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GENERATION AND REACTIONS OF 2-LITHIO-2-SUBSTITUTED-1,3-BENZODITHIOLES; NEW, CONVENIENT ACYL CARBANION EQUIVALENTS

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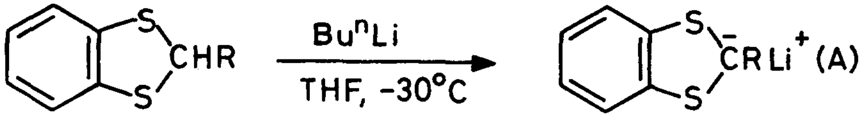
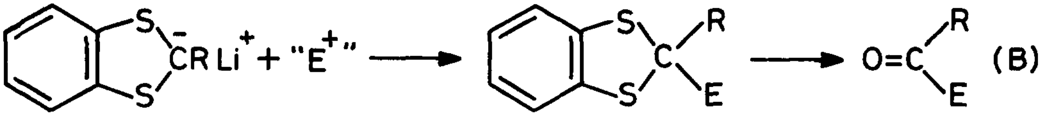
SUMMARY The reaction of Bu^nLi with 2-substituted-1,3-benzodithioles yields anions which react predictably with organic electrophiles to yield products in which the protected carbonyl group is readily unmasked. The anions constitute useful acyl carbanion equivalents.

Acyl carbanion equivalents, particularly anions derived from thioacetals, are now widely used in organic synthesis.[1] Following early recommendations,[2] 2-substituted-1,3-dithian anions have been most widely applied. However, in cases when elimination of the thiol moiety is important, 1,1-bis(phenylthio)alkane anions should have advantages.[3] Indeed, we have found these latter anions to be far superior to dithian anions in reaction with trialkylboranes, which lead to secondary or tertiary alcohols on oxidative work-up.[4] For reactions with hindered trialkylboranes we required anions with similar electronic features to the bis(phenylthio)alkane anions but which were less hindered, and we therefore chose to investigate anions (2) derived from 2-substituted-1,3-benzodithioles (1). We have previously described a convenient two stage synthesis of compounds (1) starting with anthranilic acid.[5]



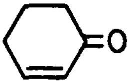
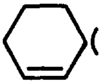
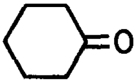
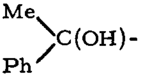
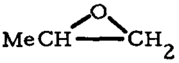
(1) (2)

We find that compounds (1) readily yield anions (2) on reaction with Bu^nLi in THF for 1.5 h at -30°C (Eq. A), at which temperature the anions are stable for long periods. The anions (2) react (Eq. B) with a variety of organic electrophiles, including alkyl halides, aldehydes, ketones, enones, and epoxides, giving good yields of adducts (3) (Table). Addition of (2, R = Me) to cyclohex-2-enone occurs overwhelmingly in the 1,2-sense.



(2) (3) (4)

TABLE[a]

R of (1) used	electrophile	Nature of E in product (3)	m.p. (°C) of product (3)	Yield (%)[b]
H	$\mathrm{Pr^nI}$	$\mathrm{Pr^n}$-	39-40	91
Me	EtCHO	EtCH(OH)-	(oil)	94
Me		(OH)-	(oil)	81
$\mathrm{Pr^i}$	PhCHO	PhCH(OH)-	103-105	78
$\mathrm{Pr^n}$	PhCHO	PhCH(OH)-	62.5	67
$\mathrm{Pr^n}$	MeCHO	MeCH(OH)-	71-74.5	94
$\mathrm{Pr^n}$	$\mathrm{Me_2CHCH_2CHO}$	$\mathrm{Me_2CHCH_2CH(OH)}$-	44.5-45	89
$\mathrm{Pr^n}$		(OH)-	60-64	79[c]
$\mathrm{Pr^n}$	MeCOPh	 $\mathrm{Me(Ph)C(OH)}$-	88.5-90	77
$\mathrm{Pr^n}$	$\mathrm{Bu^nI}$	$\mathrm{Bu^n}$-	[b.100-108° (at 0.15mm Hg)]	93
$\mathrm{Pr^n}$	MeI	Me-	[b.78-86° (at 0.2mm Hg)]	98
$\mathrm{Pr^n}$		$\mathrm{MeCH(OH)CH_2}$-[d]	(Oil)	92

a. All products have been fully characterised.

b. Yield of product after isolation and purification by crystallisation, distillation, or column chromatography (oils).

c. Yield after column chromatography, but n.m.r. showed the presence of some impurity; the oil crystallised very slowly, but only 42% of pure product was obtained in crystalline form.

d. Only one isomer isolated.

Starting material (1, R = Pr^n) and products (3, R = Pr^n, E = Bu^n) and (3, R = Pr^n, E = PhCH(OH)-) are all readily converted in good yields to the parent carbonyl compounds (4) by standard methods,[6,7] which justifies the designation of anions (2) as acyl carbanion equivalents. In our organoborane reactions these anions have advantages over all other thioacetal anions tried.[8]

Since R in (1) is derived from RBr via the Grignard reagent,[5] the simple ketone synthesis (1 ⟶ 4, E = alkyl) involves adding each side chain R and R' separately as an alkyl halide to the carbonyl carbon atom. The aldehyde synthesis is a one carbon homologation. The α-hydroxyketone synthesis is regio-specific in that the bond between the carbonyl carbon atom and the α-hydroxy carbon atom is made during the reaction and the product is released under conditions mild enough not to cause transposition of CO and CHOH.

The products (3) obtained in reactions of type (B) are themselves of chemical interest. For example, the α-hydroxythioketals obtained from reactions of anions (2) with aldehydes and ketones undergo some interesting electrophile-induced rearrangements, which are reported separately.[9]

The following procedures for generation and reaction of anion (2, R = Pr^n) and for hydrolysis of (3, R = Pr^n, E = Bu^n) are representative. To 2-propyl-1,3-benzodithiole (0.98 g, 5 mmol) in THF (5 ml), stirred magnetically under nitrogen at -30°C, was added Bu^nLi (5.5 mmol, as a solution in hexane). After 1.5 h at -30°C, Bu^nI (0.92 g, 5 mmol) was added and the mixture was allowed to warm to room temperature and remain for 2 h at this temperature. The mixture was poured into water (100 ml), extracted into light petroleum (boiling range 30-40°C, 2 x 200 ml), washed with water (3 x 100 ml), dried (Na_2SO_4), and evaporated to yield the crude product. Distillation gave pure 2-butyl-2-propyl-1,3-benzodithiole, 1.17 g, 93%, b. 100-108°C at 0.15 mm Hg.

To vigorously stirred red HgO (0.43 g, 2 mmol) and BF_3 etherate (0.28 g, 2 mmol) in 15% aqueous THF (2.5 ml), under nitrogen, was added 2-butyl-2-propyl-1,3-benzodithiole (0.25 g, 1 mmol). The mixture was refluxed for 30 min. After cooling, the product was extracted into diethyl ether, washed with aq. Na_2CO_3 and aq. NaCl, dried (Na_2SO_4), evaporated, and distilled at atmospheric pressure to yield octan-4-one, 0.114 g (89%); b. 162°C (lit.[10] 163°C); n_D^{24} = 1.413 (lit.[10] n_D^{14} = 1.417).

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