The Lithium Diisopropylamide-Induced Fragmentation of 2,2-Diphenyl-1,3-dithiolane *S*-Oxide and Several 2,2-Diaryl-1,3-dithiolane *S,S'*-Dioxides

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The reaction of 2,2-diphenyl-1,3-dithiolane *S*-oxide with lithium diisopropylamide results in fragmentation to thiobenzophenone followed by further conversion leading to alkyl diphenylmethyl sulfide on trapping with alkyl halide. The reaction of 2,2-diaryl-1,3-dithiolane *S,S'*-dioxides with lithium diisopropylamide proceeded smoothly to afford 1,1-diaryl-*N,N*-diisopropylmethanesulfinamides in moderate yields via the intermediate diaryl thioketone *S*-oxides.

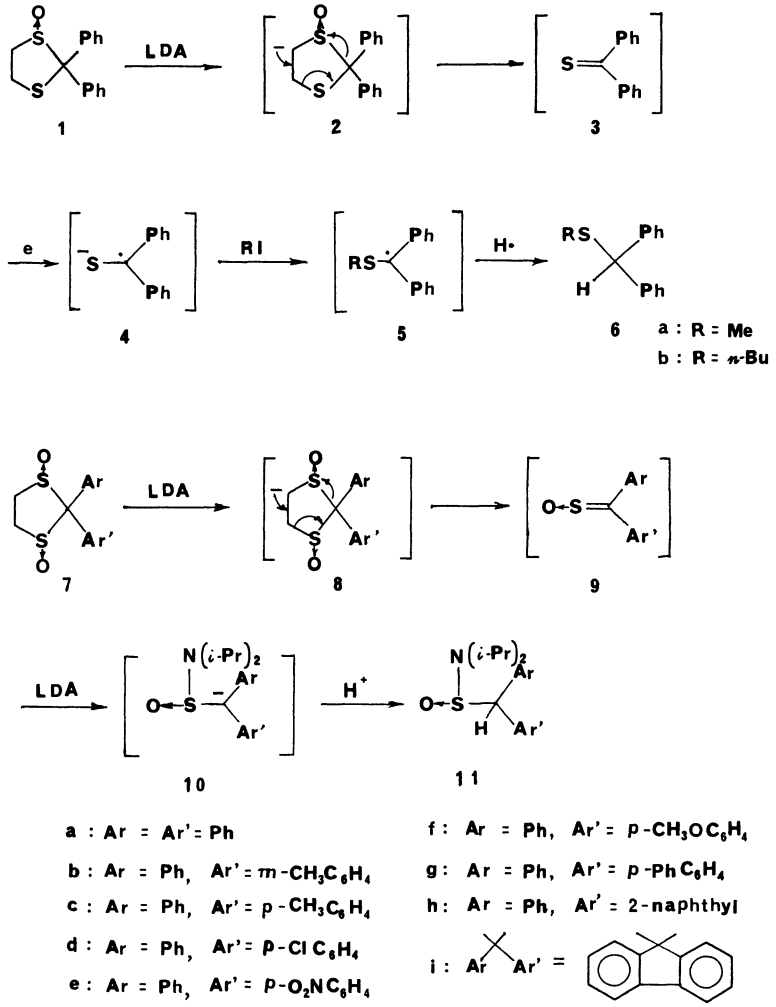
It is well-known that 2-lithio-1,3-dithiolanes undergo facile elimination to form ethylene and dithiocarbonates.[1,2] On the other hand, 4-lithio-1,3-dithiolanes, as unstable intermediates occurring in the reaction of 1,3-dithiolanes with butyllithium, undergo facile fragmentation to the corresponding thiocarbonyl compounds followed by further reaction such as reduction, *S*-addition, *C*-addition, or double addition with butyllithium.[3,4] 4-Lithio-1,3-dithiolanes bearing two aromatic substituents at *C*-2 are also formed by the reaction of 2,2-diaryl-1,3-dithiolanes with less nucleophilic lithium diisopropylamide (LDA), and diaryl thioketones arising from these 4-lithio-1,3-dithiolanes afforded alkyl diarylmethyl sulfides or their α-alkyl derivatives by quenching the reaction mixture with alkyl halides.[2] The same fragmentation-alkylation sequence using LDA has also been applied to several 2-alkyl-2-aryl-1,3-dithiolanes.[5] Moreover, it has been reported[6] that 1,3-dithiolane *S,S*-dioxides derived from benzophenone and camphor undergo facile metalation with LDA or potassium *t*-butoxide followed by fragmentation to the corresponding thiobenzophenone and thiocamphor, respectively. These thioketones have been isolated[6] without any conversion by the bases used in the reaction systems. With these considerations in mind, we have studied the reaction of 2,2-diphenyl-1,3-dithiolane *S*-oxide (**1**) and several 2,2-diaryl-1,3-dithiolane *S,S'*-dioxides (**7**) with LDA in tetrahydrofuran.

Results and Discussion

A noteworthy observation[7] on the stereoselectivity in oxidation of 2-substituted 1,3-dithiolanes with *m*-chloroperbenzoic acid is recorded in the literature. Also, the oxidation of a few 2,2-disubstituted 1,3-dithiolanes such as 2,2-diphenyl-1,3-dithiolane with H_2O_2 providing the corresponding *S*-oxides or *S,S'*-dioxides has been reported.[8] However, no report thus far appears in which the oxidation of 2,2-diaryl-1,3-dithiolanes with *m*-chloroperbenzoic acid is described. Although not proved, almost all of **1** and **7** used in this research will probably be a mixture of two or more stereoisomers. Compound **1** is a racemic mixture, and both 2,2-diphenyl-1,3-dithiolane *S,S'*-dioxide (**7a**) and spiro[1,3-dithiolane-2,9'-[9*H*]fluorene] *S,S'*-dioxide (**7i**) are mixtures of cis and trans-forms.[9] Other 2,2-diaryl-1,3-dithiolane *S,S'*-dioxides (**7b—h**) are constituted of four stereoisomers. This may be evidenced by the fact that most of **7** melt over a relatively broad range of temperature, especially 2-(2-naphthyl)-2-phenyl-1,3-dithiolane *S,S'*-dioxide (**7h**) melts abnormally.[10] Alo, according to Henbest and his coworker,[11] the competitive formation of 2,2-diaryl-1,3-dithiolane *S,S*-dioxides in the oxidative process of 2,2-diaryl-1,3-dithiolanes with *m*-chloroperbenzoic acid giving **7** seems to be negligible. Thus, **1** and **7** have been prepared using *m*-chloroperbenzoic acid and submitted to the action of LDA in tetrahydrofuran.

The reaction of **1** with an excess of LDA proceeded smoothly via proton abstraction at *C*-5 followed by cyclo-elimination affording thiobenzophenone (**3**) and an ethylenesulfinate anion. The resulting **3** is labile in this reaction system, and hence **3** is converted to alkyl diphenylmethyl sulfides (**6**) via a process involving a one-electron transfer from LDA, the charge neutralization by the added alkyl iodide (methyl iodide or butyl iodide), and the abstraction of a hydrogen radical from tetrahydrofuran. Thus, we have obtained excellent yields of diphenylmethyl methyl sulfide (**6a**) and butyl diphenylmethyl sulfide (**6b**), which are identical with those obtained[2] by the reaction of 2,2-diphenyl-1,3-dithiolane itself and LDA followed by trapping with methyl iodide and butyl iodide, respectively.

Next, 2,2-diaryl-1,3-dithiolane *S,S'*-dioxides (**7a—i**) were submitted to fragmentation with an excess of LDA in tetrahydrofuran at low temperature. These, without any trapping with alkyl halide, led to the corresponding 1,1-diaryl-*N,N*-diisopropylmethanesulfinamides (**11a—i**) via a successive attack of 2 molar equivalents of LDA to **7a—i**. Though the exact mechanism is still in doubt, it is certain that the deprotonation at *C*-4 of the ring affording **8** is the first step. Probably, the intermediate **8** undergoes cyclo-elimination leading to diaryl thioketone *S*-oxides (**9**) and an ethylenesulfinate anion. The former is converted to an anionic species (**10**) by the nucleophilic attack of a second LDA molecule. In another experiment with **7a**,



in which only a 1.2-fold excess of LDA was used, *N,N*-diisopropyl-1,1-diphenylmethanesulfinamide (**11a**) was obtained in 28% yield. This result indicates that the nucleophilic attack of a second LDA molecule to thiobenzophenone *S*-oxide (**9a**) takes place very rapidly. When D_2O was used in the quenching step of the experiment, which was conducted with **7a** and a 2.5-fold excess of LDA, 1-deuterio-*N,N*-diisopropyl-1,1-diphenylmethanesulfinamide was obtained in almost the same yield as **11a**. These experimental facts substantiate the proposed mechanical assignment of the present reaction. The results with **1** and **7a—i** are summarized in Table 1. The physical and analytical data of the products obtained are listed in Table 2.

Except **11a** and *N,N*-diisopropyl-9*H*-fluorene-9-sulfinamide (**11i**), the 1,1-diaryl-*N,N*-diisopropylmethanesulfinamides (**11b—h**) obtained possess two dissimilar asymmetric centers, and hence four stereoisomers are possible. Each of the two products, 1-(4-chlorophenyl)-*N,N*-diisopropyl-1-phenylmethanesulfinamide (**11d**) and *N,N*-diisopropyl-1-(4-nitrophenyl)-1-phenylmethanesulfinamide (**11e**), was chromatographically separated into two kinds of racemates distinguishable from each other by a difference in melting point. Each of **11a** and **11i** is a racemic mixture; the former was isolated as crystals with relatively sharp melting point and the latter was an oily substance.

Experimental

Preparation of 2,2-Diphenyl-1,3-dithiolane *S*-Oxide (1). To a stirred, cooled (0 °C) solution of 2,2-diphenyl-1,3-dithiolane (5.2 g, 20 mmol) in dichloromethane (50 ml) a solution of *m*-chloroperbenzoic acid (3.4 g, 20 mmol) in dichloromethane (40 ml) was added during 2 h, followed by stirring at reflux temperature for 3 h. The reaction mixture was cooled overnight in an ice bath. The precipitated benzoic acid was filtered off and the filtrate was washed with 10% aqueous $NaHCO_3$ (3×50 ml). The washings were extracted with dichloromethane (3×50 ml) and the dichloromethane extract obtained was combined with the above filtrate. It was dried over $MgSO_4$ and the solvent was removed in vacuo to give a residue which was recrystallized from ethanol, yield 3.7 g (65%), mp 127—129 °C (lit,[8] mp of 2,2-diphenyl-1,3-dithiolane *S*-oxide prepared from 2,2-diphenyl-1,3-dithiolane and H_2O_2 is 131—132 °C). Found: C, 65.67; H, 5.22%. Calcd for $C_{15}H_{14}OS_2$: C, 65.66; H, 5.14%. ^{1}H-NMR ($CDCl_3$) δ=2.9—4.0 (m, 4H), 7.0—8.1 (m, 10H).

Preparation of 2,2-Diaryl-1,3-dithiolane *S,S'*-Dioxides (7a—i). 2,2-Diphenyl-1,3-dithiolane *S,S'*-Dioxide (7a): To a stirred, cooled (0 °C) solution of 2,2-diphenyl-1,3-dithiolane

Table 1. The Reaction of 2,2-Diphenyl-1,3-dithiolane *S*-Oxide (**1**) and 2,2-Diaryl-1,3-dithiolane *S,S'*-Dioxides (**7a—i**) with Lithium Diisopropylamide (LDA)

Entry	Starting substrate (**1** or **7**)	Molar ratio (LDA/**1** or **7**)	Trapping agent	Eluent used in chromatographic purification	Product	
					Abbreviation	Yield/%
1	**1**	2.5	MeI	CH_3CO_2Et/Hexane (1:1)	**6a**	90
2	**1**	2.5	*n*-BuI	CH_3CO_2Et/Hexane (1:1)	**6b**	92
3	**7a**	2.5	H_2O	CH_3CO_2Et	**11a**	60
4	**7a**	2.5	*n*-BuI	CH_3CO_2Et	**11a**	59
5	**7b**	2.5	H_2O	CH_3CO_2Et/Hexane (3:1)	**11b**	69
6	**7c**	2.5	H_2O	CH_3CO_2Et/Hexane (1:4)	**11c**	67
7	**7d**	2.5	H_2O	CH_3CO_2Et/Hexane (3:2)	**11d**(I)[a]	27
					11d(II)[a]	37
8	**7e**	2.5	H_2O	CH_3CO_2Et/Hexane (5:2)	**11e**(I)[b]	31
					11e(II)[b]	28
9	**7f**	2.5	H_2O	CH_2Cl_2/Hexane (1:1)	**11f**	17
10	**7g**	2.5	H_2O	CH_2Cl_2/Hexane (1:1)	**11g**	50
11	**7h**	2.5	H_2O	CH_2Cl_2/Hexane (1:1)	**11h**	65
12	**7i**	2.5	H_2O	CH_3CO_2Et	**11i**	36

a) Column chromatography afforded two products **11d**(I) and **11d**(II), which are diastereoisomeric with each other. b) Similarly, two diastereoisomers **11e**(I) and **11e**(II) were obtained.

Table 2. Physical Properties and Analytical Data of the Products

Product	Mp or Bp θ_m/°C θ_b/°C (Torr)	^{1}H NMR Spectra (δ, in $CDCl_3$)	Found (Calcd) (%)		
			C	H	N
6a	140(2) [Lit,[12] 108—111(1)]	1.89(s, 3H), 5.00(s, 1H), 7.1—7.6(m, 10H)	78.47 (78.45)	6.88 (6.58)	
6b	164—166(1—2)	0.6—1.9(m, 7H), 2.19(t, 2H), 4.98(s, 1H), 6.8—7.4 (m, 10H)	79.53 (79.63)	7.80 (7.86)	
11a[a]	102—104 (Hexane)	0.58(d, 6H), 1.26(d, 6H), 3.63(m, 2H), 5.04(s, 1H), 7.0—7.6(m, 10H)	72.57 (72.34)	7.90 (7.99)	4.22 (4.44)
11b[b]	Oil	0.73(d, 6H), 1.25(d, 6H), 2.22(s, 3H), 3.56(m, 2H), 4.90(s, 1H), 6.7—7.4(m, 9H)	73.11 (72.90)	8.47 (8.26)	4.21 (4.25)
11c[b]	Oil	0.72(d, 6H), 1.24(d, 6H), 2.17(s, 3H), 3.55(m, 2H), 4.90(s, 1H), 6.7—7.4(m, 9H)	73.13 (72.90)	8.28 (8.26)	4.01 (4.25)
11d(I)	55—57 (Hexane)	0.74(d, 6H), 1.25(d, 6H), 3.57(m, 2H), 4.88(s, 1H), 6.9—7.3(m, 9H)	65.23 (65.22)	6.89 (6.91)	3.86 (4.00)
11d(II)	121—124 (Hexane)	0.78(d, 6H), 1.26(d, 6H), 3.57(m, 2H), 4.87(s, 1H), 6.9—7.4(m, 9H)	65.34 (65.22)	6.79 (6.91)	3.90 (4.00)
11e(I)	133—134 (Hexane)	0.77(d, 6H), 1.27(d, 6H), 3.62(m, 2H), 5.08(s, 1H), 7.0—7.6(m, 7H), 7.8—8.1 (m, 2H)	63.60 (63.31)	6.91 (6.71)	7.49 (7.77)
11e(II)	48—49 (Hexane)	0.77(d, 6H), 1.28(d, 6H), 3.60(s, 2H), 5.07(s, 1H), 7.0—7.6(m, 7H), 7.8—8.1(m, 2H)	63.26 (63.31)	6.95 (6.71)	7.80 (7.77)
11f[b]	Oil	0.76 and 0.80(d and d, 6H), 1.29(d, 6H), 3.67(m, 2H), 3.74(s, 3H), 4.94(s, 1H), 6.7—7.0(m, 2H), 7.1—7.6(m, 7H)	69.35 (69.53)	8.00 (7.88)	3.81 (4.05)
11g[b]	Oil	0.76(d, 6H), 1.62(d, 6H), 3.67(m, 2H), 5.09(s, 1H), 7.0—7.8(m, 14H)	76.43 (76.68)	7.33 (7.47)	3.54 (3.58)
11h[b]	Oil	0.65 and 0.75(d and d, 6H), 1.26(d, 6H), 3.27 and 3.30(m and m, 2H), 5.19(s, 1H), 7.0—7.9(m, 12H)	75.66 (75.57)	7.35 (7.45)	3.92 (3.83)
11i[a]	Oil	0.79(d, 6H), 1.34(d, 6H), 3.56(m, 2H), 4.99(s, 1H), 6.9—7.9(m, 8H)	72.56 (72.80)	7.15 (7.40)	4.30 (4.47)

a) Racemic mixture. b) Mixture composed of four stereoisomers unseparable from each other by column chromatography. 1 Torr = 133.322 Pa.

(5.2 g, 20 mmol) in dichloromethane (50 ml) a solution of *m*-chloroperbenzoic acid (6.9 g, 40 mmol) in dichloromethane (50 ml) was added during 3 h, followed by stirring at reflux temperature for 3 h. The reaction mixture was conducted as above. The crude product obtained was recrystallized from ethanol. If necessary, the crude product was purified by column chromatography on silica gel, using ethyl acetate as eluent, prior to the recrystallization, yield 6.51 g (56%), mp 186—189 °C. Found: C, 61.98; H, 4.95%. Calcd for $C_{15}H_{14}O_2S_2$: C, 62.04; H, 4.86%. ^{1}H-NMR ($CDCl_3$)

δ=3.42 (ddd, 2H), 3.93 (ddd, 2H), 6.9—7.6 (m, 10H).

In a similar manner, other 2,2-diaryl-1,3-dithiolane *S,S'*-dioxides (**7b—i**) were prepared from the corresponding 2,2-diaryl-1,3-dithiolanes.

2-(3-Methylphenyl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7b): 97%, mp 167—171 °C (from ethanol). Found: C, 63.01; H, 5.14%. Calcd for $C_{16}H_{16}O_2S_2$: C, 63.13; H, 5.30%. ^{1}H-NMR ($CDCl_3$) δ=3.44 (d, 2H), 3.80 (d, 2H), 6.9—7.6 (m, 9H).

2-(4-Methylphenyl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7c): 80%, mp 177—180 °C (from ethanol). Found: C, 62.88; H, 5.09%. Calcd for $C_{16}H_{16}O_2S_2$: C, 63.13; H, 5.30%. ^{1}H-NMR ($CDCl_3$) δ=3.31 (s, 3H), 3.3—4.1 (m, 4H), 6.9—7.5 (m, 9H).

2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7d): 61%, mp was not measured. Found: C, 55.24; H, 4.06%. Calcd for $C_{15}H_{13}ClO_2S_2$: C, 55.46; H. 4.03%. ^{1}H-NMR ($CDCl_3$) δ=3.2—4.1 (m, 4H), 6.8—7.6 (m, 9H).

2-(4-Nitrophenyl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7e): 83%, mp was not measured. Found: C, 53.65; H, 4.05; N, 4.11%. Calcd for $C_{15}H_{13}NO_4S_2$: C, 53.72; H, 3.91; N, 4.18%. ^{1}H-NMR ($CDCl_3$) δ=3.5—4.3 (m, 4H), 7.0—7.5 (m, 7H), 8.11 (s, 1H), 8.26 (s, 1H).

2-(4-Methoxyphenyl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7f): 84%, mp 180—183 °C (from ethanol). Found: C, 59.95; H, 5.07%. Calcd for $C_{16}H_{16}O_3S_2$: C, 59.97; H, 5.03%. ^{1}H-NMR ($CDCl_3$) δ=3.71 (s, 3H), 3.3—4.0 (m, 4H), 6.70 and 6.86 (s and s, 2H), 7.1—7.6 (m, 7H).

2-(1,1'-Biphenyl-4-yl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7g): 48%, mp 186—189 °C (from ethanol). Found: C, 68.70; H, 4.68%. Calcd for $C_{21}H_{18}O_2S_2$: C, 68.82; H, 4.95%. ^{1}H-NMR ($CDCl_3$) δ=3.2—4.1 (m, 4H), 7.0—7.8 (m, 14H).

2-(2-Naphthyl)-2-phenyl-1,3-dithiolane *S,S'*-Dioxide (7h): 59%, mp 163— °C (from ethanol). Found: C, 67.68; H, 5.05%. Calcd for $C_{19}H_{16}O_2S_2$: C, 67.03; H, 4.74%. ^{1}H-NMR ($CDCl_3$) δ=3.2—4.5 (m, 4H), 7.0—8.0 (m, 12H).

Spiro[1,3-dithiolane-2,9'-[9*H*]fluorene] *S,S'*-Dioxide (7i): 74%, mp 176—181 °C (from ethanol). Found: C, 62.22; H, 4.06%. Calcd for $C_{15}H_{12}O_2S_2$: C, 62.47; H, 4.19%. ^{1}H-NMR ($CDCl_3$) δ=3.69 (dd, 2H), 4.27 (dd, 2H), 7.1—7.9 (m, 8H).

The Reaction of 2,2-Diphenyl-1,3-dithiolane *S*-Oxide (1) with Lithium Diisopropylamide (LDA) (Entries 1 and 2 of Table 1). To a stirred, cooled (−78 °C) solution of diisopropylamine (0.35 g, 3.5 mmol) in tetrahydrofuran (7 ml) was added a 1.56 molar solution (2.1 ml, 3.3 mmol) of butyllithium in hexane under nitrogen, followed by stirring at the same temperature for 30 min and further stirring at −15 °C for 10 min. The solution of LDA thus prepared was maintained at −15 °C. It was slowly added to a stirred, cooled (−78 °C) solution of **1** (0.35 g, 1.3 mmol) in tetrahydrofuran (4 ml) under nitrogen. The reaction mixture was warmed to room temperature and the stirring was continued for 1 h. The mixture was cooled again to −78 °C, and 3.3 mmol of an alkyl halide (0.47 g of methyl iodide or 0.61 g of butyl iodide) was added with stirring. The mixture was stirred for 1 h at 0 °C, warmed to room temperature, stirred an additional 24 h, quenched with 20 ml of a saturated aqueous solution of NH_4Cl, and extracted with ether (3×60 ml). The ethereal extract was dried over $MgSO_4$ and concentrated in vacuo to give a residue, which was subjected to purification by column chromatography on silica gel.

The Reaction of 2,2-Diaryl-1,3-dithiolane *S,S'*-Dioxides (7a—i) with Lithium Diisopropylamide (LDA) (Entries 3—12 of Table 1). The LDA solution prepared in the same way as above was slowly added with stirring to a cooled (−78 °C) solution of the appropriate **7a—i** (1.3 mmol) in tetrahydrofuran (4 ml) under nitrogen. Stirring was continued for 2 h at −78 °C, and the reaction mixture was quenched with 100 ml of H_2O and 20 ml of a saturated aqueous solution of NH_4Cl. It was extracted with ether (3×60 ml). The ethereal extract was dried over $MgSO_4$, filtered, and concentrated in vacuo to give a residue, which was purified by column chromatography on silica gel. Only in the case of Entry 4 in Table 1, an excess of butyl iodide was added to the reaction mixture prior to the quenching with H_2O. However, the yield of the objective **11a** was not altered by the addition, suggesting that the anionic species **10** is unreactive to butyl iodide and hence the true trapping agent is H_2O.

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