

n-Butyl-lithium-induced Cleavage of Several Dithioacetals Derived from Diaryl Ketones

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The reaction of 2,2-diaryl-1,3-dithiolanes and -1,3-dithianes, and diaryl ketone di-n-propyl dithioacetals with n-butyl-lithium in tetrahydrofuran followed by alkylation with alkyl halides gives 1-n-butylthio-2-(1,1-diarylalkylthio)ethanes and -3-(1,1-diarylalkylthio)propanes, and 1,1-diarylalkyl n-propyl sulphides, respectively. The process probably involves S-addition of an n-butyl anion with simultaneous cleavage of the bond between the sulphur atom and the adjacent carbon atom giving an intermediate anionic species, which is then alkylated by the alkyl halide.

There have been many reports¹⁻¹¹ concerning the reactions of 1,3-dithiolane and 1,3-dithiane derivatives with a strong base such as n-butyl-lithium or, less commonly, lithium diisopropylamide. The products from these derivatives are thought to arise *via* initial deprotonation at either C-2 or C-4 of the ring.¹² Deprotonation at C-5 of 1,3-dithiane in the gas phase is also reported by Wilson and co-workers,¹² and it is obvious that this initial deprotonation plays an important part in all these reactions. We now report the reactions of several cyclic and acyclic dithioacetals derived from diaryl ketones such as 2,2-diaryl-1,3-dithiolanes and -1,3-dithianes, and diaryl ketone di-n-propyl dithioacetals with n-butyl-lithium in tetrahydrofuran, which occur by a different mechanism from the above-mentioned one. When 2,2-diaryl-1,3-dithiolanes (**1**) were treated with an excess of n-butyl-lithium in tetrahydrofuran and an appropriate alkyl halide then added, we obtained the corresponding 1-n-butylthio-2-(1,1-diarylalkylthio)ethanes (**3**) in good to near-quantitative yields (Table 1).

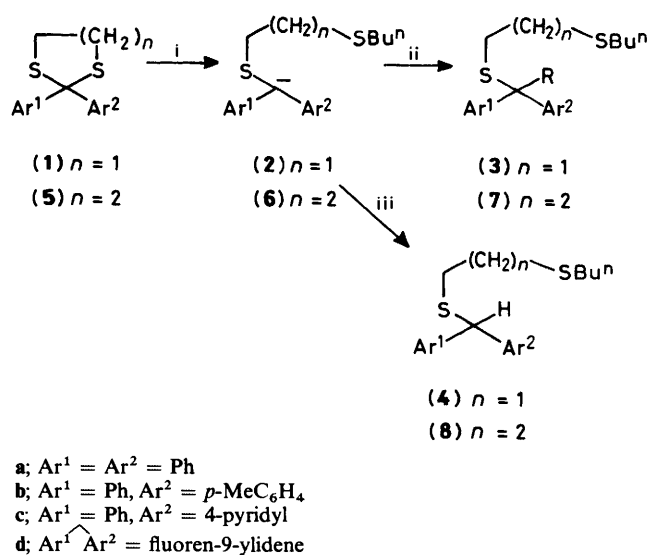
The formation of compounds (**3**) is easily understandable and occurs *via* S-addition of an n-butyl anion with simultaneous cleavage of the bond between the sulphur atom and the adjacent C-2, leading to an intermediate anion (**2**); this is then alkylated by alkyl halide to afford (**3**) (Scheme 1). When aqueous ammonium chloride was used instead of the alkyl halides as the trapping agent, the corresponding 1-n-butylthio-2-(diaryl-methylthio)ethanes (**4**) were formed (Table 1), supporting the proposed intermediate (**2**).

The reaction of 2,2-diaryl-1,3-dithianes (**5**) with an excess of n-butyl-lithium in tetrahydrofuran proceeded similarly to give an intermediate anionic species (**6**) which, when trapped by alkyl halide, gave the corresponding 1-n-butylthio-3-(1,1-diarylalkylthio)propanes (**7**) in excellent yields (Table 2). Evidence for the presence of the anion (**6**) was also obtained by treating it with aqueous ammonium chloride to yield the 1-n-butylthio-3-(diarylmethylthio)propanes (**8**). The results together with the physical properties of (**7**) and (**8**) are summarized in Table 2.

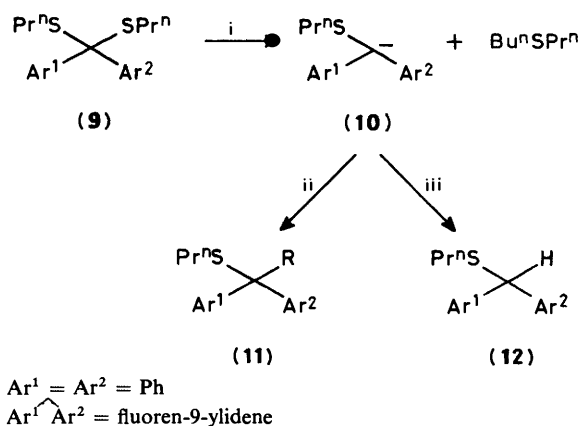
When the diaryl ketone di-n-propyl dithioacetals (**9**) were treated similarly with n-butyl-lithium in tetrahydrofuran and either an alkyl halide or aqueous ammonium chloride then added, the corresponding 1,1-diarylalkyl n-propyl sulphides (**11**) or diarylmethyl n-propyl sulphides (**12**) were isolated together with n-butyl n-propyl sulphide (Scheme 2).

The formation of product (**11**) or (**12**) is easily understandable by analogy with the mechanism proposed in the case of compound (**1**) or (**5**). The results together with the physical data of (**11**) and (**12**) are summarized in Table 3.

All the reactions using cyclic and acyclic dithioacetals, such as 2-alkyl-2-aryl-1,3-dithiolanes and -1,3-dithianes, 2,2-dialkyl-1,3-dithiolanes and -1,3-dithianes, and di-n-propyl dithioacetals



Scheme 1. Reagents: i, BuⁿLi; ii, RX; iii, H⁺



Scheme 2. Reagents: i, BuⁿLi; ii, RX; iii, H⁺

of alkyl aryl ketones and of dialkyl ketones, resulted in the recovery of the starting substrate together with a small amount of tarry substance or, in some instances, complete conversion into the tarry material. Thus, a possible requirement for the occurrence of this conversion is the presence of two aryl substituents at a carbon atom between the two sulphur atoms of the starting dithioacetals. The electron-withdrawing

Table 1. The conversion of the dithiolanes (1) into the sulphides (3) or (4)

Starting substrate	Trapping agent	Product ^a	Yield ^b (%)	B.p. (°C/Torr)	¹ H N.m.r. δ/p.p.m. (CCl ₄)
(1a)	MeI	(3a; R = Me)	97	123/2.5	0.6—1.0 (m, 3 H), 1.0—1.6 (m, 4 H), 1.99 (s, 3 H), 2.1—2.5 (m, 2 H), 2.32 (s, 4 H), 7.0—7.5 (m, 10 H)
(1a)	EtI	(3a; R = Et)	92	147/1	0.75 (t, 3 H, <i>J</i> 7 Hz), 0.7—1.1 (m, 3 H), 1.1—1.6 (m, 4 H), 2.1—2.5 (m, 2 H), 2.20 (s, 4 H), 2.28 (q, 2 H, <i>J</i> 7 Hz), 7.0—7.4 (m, 10 H)
(1b)	MeI	(3b; R = Me)	83	140/2.5	0.6—1.0 (m, 3 H), 1.0—1.7 (m, 4 H), 1.95 (s, 3 H), 2.1—2.5 (m, 2 H), 2.24 (s, 3 H), 2.38 (s, 4 H), 6.9—7.5 (m, 9 H)
(1b)	EtI	(3b; R = Et)	94	143/2.5	0.76 (t, 3 H, <i>J</i> 7 Hz), 0.7—1.1 (m, 3 H), 1.1—1.7 (m, 4 H), 2.19 (s, 3 H), 2.1—2.3 (m, 2 H), 2.28 (q, 2 H, <i>J</i> 7 Hz), 2.29 (s, 4 H), 6.8—7.4 (m, 9 H)
(1c)	MeI	(3c; R = Me)	96	115/2.5	0.7—1.0 (m, 3 H), 1.1—1.6 (m, 4 H), 1.92 (s, 3 H), 2.2—2.5 (m, 2 H), 2.24 (s, 4 H), 6.9—7.2 (m, 7 H), 8.1—8.4 (m, 2 H)
(1c)	EtI	(3c; R = Et)	96	126/4.5	0.75 (t, 3 H, <i>J</i> 7 Hz), 0.7—1.0 (m, 3 H), 1.0—1.5 (m, 4 H), 2.1—2.4 (m, 2 H), 2.18 (s, 4 H), 2.25 (q, 2 H, <i>J</i> 7 Hz), 7.0—7.3 (m, 7 H), 8.2—8.5 (m, 2 H)
(1c)	Bu ⁿ I	(3c; R = Bu ⁿ)	99	119/2.5	0.6—1.0 (m, 6 H), 1.0—1.7 (m, 8 H), 2.0—2.5 (m, 4 H), 2.18 (s, 4 H), 7.0—7.3 (m, 7 H), 8.2—8.4 (m, 2 H)
(1c)	Bu ⁿ Br	(3c; R = Bu ⁿ)	89		
(1d)	MeI	(3d; R = Me)	98	142/2.5	0.6—1.0 (m, 3 H), 1.0—1.4 (m, 4 H), 1.63 (s, 3 H), 1.82 (s, 4 H), 1.7—2.0 (m, 2 H), 7.0—7.6 (m, 8 H)
(1d)	EtI	(3d; R = Et)	92	142/1	0.40 (t, 3 H, <i>J</i> 7 Hz), 0.6—1.0 (m, 3 H), 1.0—1.4 (m, 4 H), 1.82 (s, 4 H), 1.7—2.0 (m, 2 H), 2.10 (q, 2 H, <i>J</i> 7 Hz), 7.0—7.6 (m, 8 H)
(1d)	Bu ⁿ I	(3d; R = Bu ⁿ)	98	152/2.5	0.5—1.3 (m, 14 H), 1.80 (s, 4 H), 1.7—2.2 (m, 4 H), 7.0—7.6 (m, 8 H)
(1d)	Bu ⁿ Br	(3d; R = Bu ⁿ)	91		
(1d)	Pr ⁱ Br	(3d; R = Pr ⁱ)	96	157/1.5	0.80 (d, 6 H, <i>J</i> 6 Hz), 0.6—1.0 (m, 3 H), 1.0—1.4 (m, 4 H), 1.7—2.0 (m, 2 H), 1.82 (s, 4 H), 2.2—2.7 (m, 1 H), 7.0—7.7 (m, 8 H)
(1a)	NH ₄ Cl ^c	(4a)	96	148/4.5	0.7—1.1 (m, 3 H), 1.1—1.6 (m, 4 H), 2.1—2.4 (m, 2 H), 2.47 (s, 4 H), 5.07 (s, 1 H), 7.0—7.4 (m, 10 H)
(1b)	NH ₄ Cl ^c	(4b)	97	114/2.5	0.7—1.1 (m, 3 H), 1.1—1.8 (m, 4 H), 2.25 (s, 3 H), 2.1—2.5 (m, 2 H), 2.58 (s, 4 H), 5.15 (s, 1 H), 6.9—7.5 (m, 9 H)
(1c)	NH ₄ Cl ^c	(4c)	91	122/4	0.7—1.0 (m, 3 H), 1.1—1.6 (m, 6 H), 2.2—2.5 (m, 2 H), 2.48 (s, 4 H), 5.03 (s, 1 H), 7.0—7.4 (m, 7 H), 8.1—8.7 (m, 2 H)
(1d)	NH ₄ Cl ^c	(4d)	97	120/4.5	0.6—1.0 (m, 3 H), 1.0—1.4 (m, 4 H), 1.8—2.1 (m, 2 H), 1.96 (s, 4 H), 4.71 (s, 1 H), 7.1—7.7 (m, 8 H)

^a These products (3) and (4) showed correct combustion analyses (C ± 0.30%, H ± 0.26%) and exact mass measurements by mass spectrometry.

^b Yield of isolated product based on (1). ^c Aqueous solution of ammonium chloride.

Table 2. The conversion of the dithanes (5) into the sulphides (7) or (8)

Starting substrate	Trapping agent	Product ^a	Yield ^b (%)	B.p. (°C/Torr)	¹ H N.m.r. δ/p.p.m. (CCl ₄)
(5b)	EtI	(7b; R = Et)	99	159/1	0.75 (t, 3 H, <i>J</i> 7 Hz), 0.6—1.1 (m, 3 H), 1.1—1.8 (m, 6 H), 2.15 (q, 2 H, <i>J</i> 7 Hz), 2.25 (s, 3 H), 2.0—2.6 (m, 6 H), 6.8—7.4 (m, 9 H)
(5c)	MeI	(7c; R = Me)	84	127/4	0.7—1.1 (m, 3 H), 1.1—1.9 (m, 6 H), 1.93 (s, 3 H), 2.1—2.5 (m, 6 H), 6.9—7.3 (m, 7 H), 8.1—8.6 (m, 2 H)
(5d)	MeI	(7d; R = Me)	89	151/1	0.7—1.1 (m, 3 H), 1.1—1.9 (m, 6 H), 1.67 (s, 3 H), 2.0—2.3 (m, 6 H), 7.0—7.7 (m, 8 H)
(5a)	NH ₄ Cl ^c	(8a)	98	143/1	0.7—1.1 (m, 3 H), 1.1—2.0 (m, 6 H), 2.2—2.7 (m, 6 H), 4.98 (s, 1 H), 6.9—7.5 (m, 10 H)
(5b)	NH ₄ Cl ^c	(8b)	98	156/1.1	0.7—1.1 (m, 3 H), 1.1—2.0 (m, 6 H), 2.1—2.6 (m, 6 H), 2.23 (s, 3 H), 4.93 (s, 1 H), 6.8—7.4 (m, 9 H)

^a These products (7) and (8) showed correct combustion analyses (C ± 0.29%, H ± 0.29%) and exact mass measurements by mass spectrometry.

^b Yield of isolated product based on (5). ^c Aqueous solution of ammonium chloride.

characteristics of these substituents would facilitate both the attack of the *n*-butyl anion at the sulphur atom and the subsequent electron transfer leading to the intermediate anionic species. Also, these substituents can delocalize the negative charge in the anionic species.

When compounds (4b), (4d), (12a), and (12b), all of which are obtained in the above conversion, were treated with an excess of lithium di-isopropylamide in tetrahydrofuran, and methyl iodide or ethyl iodide then added, we obtained the corresponding alkylated compounds. The delocalization of the

negative charge in the intermediate anionic species by the two aromatic substituents is also illustrated by the reaction. The results are summarized in Table 4.

Experimental

Materials.—All dithioacetals used in this research were prepared by the AlCl₃-catalysed reaction of carbonyl compounds with thiols such as ethane-1,2-dithiol, propane-1,3-dithiol, and propane-1-thiol.¹⁵ Tetrahydrofuran was dried over

Table 3. The conversion of the bis-sulphides (9) into the monosulphides (11) or (12)

Starting substrate	Trapping agent	Product ^a			
			Yield ^b (%)	B.p. (°C/Torr)	¹ H N.m.r. δ/p.p.m. (CCl ₄)
(9a)	MeI	(11a; R = Me)	98	123/4	0.83 (t, 3 H, J 6 Hz), 0.9—1.7 (m, 2 H), 1.95 (s, 3 H), 2.12 (t, 2 H, J 6 Hz), 7.0—7.4 (m, 10 H)
(9a)	EtI	(11a; R = Et)	98	138/4	0.77 (t, 3 H, J 7 Hz), 0.82 (t, 3 H, J 6 Hz), 0.9—1.7 (m, 2 H), 1.95 (t, 2 H, J 6 Hz), 2.27 (q, 2 H, J 7 Hz), 7.0—7.5 (m, 10 H)
(9a)	Bu ⁿ Br	(11a; R = Bu ⁿ)	96	152/4	0.80 (t, 3 H, J 6 Hz), 0.6—1.0 (m, 3 H), 1.0—1.5 (m, 6 H), 1.95 (t, 2 H, J 6 Hz), 2.0—2.4 (m, 2 H), 6.9—7.4 (m, 10 H)
(9b)	MeI	(11b; R = Me)	95	139/4	0.61 (t, 3 H, J 6 Hz), 0.7—1.3 (m, 2 H), 1.52 (t, 2 H, J 6 Hz), 1.63 (s, 3 H), 7.0—7.6 (m, 8 H)
(9b)	EtI	(11b; R = Et)	93	146/5	0.42 (t, 3 H, J 7 Hz), 0.62 (t, 3 H, J 6 Hz), 0.6—1.3 (m, 2 H), 1.57 (t, 2 H, J 6 Hz), 2.13 (q, 2 H, J 7 Hz), 7.0—7.7 (m, 8 H)
(9b)	Bu ⁿ Br	(11b; R = Bu ⁿ)	95	149/4.5	0.4—1.3 (m, 12 H), 1.53 (t, 2 H, J 6 Hz), 1.9—2.3 (m, 2 H), 7.0—7.7 (m, 8 H)
(9a)	NH ₄ Cl ^c	(12a) ^d	94	136/5	0.90 (t, 3 H, J 6 Hz), 1.2—1.8 (m, 2 H), 2.23 (t, 2 H, J 6 Hz), 4.99 (s, 1 H), 7.0—7.4 (m, 10 H)
(9b)	NH ₄ Cl ^c	(12b)	91	131/4.5	0.70 (t, 3 H, J 6 Hz), 0.7—1.5 (m, 2 H), 1.72 (t, 2 H, J 6 Hz), 4.68 (s, 1 H), 7.0—7.7 (m, 8 H)

^a These products (11) and (12) showed correct combustion analyses (C ± 0.31%, H ± 0.25%) and exact mass measurements by mass spectrometry. The minor product n-butyl n-propyl sulphide was not isolated. ^b Yield of isolated product based on (9). ^c Aqueous solution of ammonium chloride. ^d Of the products obtained in this work only (12a) is a known compound.^{13,14}

Table 4. The conversion of the products (4b), (4d), (12a), and (12b) to the sulphides (3b; R = Et), (3d; R = Me), (11a; R = Et), and (11b; R = Me)

Starting substrate	Trapping agent	Product ^a	
			Yield ^b (%)
(4b)	EtI	(3b; R = Et)	89
(4d)	MeI	(3d; R = Me)	96
(12a)	EtI	(11a; R = Et)	98
(12b)	MeI	(11b; R = Me)	97

^a Details of these products are given in Tables 1 and 3. ^b Isolated yield based on the starting sulphide.

lithium aluminium hydride and then distilled. The other reagents were commercially available and were used without further purification. Ether refers to diethyl ether.

Formation of the 1-n-Butylthio-2-(1,1-diaryllalkylthio)ethanes (3), the 1-n-Butylthio-3-(1,1-diaryllalkylthio)propanes (7), and the 1,1-Diaryllalkyl n-Propyl Sulphides (11).—A 1.56M-solution (2.12 ml, 3.3 mmol) of n-butyl-lithium in hexane was added under nitrogen to tetrahydrofuran (7 ml) at -78 °C, and the solution was stirred at that temperature for 10 min. To the cooled solution was added with stirring the dithioacetal (1.5 mmol) [(1), (5), or (9)] in tetrahydrofuran (4 ml). The solution was allowed to warm to -15 °C and the stirring was continued for 1 h. Thus the solution containing the intermediary anionic species [(2), (6), or (10)] was prepared. The solution was cooled again to -78 °C, an alkyl halide (3.3 mmol) was added with stirring, the reaction mixture was warmed to -10 to -5 °C, and the stirring was continued for 1 h and then for 24 h at room temperature. The reaction mixture was quenched with water (100 ml) and saturated aqueous ammonium chloride (20 ml), and then extracted with ether (3 × 60 ml). The combined ethereal extracts were dried (MgSO₄), filtered, and concentrated under reduced pressure to give a pale yellow residue, which was subjected to column chromatography.

Formation of the 1-n-Butylthio-2-(diarylmethylthio)ethanes (4) the 1-n-Butylthio-3-(diarylmethylthio)propanes (8), and the

Diarylmethyl n-Propyl Sulphides (12).—The solution containing the intermediary anionic species [(2), (6), or (10)] was cooled to -78 °C and saturated aqueous ammonium chloride (5 ml) instead of the alkyl halide was added with stirring. The mixture was allowed to warm to -10 to -5 °C and the stirring was continued for 1 h at this temperature and then for 24 h at room temperature. The mixture was quenched with water (100 ml) and saturated aqueous ammonium chloride (20 ml), and then worked up as above.

Deprotonation of Compounds (4b), (4d), (12a), and (12b) by Lithium Di-isopropylamide and Subsequent Alkylation.—To lithium di-isopropylamide prepared from di-isopropylamine (0.35 g, 3.5 mmol) in tetrahydrofuran (7 ml) and a 1.56M-solution (2.12 ml, 3.3 mmol) of n-butyl-lithium in hexane was added at -78 °C the compound [1-n-butylthio-2-[p-tolyl-(phenyl)methylthio]ethone (4b), 1-n-butylthio-2-fluoren-9-ylidenemethylthioethane (4d), diphenylmethyl n-propyl sulphide (12a), fluoren-9-ylidenemethyl n-propyl sulphide (12b)] (1.5 mmol) in tetrahydrofuran (4 ml). The reaction mixture was allowed to warm to -15 °C and the stirring was continued for 15 min. The solution was cooled to -78 °C and alkyl halide (3.3 mmol) was added with stirring. The mixture was then allowed to warm to -10 to -5 °C and stirred for 1 h at this temperature and then for 24 h at room temperature. It was then quenched with water (100 ml) and saturated aqueous ammonium chloride (20 ml) and worked up as above.

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