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N-Bromosuccinimide–thiol cobromination in basic medium: an efficient one-pot transformation of olefins into the corresponding enol thioethers

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Abstract—A convenient method for the one-pot conversion of olefins into the corresponding enol thioethers is reported. The products were obtained via the *N*-bromosuccinimide cobromination reaction of olefins with thiols in basic medium. Steric hindrance present in the product alkenes may explain the stereochemistry observed.

Zeigler[1] was the first to describe the use of *N*-bromosuccinimide (NBS) as an important reagent for allylic bromination and a radical chain mechanism was later proposed for its action by Bloomfield in 1944.[2] Since, many papers describing its widespread use as a synthetic reagent have been published,[3] NBS can be considered simply as a reservoir capable of sustaining a low steady-state concentration of bromine during a reaction.[4] Although the NBS cobromination reactions of alkenes are widely used in the presence of nucleophiles such as F^-,[5] little work has been published on these reactions with sulfur-containing nucleophiles.[6–10]

In a previous paper,[11] we reported the preparation of enol thioethers starting from the corresponding enol ethers.[12] We have also prepared β,β′-dibromodithioethers[13] via the cobromination reaction of olefins, in the presence of NBS, with dimercaptoethane. Herein, we report cobromination, in basic medium, using various thiols for the synthesis of new enol thioethers.

Inspired by our previous work[13] on the cobromination of olefins using NBS in the presence of dimercaptoethane, the one-pot transformation of alkenes with NBS and various thiols in a basic medium was carried out affording the corresponding enol thioethers **2a**–**g**.[14] The reaction proceeded via an in situ addition–elimination mechanism according to Scheme 1.

When the starting alkenes used were styrene or *tert*-butylethylene, the reaction was stereospecific and afforded *E*-alkenes exclusively (see Table 1). However, when the alkenes used were pentene derivatives **2f** and **2g**, a mixture of two isomers was observed. In addition, the DEPT ^{13}C NMR spectrum showed that each of the four double bonded carbon atoms of the two isomers is directly linked to a hydrogen atom, indicating the existence of a mixture of *Z* and *E* stereoisomers. The mechanism proposed is consistent with results reported for similar reagents by Reddy et al.[15] who showed that alkyne intermediates yielded *Z* products.

As shown in Table 1, several enol thioethers could be easily prepared and the reaction conditions are mild and efficient.

However, when the alkene used was cyclohexene, the reaction proceeded differently and allylic sulfides **3a**–**c** were obtained with no enol thioethers being formed (see Table 2). The formation of such products is explained by *trans*-Br/RS addition followed by 1,2-diaxial dehydrobromination, and was confirmed by the DEPT ^{13}C NMR spectroscopy which showed that each ethylenic carbon is linked to one hydrogen atom. The lower yields observed for these products are presumably due

Keywords: Enol thioethers; *N*-Bromosuccinimide; Cobromination; Olefins; *Z*/*E* isomers.
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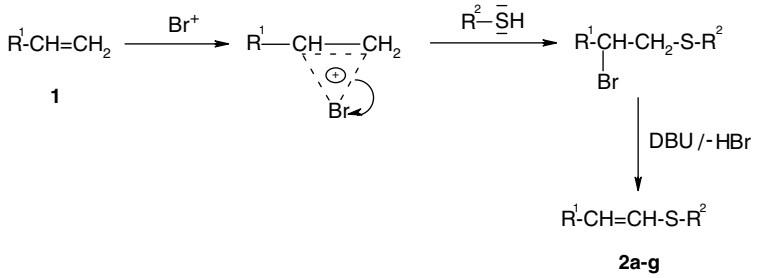
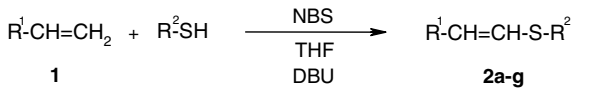


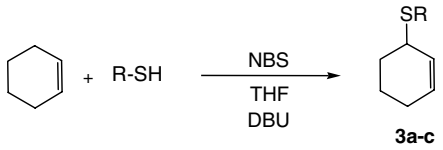
Scheme 1.

Table 1. Yields and configurations of enol thioethers **2a–g**



Enol thioether **2**	R^1	R^2	*Z*/*E*	Yield (%)
2a	$C(CH_3)_3$	Ph	0/100	82
2b	$C(CH_3)_3$	MeO–CO–CH_2	0/100	87
2c	Ph	C_6F_{13}–CH_2–CH_2	0/100	86
2d	Ph	C_8F_{17}–CH_2–CH_2	0/100	85
2e	Ph	MeO–CO–CH_2	0/100	75
2f	nC_3H_7	Ph	35/65	74
2g	nC_3H_7	MeO–CO–CH_2	15/85	82

Table 2. Yields of allylic sulfides **3a–c**



Allylic sulfide **3**	R	Yield (%)
3a	MeO–CO–CH_2	53
3b	C_6F_{13}–CH_2–CH_2	60
3c	C_8F_{17}–CH_2–CH_2	62

to the formation of dibromo derivatives as by-products[16] which, in this case, are converted to the 3-bromocyclohexene, as identified in the crude product mixture.

In summary, we have reported a one-pot preparation of novel enol thioethers. This type of enol thioether is scarcely described in the literature and the extension of this method to the preparation of substituted alkenes as well as to naturally occurring compounds is under investigation.

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14. *Preparation of enol thioethers*: To a mixture of 0.05 mol of alkene in THF (50 mL) and NBS (0.05 mol) cooled to 0 °C were added dropwise, respectively, 0.05 mol of thiol and 0.08 mol of DBU. After complete addition, the mixture was stirred at room temperature for 4 h, then diluted with ether (2 × 50 mL) and 2 N sulfuric acid solution was added until pH ≈ 5 was reached. The organic phase was washed with aqueous K_2CO_3 solution and water, dried over Na_2SO_4 and the solvent evaporated. The residue was purified by silica gel column chromatography using petroleum ether/dichloromethane as eluent (90:10).
Spectral data for compounds **2a–g** *and* **3a–c**: Compound **2a**: Oil; IR ($CHCl_3$): ν (cm^{-1}) = 1635 (C=C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.05 (s, 9H); 5.96 (d, 1H, $^3J_{HH}$ = 15.46 Hz); 6.11 (d, 1H, $^3J_{HH}$ = 15.46 Hz); 7.26 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 30.11 ($(CH_3)_3$); 34.76 ($(CH_3)_3C$); 117.20 (C–CH=); 126.24; 127.40; 128.59; 129.46 (4s, C_{arom}); 148.01 (=CH–S). ESI-HRMS: M^+ calculated 192.0973, found 192.0968, Δ (mmu) = 0.5.
Compound **2b**: Oil; IR ($CHCl_3$): ν (cm^{-1}) = 1640 (C=C); 1772 (C=O). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.00 (s, 9H); 3.29 (s, 2H); 3.66 (s, 3H); 5.71 (d, 1H, $^3J_{HH}$ = 15.06 Hz); 5.86 (d, 1H, $^3J_{HH}$ = 15.06 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 29.51 ($(CH_3)_3$); 34.26 ($(CH_3)_3C$); 34.96 (S–CH_2); 52.84 (O–CH_3); 116.78 (C–CH=); 144.34 (=CH–S); 170.30 (CO). ESI-HRMS: M^+ calculated 188.0871, found 188.0867, Δ (mmu) = 0.4.
Compound **2c**: Oil; IR ($CHCl_3$): ν (cm^{-1}) = 1642 (C=C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.49 (m, 2H); 2.99 (t, 2H, $^3J_{HH}$ = 7.1 Hz); 6.49 (d, 1H, $^3J_{HH}$ = 15.51 Hz); 6.64 (d, 1H, $^3J_{HH}$ = 15.51 Hz); 7.27 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 23.46 (t, CH_2–S, $^3J_{CF}$ = 4.35 Hz); 32.07 (t, CF_2–CH_2, $^2J_{CF}$ = 22.12 Hz); 115.37 (Ph–CH=); 125.81; 127.58; 128.41; 129.63 (4s, C_{arom}); 136.60 (s, =CH–S). ^{19}F NMR (282 MHz, $CFCl_3$): δ (ppm) = −81.65 (m, 3F, CF_3); −115.12 (m, 2F, $CF_2\alpha$); −122.43 (m, 2F, $CF_2\beta$); −123.63 (m, 2F, $CF_2\gamma$); −124.92

(m, 2F, $CF_2\delta$); −127.11 (m, 2F, $CF_2\omega$). ESI-HRMS: M^+ calculated 482.0374, found 482.0369, Δ (mmu) = 0.5.

Compound **2d**: Oil; IR ($CHCl_3$): ν (cm^{-1}) = 1640 (C=C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.47 (m, 2H); 3.01 (t, 2H, $^3J_{HH}$ = 7.1 Hz); 6.52 (d, 1H, $^3J_{HH}$ = 15.45 Hz); 6.67 (d, 1H, $^3J_{HH}$ = 15.45 Hz); 7.25 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 23.49 (t, CH_2–S, $^3J_{CF}$ = 4.33 Hz); 32.06 (t, CF_2–CH_2, $^2J_{CF}$ = 22.18 Hz); 115.33 (s, Ph–CH=); 125.86; 127.58; 128.41; 129.67 (4s, C_{arom}); 136.55 (s, =CH–S). ^{19}F NMR (282 MHz, $CFCl_3$): δ (ppm) = −81.63 (m, 3F, CF_3); −115.02 (m, 2F, $CF_2\alpha$); −122.50 (m, 2F, $CF_2\beta$); −123.52 (m, 4F, 2 $CF_2\gamma$); −124.07 (m, 2F, $CF_2\delta$); −124.94 (m, 2F, $CF_2\omega$); −127.03 (m, 2F, $CF_2\chi$). ESI-HRMS: M^+ calculated 582.0310, found 582.0304, Δ (mmu) = 0.6.

Compound **2e**: Oil; IR ($CHCl_3$): ν (cm^{-1}) = 1645(C=C); 1765 (C=O). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.34 (s, 2H); 3.69 (s, 3H); 6.57 (d, 1H, $^3J_{HH}$ = 15.32 Hz); 6.73 (d, 1H, $^3J_{HH}$ = 15.32 Hz); 7.41 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 34.96 (S–CH_2); 52.79 (O–CH_3); 117.01 (Ph–CH=); 126.02; 127.61; 128.42; 129.61 (4s, C_{arom}); 144.36 (s, =CH–S); 170.52 (s, CO). ESI-HRMS: M^+ calculated 208.0558, found 208.0554, Δ (mmu) = 0.4.

Compound **2f**: Mp = 78 °C; IR ($CHCl_3$): ν (cm^{-1}) = 1642 (C=C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.93 (m, 6H: due to overlap of the signals of the *Z* and *E* isomers); 1.44 (m, 4H: due to overlap of the signals of the *Z* and *E* isomers); 2.12 (m, 2H); 2.23 (m, 2H); 5.75 (m, 1H, $^3J_{HH(Z)}$ = 7.36 Hz); 5.90 (m, 1H, $^3J_{HH(Z)}$ = 7.36 Hz); 6.00 (m, 1H, $^3J_{HH(E)}$ = 15.23 Hz); 6.20 (m, 1H, $^3J_{HH(E)}$ = 15.23 Hz); 7.31 (m, 10H: due to overlap of the signals of the *Z* and *E* isomers). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 13.86; 14.00 (2s, CH_3); 22.45; 22.53 (2s, CH_2); 31.37; 35.35 (2s, CH_2–CH=); 121.20; 123.07 (2s, C–CH=); 133.65; 137.56 (2s, =CH–S); 126.19–129.26 (m, C_{arom}). ESI-HRMS: M^+ calculated 178.0816, found 178.0813, Δ (mmu) = 0.3.

Compound **2g**: Mp = 78 °C; IR ($CHCl_3$): ν (cm^{-1}) = 1638 (C=C); 1764 (C=O). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.90 (t, 6H: due to overlap of the signals of the *Z* and *E* isomers, $^3J_{HH}$ = 7.43 Hz); 1.41 (m, 4H: due to overlap of *Z* and *E* isomers); 2.07 (m, 4H: due to overlap of *Z* and *E* isomers); 3.35 (s, 4H: due to overlap of *Z* and *E* isomers); 3.73 (s, 6H: due to overlap of *Z* and *E* isomers); 5.62 (m, 1H, $^3J_{HH(Z)}$ = 7.45 Hz); 5.67 (m, 1H, $^3J_{HH(Z)}$ = 7.45 Hz); 5.76 (m, 1H, $^3J_{HH(E)}$ = 15.42 Hz); 5.96 (m, 1H, $^3J_{HH(E)}$ = 15.42 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 13.44 (CH_3); 22.06 (CH_2); 30.90 (CH_2); 34.85 (S–CH_2); 52.28 (OCH_3); 120.90; 122.85 (2s, C–CH=); 131.38; 133.71 (2s, =CH–S); 170.18 (s, CO). ESI-HRMS: M^+ calculated 174.0715, found 174.0713, Δ (mmu) = 0.2.

Compound **3a**: Oil; IR ($CHCl_3$): ν (cm^{-1}) = 1640 (C=C); 1770 (C=O). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.28–2.29 (m, 6H); 3.12 (m, 1H); 3.33 (s, 2H); 3.71 (s, 3H); 5.62 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 29.62–30.46 ($(CH_2)_4$); 34.91 (S–CH_2); 52.74 (O–CH_3); 117.11 (CH = C); 144.41 (=C–S); 170.47 (CO). ESI-HRMS: M^+ calculated 186.0715, found 186.0711, Δ (mmu) = 0.4.

Compound **3b**: Mp = 65 °C; IR ($CHCl_3$): ν (cm^{-1}) = 1645 (C=C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.32–2.28 (m, 6H); 2.44 (m, 2H); 3.05 (t, 2H, $^3J_{HH}$ = 7.3 Hz); 3.17 (m, 1H); 5.59 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 23.51 (t, CH_2–S, $^3J_{CF}$ = 4.41 Hz); 29.58–30.52 (m, $(CH_2)_4$); 32.04 (t, CF_2–CH_2, $^2J_{CF}$ = 22.32 Hz); 115.34 (s, CH=C); 136.67 (s, =C–S). ^{19}F NMR (282 MHz, $CFCl_3$): δ (ppm) = −81.69 (m, 3F, CF_3); −115.18 (m, 2F, $CF_2\alpha$); −122.48 (m, 2F, $CF_2\beta$); −123.59 (m, 2F, $CF_2\gamma$); −125.02 (m, 2F, $CF_2\delta$); −127.07 (m, 2F, $CF_2\omega$). ESI-HRMS: M^+ calculated 460.0530, found 460.0523, Δ (mmu) = 0.7.

Compound **3c**: Mp = 69 °C; IR ($CHCl_3$):ν (cm^{-1}) = 1646 (C=C). ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.31–2.25 (m, 6H); 2.47 (m, 2H); 3.02 (t, 2H, $^3J_{HH}$ = 7.2 Hz); 3.17 (m, 1H); 5.63 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 23.49 (t, CH_2–S, $^3J_{CF}$ = 4.33 Hz); 29.54–30.56 (m, $(CH_2)_4$); 32.06 (t, CF_2–CH_2, $^2J_{CF}$ = 22.18 Hz); 115.33 (s, CH=C); 136.55 (s, =C–S). ^{19}F NMR (282 MHz, $CFCl_3$): δ (ppm) = −81.52 (m, 3F, CF_3); −114.96 (m, 2F, $CF_2\alpha$); −122.44 (m, 2F, $CF_2\beta$); −123.54 (m, 4F, 2 $CF_2\gamma$); −123.96 (m, 2F, $CF_2\delta$); −124.92 (m, 2F, $CF_2\omega$); −126.96 (m, 2F, $CF_2\chi$). ESI-HRMS: M^+ calculated 560.0467, found 560.0462, Δ (mmu) = 0.5.

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