts.

Table I includes some experimental results and illustrates the applicability, efficiency, mildness, and scope of this method. Simple aliphatic acids are generally converted into the corresponding 1,3-dithianes in high yields within 6 h at room temperature without the contamination of other products. Alicyclic acids such as cyclohexanecarboxylic acid and sterically hindered 1-adamantanecarboxylic acid work equally well. In the case of aromatic acids, the reaction requires 20 h, and the yields are slightly lower. Carboxylic acids containing bromo, ester, and tertiary amide substituents are also cleanly converted into the corresponding 1,3-dithianes without reduction of the substituents. Furthermore, this method is sufficiently selective to distinguish between carboxylic acids and isolated olefinic double bonds, although it has been reported that 1,3,2-dithiaborolane readily hydroborates alkenes.[10]

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(5) To a stirred solution of borane–dimethyl sulfide complex (50 mmol) in THF (220 mL) in 250-mL volumetric flask at 0 °C under nitrogen was added freshly distilled 1,3-propanedithiol (5.0 mL, 50 mmol) dropwise over 20 min. The reaction mixture was stirred at room temperature for 7 days. Finally, the concentration of the reagent was adjusted to 0.2 M solution by the addition of THF. The reagent exhibited a ^{11}B NMR spectrum with a doublet at +62.4 ppm (J_{B-H} = 160 Hz) with reference to boron trifluoride etherate. IR (THF) 2540 (B–H) cm^{-1}. The reagent can be kept in a refrigerator for several weeks without little decomposition. Attempts to isolate 1,3,2-dithiaborinane–dimethyl sulfide were failed. After removal of THF and distillation with Kugelrohr apparatus [55–62 °C (55 mmHg)], ^{11}B NMR of the product showed a singlet at 62.1 ppm and broad peaks at 17.2–34.3 and 34.4–51.5 ppm, indicating that the reagent might decompose to several products during distillation.
(6) It was reported that (aryl- and alkylthio)boranes hydroborated olefins and readily reduced carboxylic acids, aldehydes, and ketones to alcohols. However, their synthetic usefulness has been limited due to the facile cleavage of etheral solvents like THF. Pasto, D. J. *J. Am. Chem. Soc.* **1962**, *84*, 3777. Pasto, D. J.; Cumbo, C. C.; Bulasubramaniyan, P. *J. Am. Chem. Soc.* **1966**, *88*, 2187.
(7) The addition of ZnI_2, LiCl, $SnCl_4$, and $TiCl_4$ did not give satisfactory results. The unique role of stannous chloride is unclear at the present time. It is assumed that stannous chloride may activate a carboxylic acid to promote direct attack of a carboxylic acid by a hydride without the evolution of appreciable amounts of hydrogen gas, producing $RCH(OH)O\overline{BS(CH_2)_3S}$ as a possible major intermediate. Another possibility we can consider is that stannous chloride may liberate dimethyl sulfide from the reagent.
(8) Reaction of carboxylic acids with the reagent did not evolve a stoichiometric amount of hydrogen gas and approximately 0.1 equiv of hydrogen gas evolved at the beginning of the reaction.
(9) In the case of phenylacetic acid, the use of 1.0, 1.3, 1.5, and 1.7 equiv of the reagent in the presence of 1.0 equiv of stannous chloride gave 2-benzyl-1,3-dithiane in 46% (with the recovery of 45% of phenylacetic acid), 55%, 77%, and 84% isolated yield, respectively. The use of more than 2 equiv of the reagent under similar conditions gave small amounts of phenethyl alcohol along with 2-benzyl-1,3-dithiane.
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Thus, undecylenic acid and vinylacetic acid are converted into the corresponding 1,3-dithianes in 72% and 75% yield, respectively.

The following procedure for the reduction of phenylacetic acid is representative. A solution of phenylacetic acid (273 mg, 2.0 mmol) and anhydrous stannous chloride (380 mg, 2.0 mmol) in tetrahydrofuran (5 mL) was stirred at room temperature for 10 min and then 1,3,2-dithiaborinane–dimethyl sulfide complex (0.2 M in THF, 17 mL, 3.4 mmol) was added to the solution. After being stirred at room temperature for 5 h, the reaction mixture was quenched with 10% aqueous KOH solution (10 mL), and the aqueous phase was extracted three times with ethyl ether. The combined extracts were washed with saturated NaCl solution, dried, filtered, and evaporated to dryness. The crude product was purified by passing through a short column of silica gel using ethyl acetate and hexane (1:5) as an eluant to give 2-benzyl-1,3-dithiane (352 mg, 84%).

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(16) **5**: ^{1}H NMR ($CDCl_3$) δ 1.63–2.41 (m, 17 H), 2.81–3.10 (m, 4 H), 4.02 (s, 1 H). **7**: ^{1}H NMR ($CDCl_3$) δ 1.90–2.21 (m, 2 H), 2.81–3.12 (m, 4 H), 5.10 (s, 1 H), 7.21–7.52 (m, 4 H). **9**: ^{1}H NMR ($CDCl_3$) δ 1.31–2.30 (m, 20 H), 2.81–3.03 (m, 4 H), 3.45 (t, J = 6 Hz, 2 H), 4.15 (t, J = 6 Hz, 1 H). **10**: ^{1}H NMR ($CDCl_3$) δ 1.41–2.54 (m, 10 H), 2.71–3.03 (m, 4 H), 3.71 (s, 3 H), 4.15 (t, J = 6 Hz, 1 H). **11**: ^{1}H NMR ($CDCl_3$) δ 1.21 (t, J = 7 Hz, 6 H), 1.50–2.45 (m, 10 H), 2.81–3.03 (m, 4 H), 3.33 (q, J = 7 Hz, 4 H), 4.12 (t, J = 6 Hz, 1 H). **12**: ^{1}H NMR ($CDCl_3$) δ 1.31–2.43 (m, 18 H), 2.85–3.10 (m, 4 H), 4.13 (t, J = 6 Hz, 1 H), 4.81–5.23 (m, 2 H), 5.51–6.10 (m, 1 H). **13**: ^{1}H NMR ($CDCl_3$) δ 1.80–2.15 (m, 2 H), 2.52–3.03 (m, 6 H), 4.05 (t, J = 6 Hz, 1 H), 4.90–5.35 (m, 2 H), 5.61–6.23 (m, 1 H).