Indium(I) iodide promoted cleavage of dialkyl disulfides — Application of the Michael addition of thiolate anions to conjugated carbonyl compounds and regioselective ring opening of epoxides

Brindaban C. Ranu and Tanmay Mandal

Abstract: Indium(I) iodide promotes cleavage of dialkyl disulfides generating thiolate anions that then undergo facile addition to α,β-unsaturated ketones, aldehydes, carboxylic esters, and nitriles under neutral conditions producing corresponding β-ketosulfides or β-cyanosulfides. This strategy has also been used for the regioselective nucleophilic ring opening of epoxides by thiolate anions in presence of indium(III) chloride producing corresponding β-hydroxyphenyl sulfides. The reactions are in general, very clean, high yielding, and reasonably fast. Thus, simple and convenient procedures for the synthesis of β-ketosulfides or β-cyanosulfides and β-hydroxyalkyl sulfides have been developed using this cleavage reaction.

Key words: indium(I) iodide, Michael addition, β-ketosulfide, β-cyanosulfide, epoxide, β-hydroxy sulfide.

Résumé : L'iodure d'indium(I) facilite le clivage des disulfures d'alkyles et génère la formation d'anions thiolates qui peuvent ensuite s'additionner facilement sur des cétones, des aldéhydes, des esters carboxyliques et des nitriles α,β-insaturés, dans des conditions neutres, pour conduire à la formation des β-céto ou β-cyanosulfures correspondants. On a aussi utilisé cette stratégie pour l'ouverture de cycle nucléophile et régiosélective d'époxydes par des anions thiolates en présence de chlorure d'indium(III) qui conduisent à la formation des sulfures de β-hydroxyphényle. Les réactions sont, en général, très propres et elles donnent des rendements élevés rapidement. Des méthodes simples et faciles utilisant cette réaction de clivage permettent donc de synthétiser des β-cétosulfures ou des β-cyanosulfures ainsi que des sulfures de β-hydroxyalkyles.

Mots clés : iodure d'indium(I), addition de Michael, β-cétosulfure, β-cyanosulfure, époxyde, β-hydroxysulfure.

[Traduit par la Rédaction]

Introduction

The importance of indium reagents in organic synthesis has been well-demonstrated through novel protocols for carbon–carbon bond formation, rearrangements, and a variety of other useful transformations over past few years (1) and increasing interest in this area is continuing (2). As a part of our activities in indium-mediated reactions (3), we are constantly looking for new indium reagents and we reported the application of indium(I) iodide (4) for the cleavage of diphenyl diselenide and disulfide followed by in situ condensation with alkyl halide (4*a*, 4*b*). We also communicated the cleavage of dialkyl disulfides promoted by InI followed by subsequent Michael addition of thiolate anions to conjugated carbonyl compounds (4*c*). We have now discovered another application of this protocol for regioselective ring opening of epoxides by thiolate anions in presence of indium(III) chloride to provide β-hydroxy sulfides. We wish to report here the results of our earlier communication (4*c*) in detail together with this new observation (Scheme 1).

The β-oxy- and β-hydroxy-sulfides are very useful molecules as they constitute a common structural component in a vast group of natural products (5). Some of the synthetic molecules are found to have biological and pharmaceutical activities (6). These molecules are also very useful intermediates in organic synthesis (7). Many methods are available in the literature for the synthesis of β-oxy- (8) and β-hydroxy-sulfides (9) and these are primarily based on reaction with thiols under base or acid catalysis. However, many of them suffer from disadvantages of harsh reaction conditions, poor regioselectivity, unsatisfactory yields, long reaction times, and are associated with undesirable side reactions owing to the oxidation of thiol or rearrangement of epoxides. Since β-oxy- and β-hydroxy-sulfides have become increasingly useful and important in organic synthesis, development of simple, efficient, and mild procedures for their

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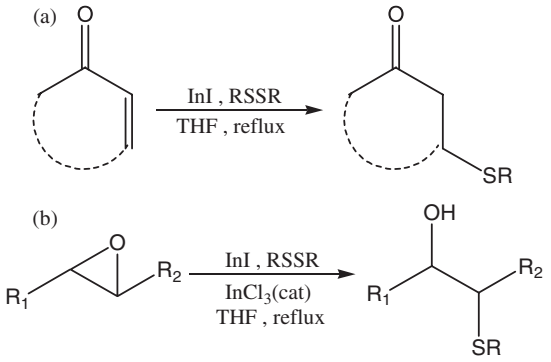
Scheme 1.



synthesis are highly desirable. Thus, we sought an alternative approach replacing thiol by a more stable sulphur reagent and we found that dialkyl disulfide can do this job more efficiently (Scheme 1).

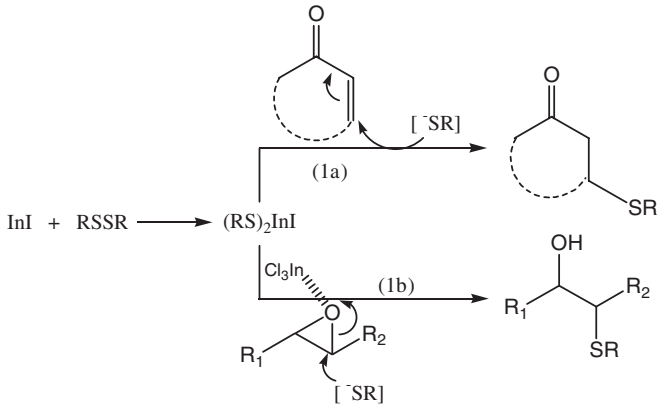
Results and discussion

The experimental procedures for both of these reactions are very simple and convenient. A solution of dialkyl disulfide and activated alkene in THF was heated under reflux in the presence of indium(I) iodide and the Michael adduct was isolated by the usual workup. On the other hand, a stirred solution of indium(I) iodide, dialkyl disulfide, and epoxide in dry THF was heated under reflux in the presence of a catalytic amount of indium trichloride (5 mol%) (TLC) and quenched with a few drops of water. Extraction with ether and the usual workup produced a pure product.

Several α,β-unsaturated ketones, aldehydes, and carboxylic esters underwent facile Michael additions to dithiolate anions generated by the cleavage of disulfides by this procedure to provide the corresponding adducts in high yields. Conjugated nitriles were also found to react with the thiolate anions, although the yields are relatively low compared with those with carbonyl compounds. The results are summarized in Table 1. Aliphatic as well as aromatic disulfides are found to undergo cleavage and subsequent reaction. On the other hand, both cyclic and acyclic conjugated carbonyl compounds participate in this reaction as Michael acceptors.

A wide range of structurally diverse epoxides underwent cleavages by reaction with dialkyl or diaryl disulfides by this procedure to provide the corresponding β-hydroxysulfides in high yields. The results are summarized in Table 2. The cleavages are highly regio- and stereo-selective. As expected, attack of thiolate anion occurred at the less-hindered carbon atom of the terminal alkyl-substituted epoxides (Table 2, entries 1–5). However, an aryl-substituted epoxide (Table 2, entry 6) attack occurs at the benzylic carbon atom. The cyclic epoxides (Table 2, entries 7–12) produced stereospecifically trans-diequatorial β-hydroxysulfides. In case of open-chain, α-keto aryl epoxides (Table 2, entries 13–15) thiolate anion also stitched at the benzylic carbon producing the corresponding γ-keto-β-hydroxysulfides. In all cases, the syn orientation of hydroxy and thiophenyl were observed as revealed by their coupling constants in ^{1}H NMR. The nonaromatic cyclic α-keto epoxides (Table 2, entries 16–18) underwent the attack of thiolate anion to the epoxycarbon atom α to the carbonyl group and simultaneous dehydration

Scheme 2.



occurred under the reaction process to produce the corresponding α-thiophenyl α,β-unsaturated ketones, although in β-methyl epoxyketone (Table 2, entry 18), a minor product (20%) from the β attack was isolated. However, in the case of α-methyl-α,β-epoxyketone (Table 2, entry 19) α-methyl-α-thiophenyl-β-hydroxyketone was obtained, as dehydration is not feasible.

In general, the reactions are considerably fast, clean, and high yielding. Presumably, these reactions are going through the intermediacy of bis(phenylthiophenyl)iodoindium(III), formed readily by the oxidative insertion of equimolar quantities of InI to diphenyl disulfide, which then releases thiolate anion to trigger the Michael addition and epoxide cleavage under the catalysis of $InCl_3$ (Scheme 2). It has also been observed that the epoxide cleavage reactions did not proceed at all without the presence of $InCl_3$.

In conclusion, this one-pot procedure for the synthesis of β-oxy- and β-hydroxyalkyl sulfides has been developed involving indium(I) iodide mediated cleavage of diorganyl disulfides and subsequent reaction with conjugated carbonyl compounds and epoxides. The significant advantages offered by this method are operational simplicity, relatively fast reaction, neutral and mild reaction conditions, general applicability, high regio- and stereo-selectivity, and good yields. Thus, it provides a better and practical alternative to the existing procedures (8, 9). Moreover, this constitutes a novel approach demonstrating the synthetic potential of indium(I) iodide, and further useful applications of this reagent are in progress.

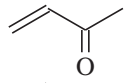
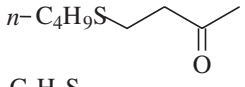
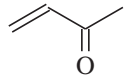
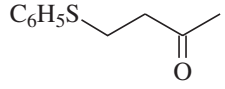
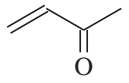
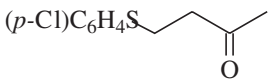
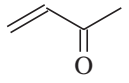
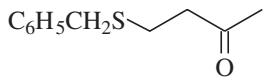
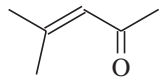
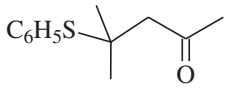
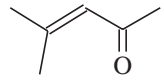
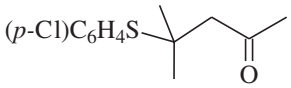
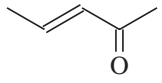
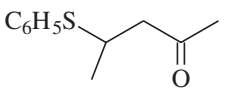
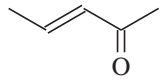
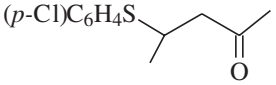
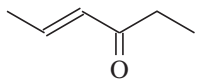
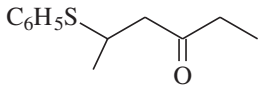
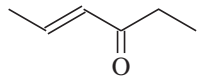
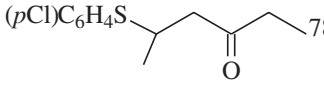
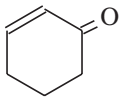
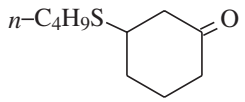
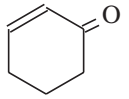
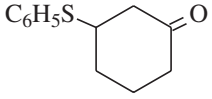
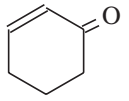
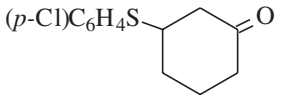
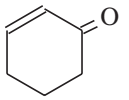
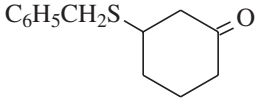
Experimental

General experimental procedure

Representative procedure for the cleavage of diphenyl disulfide and subsequent reaction with methyl vinyl ketone (Table 1, entry 2)

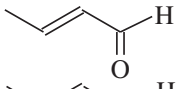
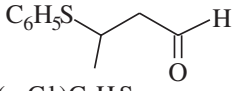
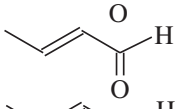
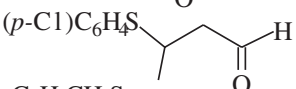
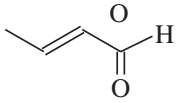
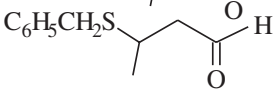
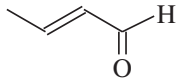
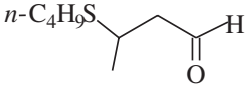
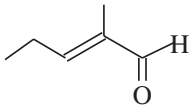
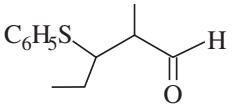
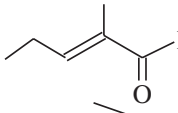
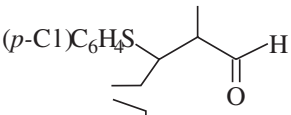
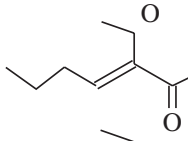
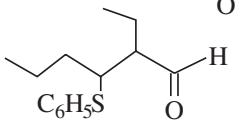
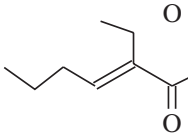
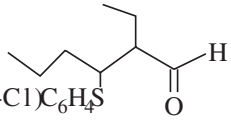
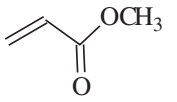
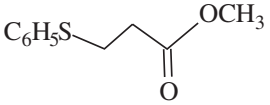
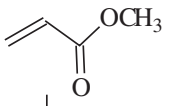
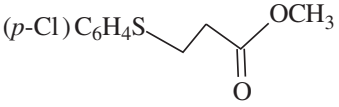
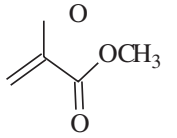
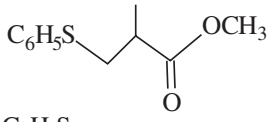
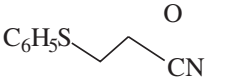
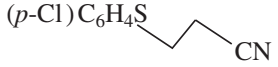
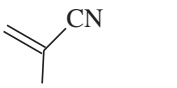
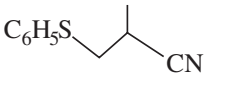
Indium(I) iodide (121 mg, 0.5 mmol) was added to a solution of diphenyl disulfide (109 mg, 0.5 mmol) in freshly distilled tetrahydrofuran (2.5 mL) under an argon atmosphere followed by the addition of methyl vinyl ketone (70 mg, 1 mmol). The reaction mixture was heated under reflux for 2.5 h (TLC). THF was then evaporated off and the residue was quenched with water and extracted with diethyl ether (3 × 10 mL). The ether extract was washed with water and

Table 1. InI-mediated cleavage of disulfides followed by Michael addition.

Entry	Disulfide	Substrate	Time (h)	Product	Yield (%)[a]	Ref.
1	n-C_4H_9S-S-n-C_4H_9		3.0		85	8*a*
2	C_6H_5S-SC_6H_5		2.5		86	10
3	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		2.5		85	
4	$C_6H_5CH_2$S-S$CH_2C_6H_5$		3.0		82	11
5	C_6H_5S-SC_6H_5		2.5		85	8*e*
6	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		3.0		81	
7	C_6H_5S-SC_6H_5		2.5		82	
8	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		3.0		80	
9	C_6H_5S-SC_6H_5		2.25		80	
10	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		3.0		78	
11	n-C_4H_9S-S-n-C_4H_9		2.5		90	8*e*
12	C_6H_5S-SC_6H_5		1.5		95	11
13	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		2.0		92	8*f*
14	$C_6H_5CH_2$S-S$CH_2C_6H_5$		2.5		89	11

dried (Na_2SO_4). The aqueous extract containing indium derivatives was discarded, although in relatively large-scale reactions indium salts may be recovered. Evaporation of the solvent left the crude product, which was purified by column chromatography over silica gel (hexane–ether, 95:5) to provide the pure addition product, 4-phenylsulfanylbutan-2-one (155 mg, 86%) as a colourless liquid. IR (neat, cm^{-1}) ν: 1716, 1477. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.14 (s, 3H), 2.76 (t, J = 7.26 Hz, 2H), 3.13 (t, J = 7.26 Hz, 2H), 7.20–7.22 (m, 2H), 7.26–7.35 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 27.9, 30.5, 43.5, 126.7, 127.9, 129.4 (2C), 130.0 (2C). These values are in good agreement with those reported for this compound (10). Several Michael adducts are known and are identified by comparison of their spectroscopic data with those reported. The new compounds are characterized by their spectroscopic data and elemental analysis. The data for a few selective representative compounds are provided here.

Table 1 (*concluded*).

Entry	Disulfide	Substrate	Time (h)	Product	Yield (%)[a]	Ref.
15	C_6H_5S-SC_6H_5		2.5		92	8*e*
16	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		3.0		90	
17	$C_6H_5CH_2S$-$SCH_2C_6H_5$		3.5		82	
18	n-C_4H_9S-S-n-C_4H_9		4.0		80	8*e*
19	C_6H_5S-SC_6H_5		3.0		80 (61:39)[b]	
20	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		3.5		78 (59:41)[b]	
21	C_6H_5S-SC_6H_5		3.0		80 (53:47)[b]	
22	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		3.5		76 (51:49)[b]	
23	C_6H_5S-SC_6H_5		4.0		73	8*e*
24	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		4.25		70	
25	C_6H_5S-SC_6H_5		5.0		60	8*e*
26	C_6H_5S-SC_6H_5		4.0		72	8*e*
27	(*p*-Cl)C_6H_4S-SC_6H_4(*p*-Cl)		4.5		65	
28	C_6H_5S-SC_6H_5		5.0		55	

[a]Yields refer to those of pure isolated products characterized by spectroscopic data (IR and ^{1}H and ^{13}C NMR).
[b]Ratio of diastereoisomers as determined by ^{1}H NMR.

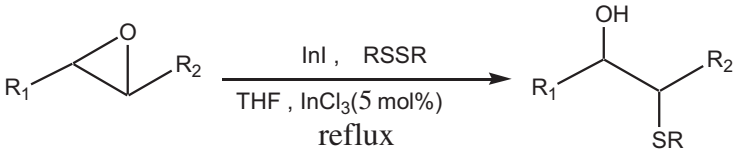
4-(4-Chlorophenylsulfanylbutan-2-one (Table 1, entry 3)

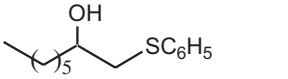
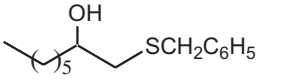
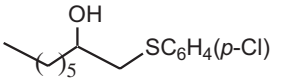
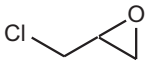
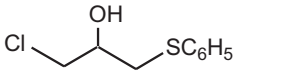
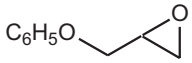
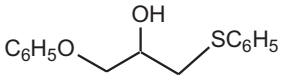
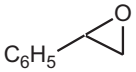
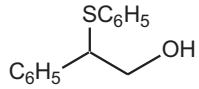
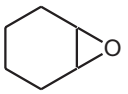
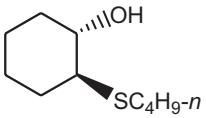
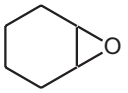
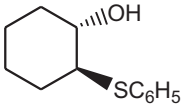
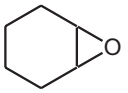
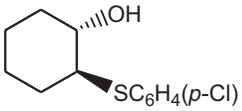
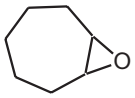
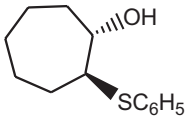
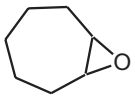
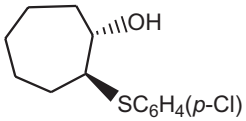
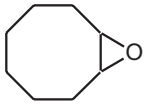
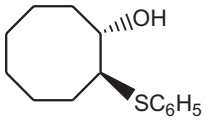
Colourless liquid. IR (neat, cm^{-1}) ν: 1438, 1477, 1578, 1716. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.14 (s, 3H), 2.73 (t, *J* = 7.2 Hz, 2H), 3.10 (t, *J* = 7.2 Hz, 2H), 7.25 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.1, 30.5, 43.3, 129.5 (2C), 131.2 (2C), 132.8, 134.7, 206.7. Anal. calcd. for $C_{10}H_{11}ClOS$: C 55.94, H 5.16; found: C 55.81, H 5.09.

4-(4-Chlorophenylsulfanyl)-4-methyl-pentan-2-one (Table 1, entry 6)

Colourless liquid. IR (neat, cm^{-1}) ν: 1438, 1473, 1573, 1715. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.36 (s, 6H), 2.11 (s, 3H), 2.62 (s, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.1 (2C), 32.0, 47.2, 54.2, 128.8 (2C), 129.8, 136.9, 138.7 (2C), 206.2.

Table 2. Cleavages of epoxides by dialkyl and diaryl disulfides.



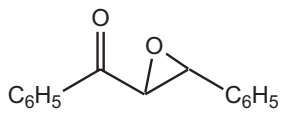
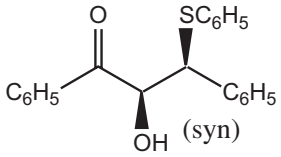
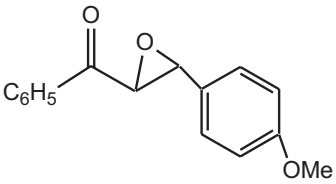
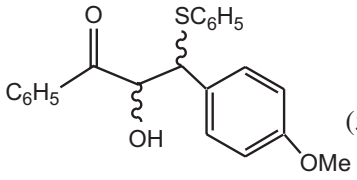
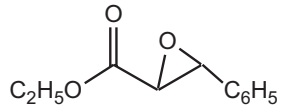
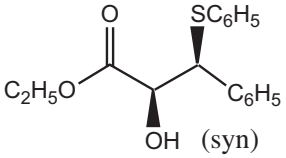
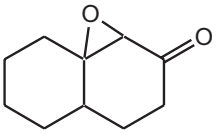
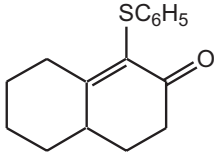
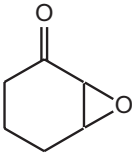
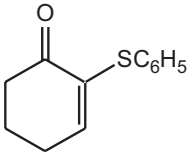
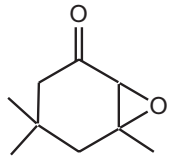
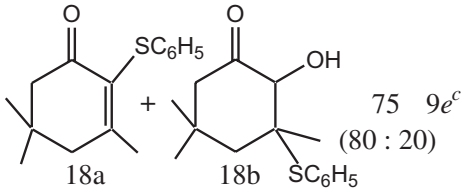
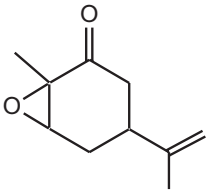
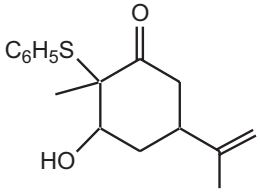
Entry	Epoxide	R	Time (h)	Product	Yield (%)[a]	Ref.
1		C_6H_5	3.0		98	9*g*
2		$C_6H_5CH_2$	4.0		78	9*b*
3		C_6H_4(*p*-Cl)	4.5		80	
4		C_6H_5	2.5		76	9*g*
5		C_6H_5	3.0		80	9*g*
6		C_6H_5	2.75		60	9*b*
7		*n*-C_4H_9	4.5		69	9*b*
8		C_6H_5	3.0		82	9*e*
9		C_6H_4(*p*-Cl)	3.0		80	
10		C_6H_5	3.5		82	9*g*
11		C_6H_4(*p*-Cl)	3.5		72	
12		C_6H_5	3.5		78	9*g*

Anal. calcd. for $C_{12}H_{15}ClOS$: C 59.37, H 6.23; found: C 59.22, H 6.09.

4-Phenylsulfanylpentan-2-one (Table 1, entry 7)

Colourless liquid. IR (neat, cm^{-1}) ν: 1438, 1477, 1583, 1714. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.28 (d, J = 6.6 Hz, 3H), 2.12 (s, 3H), 2.55 (dd, J_1 = 8.5 Hz, J_2 = 17.0 Hz, 1H), 2.75 (dd, J_1 = 5.3 Hz, J_2 = 17.0 Hz, 1H), 3.63–3.72 (m, 1H), 7.22–7.35 (m, 3H), 7.39–7.49 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.9, 30.5, 38.1, 50.2, 127.1, 128.8 (2C), 132.3 (2C), 134.1, 206.4. Anal. calcd. for $C_{11}H_{14}OS$: C 68.00, H 7.26; found: C 67.73, H 7.11.

Table 2 (*concluded*).

Entry	Epoxide	R	Time (h)	Product	Yield (%)[a]	Ref.
13		C_6H_5	2.25	 (syn)	81	
14		C_6H_5	2.5		80 (52:48)[b]	
15		C_6H_5	5.5	 (syn)	85	
16		C_6H_5	3.25		70	
17		C_6H_5	3.0		75	9*e*
18		C_6H_5	2.75	 18a 18b	75 (80 : 20)	9*e*[c]
19		C_6H_5	3.0		76	9*e*

[a]Yields refer to pure isolated products characterized by spectroscopic data (IR and ^{1}H and ^{13}C NMR).
[b]The ratio was determined by ^{1}H NMR spectroscopic data.
[c]Corresponds to compound 18a.

4-(4-Chlorophenylsulfanyl)pentan-2-one (Table 1, entry 8)

Colourless liquid. IR (neat, cm^{-1}) ν: 1475, 1716. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.27 (d, J = 6.5 Hz, 3H), 2.12 (s, 3H), 2.55 (dd, J_1 = 8.3 Hz, J_2 = 17.2 Hz, 1H), 2.72 (dd, J_1 = 5.3 Hz, J_2 = 17.2 Hz, 1H), 3.65 (m, 1H), 7.26 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.9, 30.5, 38.4, 50.0, 129.0 (2C), 132.5, 133.4, 133.6 (2C), 206.2. Anal. calcd. for $C_{11}H_{13}ClOS$: C 57.76, H 5.73; found: C 57.84, H 5.81.

5-Phenylsulfanyl-hexan-3-one (Table 1, entry 9)

Colourless liquid. IR (neat, cm^{-1}) ν: 1477, 1712. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.03 (t, J = 7.3 Hz, 3H), 1.27 (d, J = 6.7 Hz, 3H), 2.39 (q, J = 14.8 Hz, 2H), 2.53 (dd, J = 8.5 Hz, 16.9 Hz, 1H), 2.73 (dd, J = 5.3 Hz, 16.9 Hz, 1H), 3.71 (m, 1H), 7.23–7.32 (m, 3H), 7.38–7.42 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 7.5, 20.9, 36.6, 38.2, 48.9, 124.5, 127.1 (2C), 132.2 (2C), 134.2, 209.2. Anal. calcd. for $C_{12}H_{16}OS$: C 69.19, H 7.74; found: C 68.93, H 7.60.

5-(4-Chlorophenylsulfanyl)hexan-3-one (Table 1, entry 10)

Colourless liquid. IR (neat, cm^{-1}) ν: 1475, 1714. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.03 (t, *J* = 7.3 Hz, 3H), 1.26 (d, *J* = 6.7 Hz, 3H), 2.39 (q, *J* = 14.3 Hz, 2H), 2.52 (dd, *J* = 8.3 Hz, 16.4 Hz, 1H), 2.69 (dd, *J* = 5.5 Hz, 16.3 Hz, 1H), 3.68 (m, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 7.5, 20.9, 36.6, 38.5, 48.8, 128.9 (2C), 132.8, 132.9, 133.3 (2C), 208.9. Anal. calcd. for $C_{12}H_{15}ClOS$: C 59.37, H 6.23; found: C 59.21, H 6.07.

3-(4-Chlorophenylsulfanyl)butanal (Table 1, entry 16)

Colourless liquid. IR (neat, cm^{-1}) ν: 1437, 1475, 1724. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.34 (d, *J* = 6.6 Hz, 3H), 2.54–2.73 (m, 2H), 3.63–3.69 (m, 1H), 7.23–7.37 (m, 4H), 9.74 (t, *J* = 1.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.5, 38.2, 50.4, 128.1, 129.6 (2C), 132.3, 134.7 (2C), 200.5. Anal. calcd. for $C_{10}H_{11}ClOS$: C 55.94, H 5.16; found: C 55.73, H 5.07.

3-Benzylsulfanyl-butanal (Table 1, entry 17)

IR (neat, cm^{-1}) ν: 1477, 1724. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.33 (d, *J* = 6.8 Hz, 3H), 2.55–2.61 (m, 2H), 3.13–3.19 (m, 1H), 3.78 (s, 2H), 7.24–7.33 (m, 5H), 9.66 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.3, 33.6, 35.2, 50.1, 127.1, 128.5 (2C), 128.7 (2C), 137.9, 200.5. Anal. calcd. for $C_{11}H_{14}OS$: C 68.0, H 7.26; found: C 68.09, H 7.17.

2-Methyl-3-phenylsulfanyl-pentanal (Table 1, entry 19)

Obtained as a mixture of diastereoisomers (61:39). IR (neat, cm^{-1}) ν: 1447, 1722, 2721. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.08 (t, *J* = 7.2 Hz, 3H), 1.20 (d, *J* = 7.2 Hz, 3H), 1.54–1.67 (m, 2H), 2.55–2.59 (m, 1H), 3.39–3.45 (m, 1H), 7.22–7.33 (m, 3H), 7.41–7.44 (m, 2H), 9.68 (d, *J* = 1.6 Hz, 1H major), 9.69 (d, *J* = 1.0 Hz, 1H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 9.7 (minor), 10.1 (major), 11.8 (major), 12.1 (minor), 24.2 (major), 26.2 (minor), 49.1 (minor), 49.7 (major), 51.3 (major), 52.7 (minor), 127.2, 128.9 (2C), 132.3 (2C), 133.2, 203.5. Anal. calcd. for $C_{12}H_{16}OS$: C 69.19, H 7.74; found: C 69.03, H 7.60.

3-(4-Chlorophenylsulfanyl)-2-methyl-pentanal (Table 1, entry 20)

Colourless liquid obtained as a mixture of diastereoisomers (59:41). IR (neat, cm^{-1}) ν: 1475, 1724, 2721. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.04 (t, *J* = 7.2 Hz, 3H), 1.20 (d, *J* = 7.21 Hz, 3H), 1.62–1.73 (m, 2H), 2.63–2.67 (m, 1H), 3.34–3.40 (m, 1H), 7.26 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 9.67 (d, *J* = 1.6 Hz, 1H, minor), 9.68 (d, *J* = 1.0 Hz, 1H, major). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 9.7 (major), 10.2 (minor), 11.8 (minor), 12.1 (major), 24.2 (minor), 26.2 (major), 48.9 (major), 49.6 (minor), 51.7 (minor), 52.9 (major), 129.1 (2C), 133.4, 133.5 (2C), 133.6, 203.2. Anal. calcd. for $C_{12}H_{15}ClOS$: C 59.37, H 6.23; found: C 59.41, H 6.17.

2-Ethyl-3-phenylsulfanyl-hexanal (Table 1, entry 21)

Colourless liquid obtained as a mixture of diastereoisomers (53:47). IR (neat, cm^{-1}) ν: 1479, 1720, 2715. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88–0.96 (m, 6H), 1.51–1.71 (m, 6H), 2.33–2.37 (m, 1H), 3.35–3.43 (m, 1H), 7.21–7.32 (m, 3H), 7.38–7.43 (m, 2H), 9.66 (d, *J* = 2.7 Hz, 1H, major), 9.75 (d, *J* = 2.3 Hz, 1H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 11.9 (major), 12.0 (minor), 13.6 (major), 13.7 (minor), 19.3 (major), 19.3 (minor), 20.2 (major), 20.5 (minor), 34.1 (minor), 34.6 (major), 49.2 (major), 49.8 (minor), 56.5 (minor), 56.9 (major), 127.2, 128.9 (2C), 132.3 (2C), 134.8, 203.5 (major), 204.1 (minor). Anal. calcd. for $C_{14}H_{20}OS$: C 71.14, H 8.53; found: C 70.93, H 8.39.

3-(4-Chlorophenylsulfanyl)-2-ethyl-hexanal (Table 1, entry 22)

Colourless liquid obtained as a mixture of diastereoisomers (51:49). IR (neat, cm^{-1}) ν: 1475, 1722, 2719. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88, 0.94 (m, 6H), 1.49–1.84 (m, 6H), 2.32–2.36 (m, 1H), 3.31–3.37 (m, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 9.66 (d, *J* = 2.7 Hz, 1H, minor), 9.73 (d, *J* = 2.2 Hz, 1H, major). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 11.9 (major), 12.0 (minor), 13.6 (major), 13.6 (minor), 19.2 (major), 19.3 (minor), 20.2 (major), 20.5 (minor), 34.0 (major), 34.6 (minor), 49.6 (major), 50.2 (minor), 56.8 (major), 56.4 (minor), 129.1 (2C), 133.3, 133.4, 133.6 (2C), 203.3 (major), 203.6 (minor). Anal. calcd. for $C_{14}H_{19}ClOS$: C 62.09, H 7.07; found: C 61.89, H 6.94.

3-(4-Chlorophenylsulfanyl)propionic acid methyl ester (Table 1, entry 24)

Colourless liquid. IR (neat, cm^{-1}) ν: 1477, 1737. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.59 (t, *J* = 7.5 Hz, 2H), 3.13 (t, *J* = 7.5 Hz, 2H), 3.67 (s, 3H), 7.19–7.29 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 29.7, 34.4, 52.3, 129.5 (2C), 131.8 (2C), 134.1, 134.2, 172.4. Anal. calcd. for $C_{10}H_{11}ClO_2S$: C 52.06, H 4.77; found: C 52.11, H 4.71.

3-(4-Chlorophenylsulfanyl)propionitrile (Table 1, entry 27)

Pale yellow gummy liquid. IR (neat, cm^{-1}) ν: 1431, 1477, 2243. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.55–2.61 (m, 2H), 3.07–3.13 (m, 2H), 7.25–7.37 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.1, 30.4, 117.6, 129.5 (2C), 131.6, 132.7 (2C), 133.9. Anal. calcd. for C_9H_8ClNS: C 54.68, H 4.08, N 7.09; found: C 54.49, H 4.01, N 7.02.

2-Methyl-3-phenylsulfanyl-propionitrile (Table 1, entry 28)

Pale yellow liquid. IR (neat, cm^{-1}) ν: 1438, 1481, 1583, 2241. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.40 (d, *J* = 6.9 Hz, 3H), 2.71–2.78 (m, 1H), 2.93–3.02 (m, 1H), 3.12–3.28 (m, 1H), 7.23–7.35 (m, 3H), 7.38–7.43 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.1, 26.0, 38.2, 121.4, 127.4, 129.3 (2C), 131.1 (2C), 137.0. Anal. calcd. for $C_{10}H_{11}NS$: C 67.75, H 6.25, N 7.90; found: C 75.43, H 6.16, N 7.81.

General procedure for the synthesis of β-hydroxyalkyl/aryl sulfides

Representative procedure for 1-phenylsulfanyloctan-2-ol (Table 2, entry 1)

To a stirred solution of indium(I) iodide (121 mg, 0.5 mmol) and diphenyldisulphide (109 mg, 0.5 mmol) in dry THF (2.5 mL) was added 1-octene oxide (128 mg, 1 mmol) and indium trichloride (11.05 mg, 5 mol%) under nitrogen. The reaction mixture was heated under reflux for 3 h (TLC) and quenched with a few drops of water. THF was then evaporated off and the residual mixture was then extracted with ether (3 × 20 mL). The combined ether ex-

tract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent left the crude product, which was purified by column chromatography over silica gel (hexane–ether, 85:15) to furnish the pure product, 1-thiophenyloctan-2-ol as a colourless oil (233 mg, 98%). The product was identified by comparison of its spectroscopic data (IR and ^{1}H and ^{13}C NMR) with the reported values (8*g*).

This procedure was followed for all the reactions listed in Table 2. All the products are adequately characterized by their spectroscopic data (IR and ^{1}H and ^{13}C NMR). The values for the known compounds are in good agreement with those reported (Table 2). The spectroscopic data and elemental analysis for new compounds that are not available in the literature are provided here.

1-(4-Chlorophenylsulfanyl)octan-2-ol (Table 2, entry 3)

Colourless liquid. IR (neat, cm^{-1}) ν: 1439, 1479, 1580, 3467. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.87 (t, *J* = 6.36 Hz, 3H), 1.26–1.41 (m, 7H), 1.42–1.53 (m, 3H), 2.36 (bs, 1H), 2.84 (dd, *J* = 8.49, 13.56 Hz, 1H), 3.08 (dd, *J* = 3.39 Hz, 13.56 Hz, 1H), 3.62–3.70 (m, 1H), 7.23–7.32 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.4, 22.9, 25.9, 29.6, 32.1, 36.5, 42.7, 69.9, 129.5 (2C), 131.6 (2C), 132.9, 134.5. Anal. calcd. for $C_{14}H_{21}ClOS$: C 61.63, H 7.76; found: C 61.50, H 7.61.

2-(4-Chlorophenylsulfanyl)cyclohexanal (Table 2, entry 9)

Colourless liquid. IR (neat, cm^{-1}) ν: 1446, 1477, 1581, 3398. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.17–1.38 (m, 4H), 1.67–1.79 (m, 2H), 2.03–2.12 (m, 2H), 2.70–2.77 (m, 1H), 2.80 (s, 1H), 3.30 (ddd, *J* = 4.20, 9.86, 10.01 Hz, 1H), 7.23–7.26 (m, 2H), 7.35–7.39 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.6, 26.4, 32.9, 34.3, 56.9, 72.4, 129.4 (2C), 131.7, 134.3, 135.3 (2C). Anal. calcd. for $C_{12}H_{15}ClOS$: C 59.37, H 6.23; found: C 59.21, H 6.11.

2-(4-Chlorophenylsulfanyl)cycloheptanol (Table 2, entry 11)

Colourless liquid. IR (neat, cm^{-1}) ν: 1438, 1478, 1582, 3473. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.46–1.61 (m, 4H), 1.69–1.77 (m, 2H), 1.99–2.25 (m, 2H), 2.27–2.40 (m, 2H), 2.41 (s, 1H), 3.64 (ddd, *J* = 3.21, 8.73, 9.87 Hz, 1H), 4.02–4.09 (m, 1H), 7.24–7.38 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.0, 25.0, 26.9, 32.6, 35.3, 66.1, 79.2, 126.4, 127.7, 129.5 (2C), 133.5 (2C). Anal. calcd. for $C_{13}H_{17}ClOS$: C 60.80, H 6.67; found: C 60.62, H 6.51.

3-Hydroxy-1,3-diphenyl-2-phenylsulfanyl-propan-1-one (Table 2, entry 13)

Yellow oil. IR (neat, cm^{-1}) ν: 1438, 1477, 1597, 1683, 3460. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.94 (bs, 1H), 4.64 (d, *J* = 2.58 Hz, 1H), 5.48 (d, *J* = 2.58 Hz, 1H), 7.10–7.13 (m, 2H), 7.20–7.24 (m, 6H), 7.45–7.62 (m, 4H), 7.62–7.68 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 58.0, 75.1, 128.2, 128.5 (2C), 128.6, 128.7 (2C), 129.0 (2C), 129.2 (2C), 129.3 (2C), 129.4, 129.5, 133.3 (2C), 134.5, 135.9, 198.9. Anal. calcd. for $C_{21}H_{18}O_2S$: C 75.42, H 5.42; found: C 75.31, H 5.33.

2-Hydroxy-3-(4-methoxy-phenyl)-1-phenyl-3-phenylsulfanyl-propan-1-one (as a mixture of diastereomers, 52:48) (Table 2, entry 14)

Yellowish, low-melting solid; mp 40–43 °C. IR (neat, cm^{-1}) ν: 1438, 1477, 1581, 1682, 3465. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.74 (s, 3H, major), 3.78 (s, 3H, minor), 4.57 (d, *J* = 2.64 Hz, 1H, minor), 4.64 (d, *J* = 2.58 Hz, 1H, major), 5.42 (d, *J* = 2.64 Hz, 1H, minor), 5.45 (d, *J* = 2.58 Hz, 1H, major), 6.74 (d, *J* = 7.32 Hz, 2H, minor), 6.86 (d, *J* = 8.70 Hz, 2H, major), 7.04–7.07 (m, 4H, (2H for major and 2H for minor)), 7.29–7.32 (m, 4H (2H for major and 2H for minor)), 7.41–7.50 (m, 8H (4H for major and 4H for minor)), 7.62–7.64 (m, 4H (2H for major and 2H for minor)), 7.66 (d, *J* = 8.70 Hz, 2H, major), 7.84 (d, *J* = 7.32 Hz, 2H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.5 (major), 55.6 (minor), 57.3 (minor), 58.4 (major), 75.2 (minor), 77.1 (major), 113.9 (minor, 2C), 114.3 (major, 2C), 127.6 (minor), 127.8 (major), 128.1 (minor), 128.2 (major), 128.8 (major, 2C), 128.9 (minor, 2C), 129.1 (major, 2C), 129.2 (minor, 2C), 129.4 (major, 2C), 129.5 (minor, 2C), 129.9 (minor, 2C), 130.1 (minor), 130.4 (major, 2C), 130.5 (major), 132.8 (minor, 2C), 133.3 (major, 2C), 134.2 (minor), 134.5 (major), 134.7 (minor), 135.1 (major), 159.5 (minor), 159.7 (major), 199.1 (minor), 199.7 (major). Anal. calcd. for $C_{22}H_{20}O_3S$: C 72.50, H 5.53; found: C 72.41, H 5.43.

2-Hydroxy-3-phenyl-3-phenylsulfanyl propionic acid ethyl ester (Table 2, entry 15)

Colourless liquid. IR (neat, cm^{-1}) ν: 1439, 1479, 1583, 1732, 3484. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.07 (t, *J* = 7.20 Hz, 3H), 2.88 (bs, 1H), 3.99 (q, *J* = 7.20 Hz, 2H), 4.49 (d, *J* = 3.69 Hz, 1H), 4.52 (d, *J* = 3.69 Hz, 1H), 7.11–7.18 (m, 6H), 7.28–7.33 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.9, 56.5, 61.8, 72.6, 127.4, 127.9, 128.2 (2C), 128.3 (2C), 128.7 (2C), 132.1 (2C), 134.2, 136.4, 171.8. Anal. calcd. for $C_{17}H_{18}O_3S$: C 67.52, H 6.00; found: C 67.45, H 5.91.

1-Phenylsulfanyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one (Table 2, entry 16)

Yellowish liquid. IR (neat, cm^{-1}) ν: 1439, 1477, 1582, 1674, 3477. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.97–1.51 (m, 4H), 1.52–2.13 (m, 5H), 2.44–2.83 (m, 3H), 3.59–3.69 (m, 1H), 7.07–7.44 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.3, 27.2, 28.2, 34.6, 35.2, 37.0, 41.0, 125.3, 127.2 (2C), 128.9 (2C), 137.2, 137.4, 174.0, 195.1. Anal. calcd. for $C_{16}H_{18}OS$: C 74.38, H 7.02; found: C 74.25, H 6.92.

2-Hydroxy-3,5,5-trimethyl-3-phenylsufanyl-cyclohexanone (Table 2, entry 18b)

Colourless liquid. IR (neat, cm^{-1}) ν: 1439, 1477, 1582, 1740. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.15 (s, 3H), 1.27 (s, 3H), 1.42 (s, 3H), 1.81–1.86 (m, 1H), 2.25–2.34 (m, 2H), 2.53–2.59 (m, 1H), 4.44 (s, 1H), 7.15–7.26 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.3, 30.7, 31.1, 32.9, 47.1, 54.7, 56.8, 71.3, 128.0, 129.0 (2C), 133.2, 133.8, 134.2, 220.7. Anal. calcd. for $C_{15}H_{20}O_2S$: C 68.14, H 7.62; found: C 67.95, H 7.48.

3-Hydroxy-5-isopropenyl-2-methyl-2-phenylsulfanyl-cyclohexanone (Table 2, entry 19)

Colourless liquid. IR (neat, cm^{-1}) ν: 1439, 1474, 1646, 1696, 3464. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.18 (s, 3H), 1.76 (s, 3H), 1.89–1.97 (m, 1H), 2.32–2.42 (m, 2H), 2.57 (bs, 1H), 2.84–2.94 (m, 1H), 3.30–3.41 (m, 1H), 4.18–4.20 (m, 1H), 4.79 (d, *J* = 0.75 Hz, 2H), 7.24–7.35 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.8, 20.4, 33.4, 39.2, 41.7, 59.9,

76.0, 110.3, 129.0 (2C), 129.6, 129.7, 136.5 (2C), 147.0, 208.5. Anal. calcd. for $C_{16}H_{20}O_2S$: C 69.53, H 7.29; found: C 69.43, H 7.13.

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