Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 5263–5265

TETRAHEDRON LETTERS

N-Bromosuccinimide-dimercaptoethane cobromination of alkenes: synthesis of β,β′-dibromodithioethers

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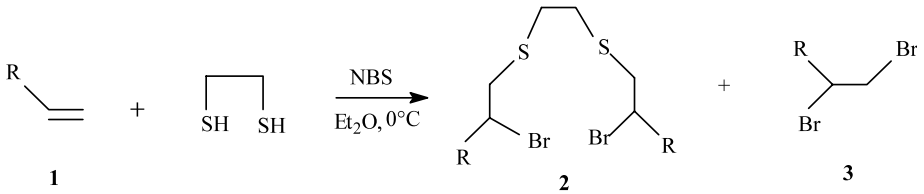
Received 1 April 2003; revised 5 May 2003; accepted 16 May 2003

Abstract—Alkenes react in diethyl ether with *N*-bromosuccinimide (NBS) and dimercaptoethane to afford the corresponding β,β′-dibromodithioethers. Bromine and dimercaptoethane are added to the aliphatic terminal olefins in an anti-Markovnikov fashion.

The cohalogenation of alkenes with halogens and nucleophilic solvents like water, dimethylsulfoxide, dimethylformamide, carboxylic acids, alcohols, nitriles and ethers is well documented,[1] but little work has been carried out on the formation of a C–S bond with sulfur-containing nucleophiles. The two reactions reported in the literature are related to the incorporation of the thiocyanate or the sulfone functionality by cohalogenation of an olefin in the presence of thiocyanate[2–5] or by using sodium benzenesulfinate,[6] but to our knowledge, the use of thiols has not been described previously. In this paper, we report the preparation of β,β′-dibromodithioethers resulting from electrophilic bromination by *N*-bromosuccinimide (NBS) followed by dimercaptoethane addition to two mole equivalents of olefins (Scheme 1).

As shown in Table 1, this electrophilic cobromination reaction allows the preparation of β,β′-dibromodithioethers in good yields. With aliphatic terminal alkenes **1a–c** the addition proceeds with a marked anti-Markovnikov regioselectivity, probably because nucleophilic attack of dimercaptoethane onto bromonium cyclic ion takes place with steric factors controlling the regioselectivity. This regioselectivity was not observed in the case of styrene **1d**, which gave a mixture of Markovnikov and anti-Markovnikov products.[7] In resonance terms the bromonium ion formed from styrene is in equilibrium with a carbocation form which is stabilized by conjugation.

In all cases, variable amounts (16–33%) of the corresponding dibromo compounds were found, except in the case of alkene **1c**. However, the separation of the undesired side products from the corresponding dithioethers was remarkably easy by evaporation at reduced pressure (1.5 Torr) at 50°C and then by conventional column chromatography on silica gel. After a literature search, we have found that the formation of dihalo derivatives is observed in the halofluorination reaction of a variety of alkenes and a mechanism for this side reaction was postulated.[8]



1 **2** **3**

R = *n*-C_3H_7 ; *n*-C_4H_9 ; *t*-Bu ; Ph ; $(CH_2)_4$

Scheme 1.

Keywords: alkenes; dimercaptoethane; cohalogenation; thioethers.
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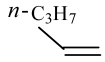
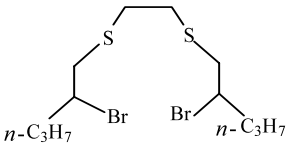
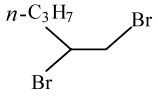
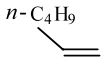
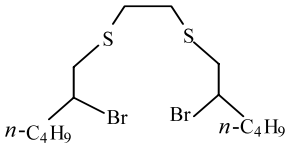
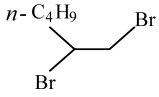
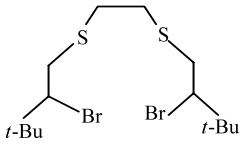
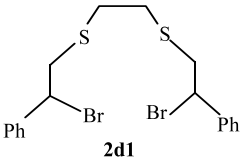
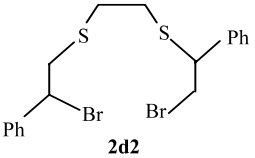
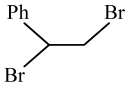
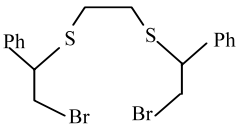
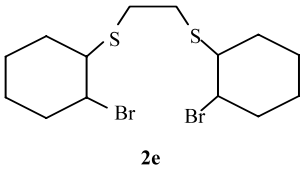
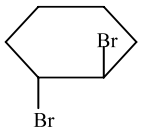
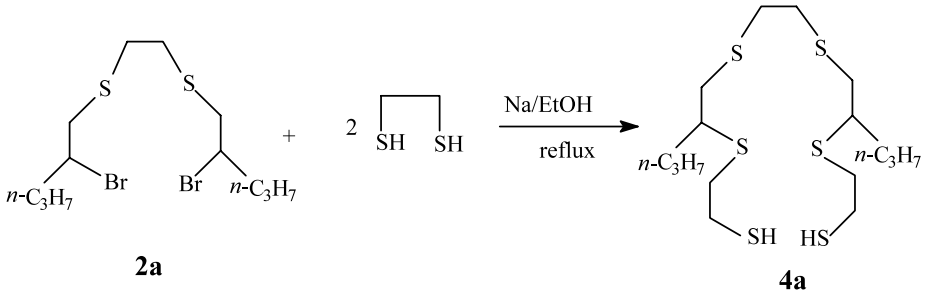
0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)01221-8

Table 1. Cobromination of alkenes with NBS and dimercaptoethane

Alkene	β,β'-Dibromo-dithioether	(%)[a]	Dibromo compound	(%)[a]	conv. (%)[b]
 **1a**	 **2a**	83	 **3a**	17	70
 **1b**	 **2b**	84	 **3b**	16	78
 **1c**	 **2c**	100	-		89
	 **2d1**				
 **1d**	 **2d2**	72	 **3d**	28	65
	 **2d3**				
 **1e**	 **2e**	67	 **3e**	33	62

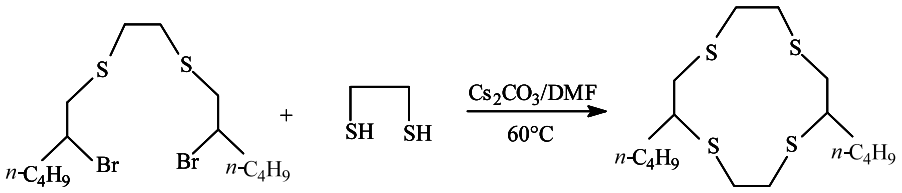
[a]The ratio of isomers was determined by ^{1}H NMR analysis.
[b]Isolated yield of β,β'-dibromodithioether **2**.

A typical procedure used in the synthesis of β,β′-dibromodithioethers is as follows: Dimercaptoethane (27 mmol) was added dropwise over 30 min to a stirred solution of alkene **1** (50 mmol) and *N*-bromosuccinimide (8.89 g, 50 mmol) in diethyl ether (50 mL) at 0°C under nitrogen. After addition, the reaction mixture was stirred at rt for 30 min. The mixture obtained was filtered, washed with water, dried over $MgSO_4$ and concentrated. After evaporation of the dibromo product at 50°C/1.5 Torr, the residue was purified by column chromatography on silica gel, eluting with light petroleum. All products were fully characterized by ^{1}H and ^{13}C NMR spectroscopy and HRMS methods.[9]



2a **4a**

Scheme 2.



2b **5b**

Scheme 3.

Some applications of β,β′-dibromodithioethers in organic synthesis are summarized in Schemes 2 and 3. Dithiol **4a**[10] (Scheme 2) was synthesized from dibromodithioether **2a** by reaction of two mole equivalents of dimercaptoethane in absolute ethanol in the presence of sodium metal.

When Cs_2CO_3 was used as the base in DMF,[11,12] the dibromide **2b** reacted with dimercaptoethane to afford the thiacrown ether **5b**[13] (Scheme 3).

In conclusion, this paper describes a simple route to β,β′-dibromodithioethers. We have shown that the addition of bromine and sulfur to terminal olefins takes place regioselectively in an anti-Markovnikov manner. The reaction products may prove to be useful, except in the case of styrene, in synthesis and particularly for thiacrown ethers as realized from the conversion of **2b** into **5b**.

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7. Compound **2d**, HRMS: mol. mass calcd 458.94516 (for $C_{18}H_{21}S_2Br_2$), found 458.94515 $(M+H)^+$.
8. Camps, F.; Chamorro, E.; Gasol, V.; Guerrero, A. *J. Org. Chem.* **1989**, *54*, 4294–4298.
9. Spectral data: compound **2a**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.93$ (t, $J=6.9$ Hz, 6H), 1.39–1.49 (m, 8H), 2.77 (s, 4H), 3.02 (m, 4H), 3.68 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=13.78$, 18.80, 33.84, 38.24, 40.09, 69.39. Compound **2b**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.92$ (t, $J=6.9$ Hz, 6H), 1.30–1.60 (m, 8H), 1.79 (m, 2H), 2.03 (m, 2H), 2.79 (s, 4H), 3.05 (m, 4H), 4.09 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=13.83$, 21.93, 29.33, 33.08, 36.73, 40.90, 55.09. Compound **2c**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.08$ (s, 18H), 2.83–3.15 (m, 8H), 3.97 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=27.33$, 33.09, 36.38, 37.73, 69.91. HRMS: mol. mass calcd 419.00776 (for $C_{14}H_{29}S_2Br_2$), found 419.00765 $(M+H)^+$. Compound **2e**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.43$–1.90 (m, 12H), 2.27–2.39 (m, 4H), 2.83 (s, 4H), 3.02 (m, 2H), 4.29 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=23.02$, 30.29, 32.29, 33.48, 38.42, 50.34, 56.79.
10. Spectral data: compound **4a**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.93$ (t, $J=6.9$ Hz, 6H), 1.39–1.56 (m, 8H), 1.76 (br, 2H), 2.76 (m, 8H), 2.88 (m, 8H), 3.01 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=13.84$, 19.82, 30.25, 32.34, 35.78, 37.49, 38.54, 46.04. MS (CI-NH_3) m/z 435 $(M+17)^+$, 419 $(M+1)^+$, 418 (M^+).
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12. Edema, J. J. H.; Buter, J.; Kellogg, R. M. *Tetrahedron* **1994**, *50*, 2095–2098.
13. Spectral data: compound **5b**: ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.92$ (t, $J=6.9$ Hz, 6H), 1.34–1.60 (m, 12H), 2.77–3.10 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 13.70, 22.33, 28.37, 29.00, 34.82, 35.13, 35.33, 41.60. MS (CI-NH_3) m/z 369 $(M+17)^+$, 353 $(M+1)^+$, 352 (M^+).