Alkylation of 2-Lithio-1,3-dithianes with Arenesulfonates of Primary Alcohols

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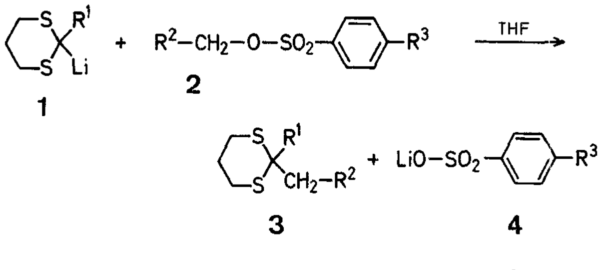
Many preparatively useful, highly reactive organolithium reagents cannot be alkylated by tosylates of primary or secondary alcohols in good yields[1,2,3]. This means that for coupling reactions the simple and "mild" sequence R—OH→R—OTos→R—R′ cannot be used. Thus, the alkyl halides have to be prepared from the alcohols and submitted to the coupling reaction. There is an evident relation between anion stabilization ("softness") and yield of substitution reactions of this type. Metallation at the methyl group or at the *ortho* position[5] of tosylates as well as one-electron transfer (cf. halides[6]) are possible side reactions with the more reactive species. Thus, in the field of nucleophilic acylation, the lithio derivatives of the more stabilized anions derived from thioacetal mono-*S*-oxides or from cyanohydrins have been reported to react with tosylates[7] while 2-lithio-1,3-dithianes (**1**) undergo this coupling only intramolecularly[8] under the standard conditions (<0°, tetrahydrofuran/hexane)[9].



We have now found that benzenesulfonates (**2**, $R^3 = H$) of primary alcohols react smoothly with the lithio derivatives of 1,3-dithiane and 2-phenyl-1,3-dithiane (**1**, $R^1 = H$, C_6H_5) at room temperature (24 h) to give the 2-alkyl derivatives **3** in high yields. Since **1**, $R^1 = H$, normally decomposes by proton abstraction from the solvent under these conditions, it is obviously stabilized in the above reaction by the formation of an ate-complex[10] with the sulfonate salt **4**. Tosylates (**2**, $R^3 = CH_3$) give relatively low yields in the reaction with 2-lithio-1,3-dithiane (**1**, $R^1 = H$), while they are as suitable as benzenesulfonates (**2**, $R^3 = H$) in the case of 2-lithio-2-phenyl-1,3-dithiane (**1**, $R^1 = C_6H_5$).

The present procedure gives good results only with *prim*-alkyl arenesulfonates and with the lithio derivatives of 1,3-dithiane and 2-phenyl-1,3-dithiane. As shown by one example in the table, methyl benzenesulfonate alkylates even the hindered, highly reactive 2-lithio-2-isopropyl-1,3-dithiane.

Alkylation of 2-Lithio-1,3-dithianes (1) with Arenesulfonates (2); General Procedure:

A solution of the 2-lithio-1,3-dithiane **1** is prepared in the usual manner[1] from the corresponding 1,3-dithiane (10 mmol) in tetrahydrofuran (20 ml) and a 1.6 *M* solution of butyllithium (10–10.5 mmol) in hexane at −30°. To this solution, the arenesulfonate (10 mmol) in tetrahydrofuran (8 ml) is added with stirring. The cooling bath is then removed, and stirring is continued for 24 h. A colorless precipitate separates from the slightly yellow solution. The mixture is poured into water (3 vol), and then extracted several times with pentane. The extract is washed with aqueous potassium hydroxide, dried with potassium carbonate, and evaporated to leave crude **3**. Purification may be effected by recrystallization, distillation in vacuo, or chromatography on silica gel.

Table. Alkylation of 2-Lithio-1,3-dithianes (**1**) with *prim*-Alkyl Arenesulfonates (**2**) at 25° (24 h)

R^1	R^2	R^3	Yield[a] of **3** [%]	m.p. or b.p.
H	CH_3	H	85	b.p. 83°/14 torr
H	C_2H_5	H	83	b.p. 43°/0.3 torr
H	C_2H_5	CH_3	61	
H	n-C_3H_7	H	75	b.p. 51°/0.5 torr
H	n-C_3H_7	CH_3	43	
H	n-C_8H_{17}	H	68[b]	b.p. 112°/0.5 torr
i-C_3H_7	CH_3	H	90	b.p. 58°/0.3 torr
C_6H_5	CH_3	H	92	b.p. 74°/0.005 torr; m.p. 36° (from methanol)
C_6H_5	C_2H_5	H	87[c]	b.p. 77–78°/0.005 torr; m.p. 35° (from methanol)
C_6H_5	C_2H_5	CH_3	85	
C_6H_5	n-C_3H_7	H	89[d]	b.p. 87°/0.01 torr
C_6H_5	n-C_8H_{17}	H	90[e]	b.p. 111°/0.01 torr

[a] Yield of crude product. All compounds were identified by comparison of their physical properties and their ^{1}H-N.M.R. spectra with those of authentic samples[1].

[b] Reaction time: 3 days.

$C_7H_{14}S_2$	calc.	C 62.00	H 10.41
(162.2)	found	61.80	10.43
[c] $C_{12}H_{16}S_2$	calc.	C 64.23	H 7.18
(224.3)	found	64.00	7.11
[d] $C_{13}H_{18}S_2$	calc.	C 65.49	H 7.61
(238.3)	found	65.27	7.45
[e] $C_{18}H_{28}S_2$	calc.	C 70.06	H 9.14
(308.4)	found	69.99	9.16

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