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The Formation of 1,2-Bis(alkylthio)-1,2-diphenylethanes by the Lithium Diisopropylamide-induced Fragmentation of Dibenzyl Disulfide Followed by the Trapping with Some Alkyl Halides

Hideyuki IKEHIRA* and Shigeo TANIMOTO*
Institute for Chemical Research, Kyoto University, Uji, Kyoto 611

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Synopsis. It was found that dibenzyl disulfide undergoes lithium diisopropylamide-induced fragmentation to afford several intermediate species which, on trapping with alkyl halides, lead to the formation of 1,2-bis(alkylthio)-1,2-diphenylethanes and α-alkylbenzyl alkyl sulfides.

The use of carbanions stabilized by the presence of one or more adjacent thioether groups has become an established technique in organic synthesis.[1–12] In some related works, we were interested in utilizing a carbanion that could be easily generated by the action of a strong base on disulfide possessing α-hydrogens. We chose dibenzyl disulfide (**1**) as a starting substrate in this research since it is easily available and relatively nontoxic. Since most of the reaction products from it are nonvolatile, it thus has advantages for small scale work. The removal of the α-hydrogens of **1** could be achieved by the addition of an easily available metalating agent such as lithium diisopropylamide (LDA). Presumably, the initially formed anionic species undergoes fragmentation followed by further conversion to the other intermediate species. These species were trapped by the addition of some alkyl halides to the reaction mixture. In this way a series of 1,2-bis(alkylthio)-1,2-diphenylethanes (**9**) were produced in fairly good yields, along with α-alkylbenzyl alkyl sulfides (**10**) (see Table 1). The structures of **9** and **10** were established from satisfactory analytical and spectral data. Table 2 shows the physical properties and analytical data of the isolated products.

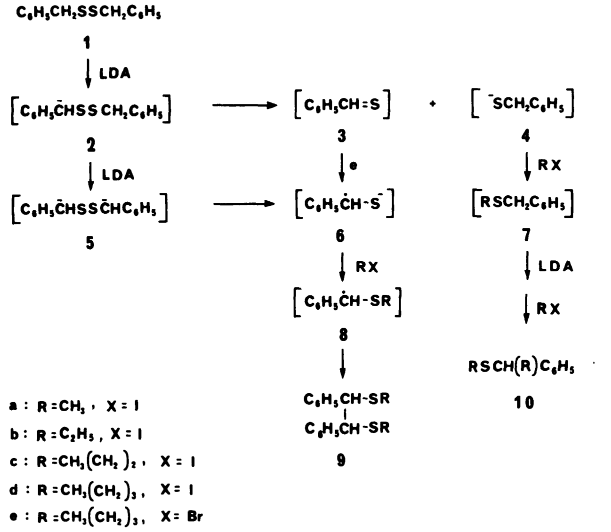

TABLE 1. LITHIUM DIISOPROPYLAMIDE-INDUCED FRAGMENTATION OF DIBENZYL DISULFIDE(**1**), FOLLOWED BY TRAPPING WITH SOME ALKYL HALIDES

Run	RX	Product (Yield/%[a])
1	CH_3I	**9a** (72), **10a** —[b]
2	C_2H_5I	**9b** (60), **10b** —[b]
3	$CH_3(CH_2)_2I$	**9c** (68), **10c** (39)
4	$CH_3(CH_2)_3I$	**9d** (77), **10d** (38)
5	$CH_3(CH_2)_3Br$	**9e**[c] (76), **10e**[c] (39)

a) Yield was calculated assuming that 1 mol of **1** produces 1 mol of product. b) Not isolated. c) The compounds **9e** and **10e** are identical to **9d** and **10d**, respectively.

Possible routes for the formation of **9** and **10** are shown by the accompanying equations. Presumably, the initially formed anion (**2**) undergoes fragmentation to afford thiobenzaldehyde (**3**) and α-toluenethiolate anion (**4**). This type of fragmentation may be certain from the fact that, in a preliminary experiment in which **1** was treated with equimolar amounts of LDA in tetrahydrofuran at −78 °C followed by addition of ethyl iodide, the formation of benzyl ethyl sulfide was observed (76% yield) together with small amounts of **9b**, **10b**, and tarry substance. Thus, the anion (**4**) which would be formed similarly in the present reaction undergoes trapping by alkyl halides and subsequent deprotonation-alkylation sequence to afford **10**. Although the deprotonation of **4** by butyllithium leading to a dianion such as $^{-}S\bar{C}HC_6H_5$ has already been recognized by Seebach and Geiss,[14] the possibility that **4** is further deprotonated by LDA to give the same dianionic species seems to be less reasonable, since LDA is less basic than butyllithium and also, in all runs, the formation of alkyl benzyl sulfides was observed, albeit in very low yields. Hiskey and Dennis[15] have previously proposed a mechanism for the alkoxide cleavage of bis(2-oxo-2-phenylethyl) disulfide. If such a mechanism also prevails in the LDA cleavage of **1**, **3** would be attacked by **4** to afford an anion of the hemidithioacetal which undergoes deprotonation with LDA and the subsequent intramolecular rearrangement leading to dianion of 1,2-diphenyl-1,2-ethanedithiol. However, this mechanism is incompatible with the fact that, in all runs of Table 1, the sum of the yield of **9** and that of **10** is beyond 100%. Thus, it seems reasonable that there is no occurrence of any recombination of **4** with **3**. On the basis of these considerations, the source of **9** could hardly be anything else than **3**. Concerning the trapping of thioaldehydes such as thiobenzaldehyde, one or two papers[16,17] have appeared in the literature. However, the isolation of **3** by the application of a similar method failed, presumably because it is immediately converted to the radical anion (**6**) by one-electron transfer from LDA. Such one-electron transfer has already been observed[12,18,19] in the reaction of several thioketones. The formation of **6** was also evident from the appearance of its characteristic color (blue-black). Thus, **6** undergoes charge neutralization by the applied alkyl halide to

Table 2. Physical properties and analytical data of the isolated products

Product[a]	Mp θ_m/°C or [Bp θ_b/°C(Torr)]	^{1}H-NMR[b] (δ, $CDCl_3$ or CCl_4)	^{13}C-NMR (δ, $CDCl_3$)	Found(Calcd)(%)	
				C	H
9a	102—103 (lit,[13] 99.3—101 °C)	1.81(s, 6H), 4.11(s, 2H), 7.01(s, 10H)	15.15(q), 57.63(d), 127.07(d), 127.95(d), 128.59(d), 139.76(s)	69.79 (70.02)	6.52 (6.61)
9b	[163(3.5)]	1.10(t, 6H, J=7 Hz), 2.19 (q, 4H, J=7 Hz), 4.20(s, 2H), 6.9—7.3(m, 10H)	14.10(q), 25.74(t), 55.70(d), 126.95(d), 127.83(d), 128.59(d), 140.11(s)	71.28 (71.47)	7.32 (7.33)
9c	[159(2.5)]	0.83(t, 6H, J=6 Hz), 1.1—1.8 (m, 4H), 2.13(t, 4H, J=6 Hz), 4.13(s, 2H), 6.8—7.1(m, 10H)	13.51(q), 22.41(t), 33.87(t), 56.10(d), 126.95(d), 127.83(d), 128.71(d), 140.29(s)	72.74 (72.67)	7.80 (7.93)
9d	[150(2)]	0.6—1.0(m, 6H), 1.0—1.6(m, 8H), 2.0—2.4(m, 4H), 4.17(s, 2H), 6.9—7.2(m, 10H)	13.57(d), 21.94(t), 31.12(t), 31.53(t), 56.16(d), 126.95(d), 127.83(d), 128.71(d), 140.29(s)	73.69 (73.68)	8.46 (8.43)
10c	[87(1.5—2.0)]	0.7—1.0(m, 6H), 1.0—1.8(m, 4H), 2.0—2.7(m, 4H), 3.55(t, 1H, J=7 Hz), 7.0—7.4(m, 5H)	—[c]	74.80 (74.93)	9.51 (9.68)
10d	[111(2.5)]	0.7—1.2(m, 6H), 1.2—2.0(m, 8H), 2.0—2.7(m, 4H), 3.67(t, 1H, J=7 Hz), 7.0—7.4(m, 5H)	—[c]	76.07 (76.20)	9.93 (10.23)

a) The research for stereochemical assignment of the structures of **9a–d** has not been done. b) The measurement of ^{1}H-NMR was carried out with **9a–d** in $CDCl_3$ and with **10c**, **10d** in CCl_4. c) Not measured.

generate the radical species (**8**), which on subsequent dimerization of itself leads to **9**. This explanation would mean that only half of the dibenzyl disulfide molecule is utilized in the formation of **9**. However, it is not tenable since it does not accommodate the experimental fact that the yields of **9**, which are calculated provided that 1 mol of **1** produce 1 mol of **9**, are beyond 50%. This problem could be solved by postulating that another process involving a further deprotonation of **2** followed by the S–S bond fission of the resulting dianion (**5**) to afford **6** is competitively operative. Such an assumption is also compatible with the facts that, in all runs of Table 1, **9** has been produced in more excess than **10** and that the employment of a fourfold excess or more of LDA under otherwise identical conditions results in increased yields of **9** and slightly decreased yields of **10**. For example, with propyl iodide as the trapping agent, the yield of **9c** was 75% and that of **10c** was 34%. However, there has not been any direct evidence for the occurrence of the conversion of **5** to **6**.

Experimental

Lithium Diisopropylamide(LDA)-induced Fragmentation of Dibenzyl Disulfide (1) Followed by the Trapping with Some Alkyl Halides. General Procedure: To LDA, prepared from diisopropylamine (0.36 g, 3.6 mmol) in tetrahydrofuran (7 ml) and 1.56 molar solution (2.18 ml, 3.4 mmol) of butyllithium in hexane, was added at −78 °C 0.27 g (1.1 mmol) of **1** in tetrahydrofuran (4 ml). The reaction mixture was allowed to warm to −15 °C and the stirring was continued for 1 h at that temperature. The mixture was cooled again to −78 °C, and an appropriate alkyl halide (3.3 mmol) was added with stirring. The stirring was continued for 1 h at −10—−5 °C and then for 24 h at room temperature. The mixture was quenched with water (100 ml) and a saturated aqueous solution (20 ml) of ammonium chloride, and then extracted with ether (3×60 ml). The combined ethereal extract was dried over magnesium sulfate and concentrated under reduced pressure to give a residue, which was sujected to preparative TLC on silica gel using ethyl acetate–hexane as the eluent. In Runs 1 and 2, however, the R_f values of **9a** and **9b** were almost same with those of **10a** and **10b**, respectively. Thus, the obtained mixture, which is composed of **9a** and **10a**, was distilled under vacuum to remove **10a** from the mixture, and the residue was again subjected to preparative TLC on silica gel using the same eluent. In the similar manner, only **9b** was isolated in Run 2.

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