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A short and stereoselective synthesis of highly substituted cyclopropanes from α,β-unsaturated carbonyl compounds with dichloromethyl *p*-tolyl sulfoxide

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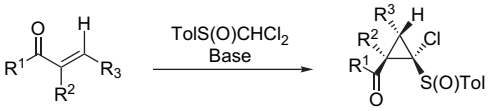
ABSTRACT

The reaction of the α-sulfinyl carbanion of dichloromethyl *p*-tolyl sulfoxide with a variety of α,β-unsaturated carbonyl compounds gave highly substituted cyclopropanes (up to five substituents) in good to high yields with high stereoselectivity.

1. Introduction

Cyclopropanes are unambiguously one of the most important and fundamental compounds in organic and synthetic organic chemistry. Because of their highly strained nature, cyclopropanes have long been recognized to be highly versatile and useful compounds in organic synthesis and innumerable studies on their chemistry, synthesis, and synthetic utilities have been studied.[1] From a synthetic viewpoint of cyclopropanes, cyclopropanation of olefins with carbenes or carbenoids (Simmons–Smith-type cyclopropanation) has been most widely studied.[2] However, this method is frequently not useful for preparing highly substituted and/or functionalized cyclopropanes.

Recently, we are interested in the use of aryl dichloromethyl sulfoxides in organic synthesis and reported a new method for a short synthesis of 2-arylfurans from alkenyl aryl ketones.[3] In continuation of our investigation for the development of new synthetic method utilizing aryl dichloromethyl sulfoxides, we found that the reaction of α-sulfinyl carbanion of dichloromethyl *p*-tolyl sulfoxide with α,β-unsaturated esters and α,β-unsaturated ketones gave highly substituted cyclopropanes in good to high yields with high stereoselectivity. This reaction offers a new method for a short synthesis of highly substituted cyclopropanes **2** from relatively easily available α,β-unsaturated carbonyl compounds **1** (Scheme 1).

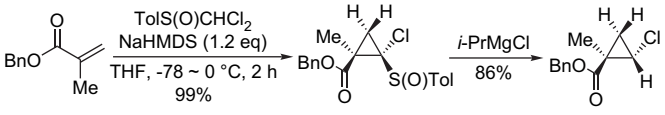


1 **2**

Scheme 1.

2. Results and discussion

At first, to a solution of benzyl methacrylate **3** (1.2 equiv) and dichloromethyl *p*-tolyl sulfoxide[3] (1.0 equiv) in THF at −78 °C was added a solution of sodium hexamethyldisilazide (NaHMDS; 1.2 equiv) and the temperature of the reaction mixture was slowly allowed to warm to 0 °C for 2 h to give cyclopropane **4** in a quantitative yield (Scheme 2). Surprisingly, although the product **4** has three stereogenic centers, only a single product was obtained. The structure of the product **4** was easily determined from NOESY spectral measurement of the stereospecifically desulfinylated product **5**.[4]



3 **4** **5**

Scheme 2.

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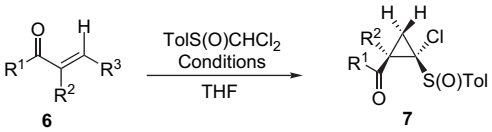
Table 1
Synthesis of cyclopropanes **7** from α,β-unsaturated carbonyl compounds **6** with dichloromethyl *p*-tolyl sulfoxide



Entry	**6**				Conditions	**7**	
		R^1	R^2	R^3			Yield/%
1	**6a**	OEt	Me	H	NaHMDS (1.2 equiv), −78 to 0 °C, 2 h	**7a**	99
2	**6b**	OEt	*n*-Bu	H	NaHMDS (1.2 equiv), −78 to 0 °C, 2 h	**7b**	77
3	**6c**	Ph	Me	H	NaH (4.0 equiv), 0 °C to rt, o.n.	**7c**	83
4	**6d**	Ph	*n*-Pr	H	NaH (4.0 equiv), 0 °C to rt, o.n.	**7d**	96
5	**6e**	Ph	H	Me	NaH (4.0 equiv), 0 °C to rt, o.n.[a]		—[b]
6	**6f**	$CH_2CH_2CH_2Ph$	Me	H	LDA (1.2 equiv), −78 °C to rt, o.n.	**7f**	88
7	**6g**	NEt_2	Me	H	NaHMDS (1.2 equiv), −78 to 0 °C, 2 h[a]		—[c]
8		Methacrylonitrile			NaHMDS (1.2 equiv), −78 to 0 °C, 2 h[a]		—[c]

[a] Various other basic conditions were investigated.
[b] Conjugate adduct was obtained in a quantitative yield.
[c] See the text.

As we recognized that this reaction offers a good method for a short and stereoselective synthesis of highly substituted cyclopropanes, we first investigated the generality of this reaction and the results are summarized in Table 1. α,β-Unsaturated esters **6a** and **6b** gave cyclopropanes **7a** and **7b**, respectively, in high yields both as a single isomer (entries 1 and 2). The results from reaction of the α-sulfinyl carbanion of dichloromethyl *p*-tolyl sulfoxide with α,β-unsaturated ketones are summarized in entries 3–6. Thus, the reaction of phenyl vinyl ketones (**6c** and **6d**) proved to proceed better with excess NaH instead of NaHMDS (entries 3 and 4). In case of alkyl vinyl ketone **6f**, LDA was found to be the best base investigated to give **7f** in 88% yield (entry 6).

Very interestingly, the cyclopropanation did not proceed at all with α,β-unsaturated ketone that has a hydrogen as R^2 (**6e** in entry 5). We investigated the reaction of **6e** with several bases; however, only conjugate adduct, usually in near quantitative yield, was obtained. In 1989, Reutrakul et al.[5] reported that the reaction of dichloromethyl phenyl sulfoxide with 2-cyclohexenone, 2-cyclopentenone, and 3-penten-2-one in the presence of LDA–HMPA gave cyclopropanes. We reinvestigated their chemisty; however, only conjugate adducts, not cyclopropanes, were obtained by using the same conditions reported. We are not sure of the real reason for the differences between their results and ours; however, at this point, we assume that the presence of a substituent at R^2 is very important to this cyclopropanation. As shown in entries 7 and 8, the α-sulfinyl carbanion of dichloromethyl *p*-tolyl sulfoxide did not react at all with α,β-unsaturated amide **6g** and α,β-unsaturated nitrile. In these reactions, decomposition of dichloromethyl *p*-tolyl sulfoxide was observed upon warming the reaction mixture.

Because the structure of the cyclopropanes derived from the α,β-unsaturated ketones was not clearly determined by ^{1}H NMR, the structure of **7c** was determined by X-ray analysis (see Fig. 1).[6] From the result, it was disclosed that the same relative stereochemistry was induced in the reaction of both the α,β-unsaturated esters and α,β-unsaturated ketones.

Next, the reaction of α,β-disubstituted unsaturated ester **8** was investigated (Scheme 3). Interestingly, LiHMDS, instead of NaHMDS (see Scheme 2 and Table 1, entries 1 and 2), was found to be the best base to afford the desired cyclopropane **9** in 90% yield. Furthermore, the product was found to be a mixture of inseparable two diastereomers. When the mixture of two diastereomers was oxidized or desulfinylated with *i*-PrMgCl,[4] the products **10** and **11**, respectively, were obtained both as a single isomer. It is obvious that the stereogenic center of the sulfur atom is the cause of the presence of two diastereomers. The stereochemistry of **9** was determined from NOESY spectrum of **11** and comparison of the similar compound **13f**, whose stereochemistry was established by X-ray analysis (Table 2, Fig. 1, vide infra).[6]

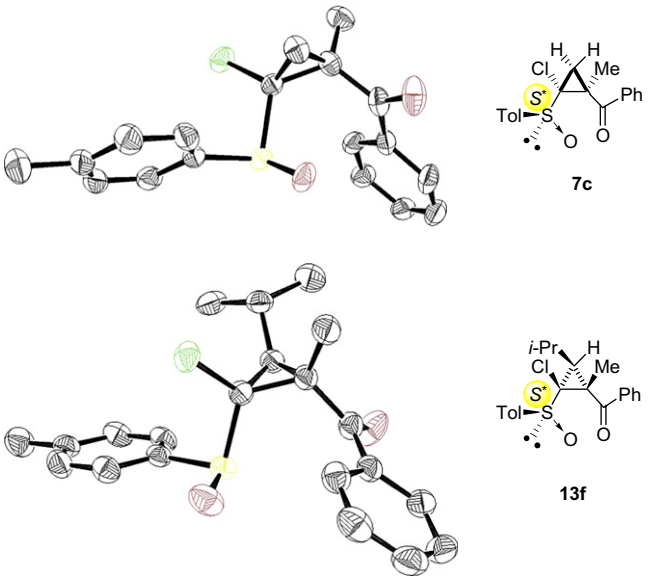
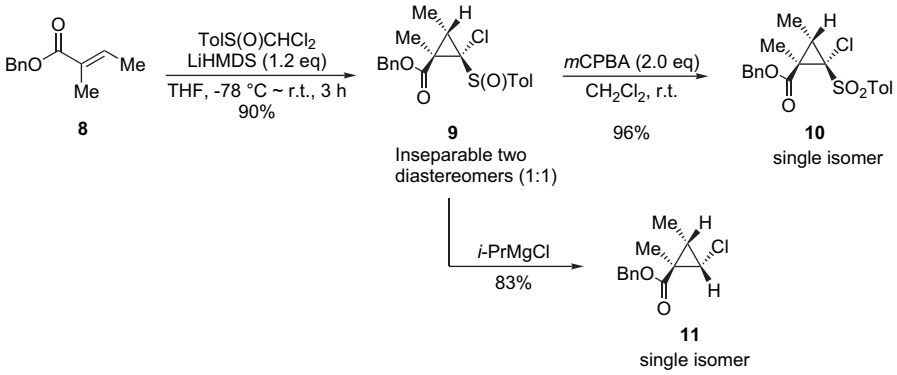


Figure 1. Crystal structure of cyclopropanes **7c** and **13f**.

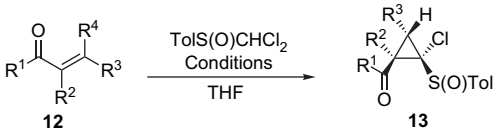
Results for the reactions of α,β-disubstituted, including α,β,β-trisubstituted, unsaturated esters and ketones (**12a**–**12j**) are summarized in Table 2. The reaction with α,β-disubstituted unsaturated esters (**12a**–**12d**) gave almost quantitative yields of the desired cyclopropanes except one case (entries 1–4). Interestingly, no reaction was observed with α,β,β-trisubstituted unsaturated ester **12e**, presumably because of the steric hindrance of the ester. This result implied that fully substituted cyclopropanes could not be synthesized by the method presented here.

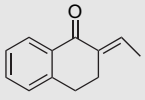
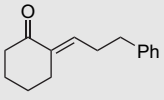
The reaction with α,β-disubstituted unsaturated ketones (**12f**–**12j**) gave high yields of the desired cyclopropanes (entries 6–10). The diastereomeric ratio was found to be variable depending on the substrate. In general, the ratio becomes larger when the substituent R^3 becomes bigger. Spiro[5.2]alkanone derivatives could be synthesized by using ketones such as **12i** and **12j** (entries 9 and 10). In order to confirm the configuration of the product **13**, X-ray analysis



Scheme 3.

Table 2
Synthesis of cyclopropanes **13** from α,β-unsaturated carbonyl compounds **12** with dichloromethyl *p*-tolyl sulfoxide



Entry	12					Conditions	13		
		R^1	R^2	R^3	R^4			Yield/%	Diastereomeric ratio[a]
1	**12a**	OEt	Me	Me	H	LiHMDS (1.2 equiv), −78 to rt, 3 h	**13a**	99	1:1
2	**12b**	OBn	Me	Et	H	LiHMDS (1.2 equiv), −78 to rt, 3 h	**13b**	94	1.5:1
3	**12c**	OBn	*n*-Bu	Me	H	LiHMDS (1.2 equiv), −78 to rt, 3 h	**13c**	99	1.5:1
4	**12d**	OEt	Me	CH_2CH_2Ph	H	LiHMDS (1.2 equiv), −78 to rt, 3 h	**13d**	44[b]	Single isomer
5	**12e**	OBn	Me	Me	Me	LiHMDS (1.2 equiv), −78 to rt, 3 h	No reaction		
6	**12f**	Ph	Me	*i*-Pr	H	NaHMDS (1.2 equiv), −78 to 0 °C, 2 h	**13f**	68	Single isomer
7	**12g**	Et	Me	CH_2CH_2Ph	H	LDA (1.2 equiv), −78 to rt, o.n.	**13g**	94	3:1
8	**12h**	*n*-Pr	Et	CH_2CH_2Ph	H	LDA (1.2 equiv), −78 to rt, o.n.	**13h**	96	6:1
9	**12i**					LDA (1.2 equiv), −78 to rt, o.n.	**13i**	87	1:1
10	**12j**					LDA (1.2 equiv), −78 to rt, o.n.	**13j**	90	Single isomer

[a] Determined by ^1H NMR.
[b] Conjugate adduct was obtained in 42% yield as a byproduct.

of crystalline product **13f** was carried out and the ORTEP drawing is shown in Figure 1.[6]

Although all the structures of the produced cyclopropanes were unambiguously determined, we still find it very difficult to propose a rational transition state model for explaining the stereochemistry of these cyclopropanation reactions. Instead of the model, we would like to present a summary of the trend for the correlation of the stereochemistry of the starting α,β-unsaturated carbonyl compounds and produced cyclopropanes (Fig. 2). Thus, in case of R^3=H in the α,β-unsaturated carbonyl compounds (**6a**–**6d** and **6f**; see Table 1) the reaction gives **14** (**14**=**7**; R^3=H). On the other hand, in case of the R^3=medium-sized alkyl group such as methyl and ethyl groups, the reaction gives a mixture of diastereomers **14** and **15** (see Table 2). The diastereomeric ratios were found to be 1:1–1.5:1 when R^3=Me or Et (entries 1–3 and 9). However, when R^3 is a much bulkier substituent, for example, $PhCH_2CH_2$ or isopropyl group, the reaction predominantly or exclusively gives **15** (entries 4–8 and 10).

Finally, the sulfinyl group in the produced cyclopropanes having an ester group is easily removed with retention of the stereochemistry of the cyclopropanes by the action of a Grignard reagent at low temperature.[5] In case of the cyclopropane having an alkyl ketone group **7f**, the ketone group was initially treated with LDA (formation of an enolate) followed by EtMgCl. The results are summarized in Table 3.

In conclusion, a method for a short and stereoselective synthesis of highly substituted cyclopropanes was established starting from α,β-unsaturated esters and ketones with dichloromethyl *p*-tolyl sulfoxide. The stereochemistry of the produced cyclopropanes can be deduced from the structure of the α,β-unsaturated esters and ketones. We believe that the results described in this paper will contribute to a synthesis of highly substituted cyclopropanes.

3. Experimental

3.1. General

All melting points were measured on Yanaco MP-S3 apparatus and are uncorrected. ^1H NMR spectra were measured in a $CDCl_3$ solution with Burker XWIN-300, 400, and 600 spectrometer.

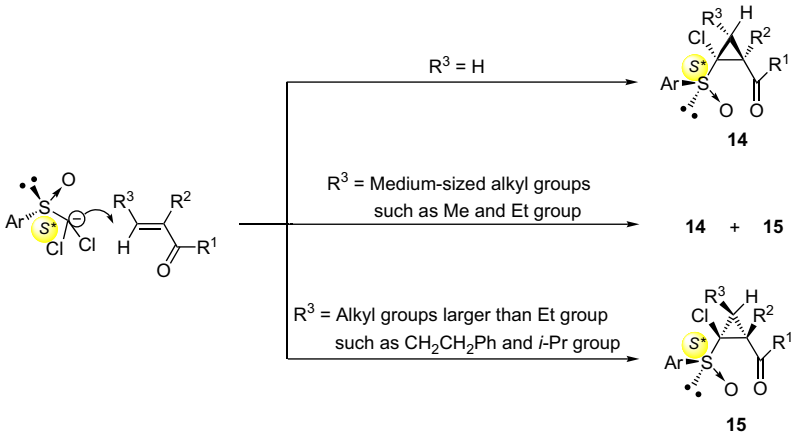
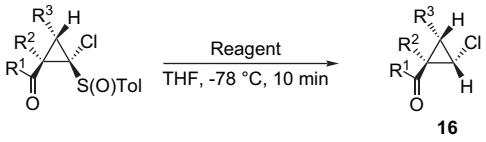


Figure 2. Trend for the correlation of the stereochemistry of the produced cyclopropanes and structure of the α,β-disubstituted α,β-unsaturated carbonyl compounds.

Table 3
Stereospecific desulfinylation of the α-chloro sulfinylcyclopropanes



Entry	1-Chlorocyclopropyl *p*-tolyl sulfoxide				Reagent	**16**	
		R^1	R^2	R^3			Yield/%
1	**13b**	OBn	Me	Et	*i*-PrMgCl	**16a**	91
2	**13c**	OBn	*n*-Bu	Me	*i*-PrMgCl	**16b**	87
3	**7f**	$CH_2CH_2CH_2Ph$	Me	H	LDA then EtMgCl	**16c**	63

Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion by HITACHI M-80B mass spectrometer. IR spectra were recorded on a Perkin–Elmer Spectrum One FT-IR instrument. Silica gel 60N (KANTO CHEMICAL) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry reagent, *N*,*N*-diisopropylamine, and 1,1,1,3,3,3-hexamethyldisilazane were distilled from CaH_2, THF was distilled from diphenylketyl.

*3.1.1. 2-Chloro-1-methyl-2-(toluene-4-sulfinyl)cyclopropanecarboxylic acid benzyl ester **4***

To a solution of benzyl methacrylate (0.2 mL; 1.2 mmol) and dichloromethyl *p*-tolyl sulfoxide (223 mg; 1.0 mmol) in 10 mL of dry THF at −78 °C was added a solution of sodium hexamethyldisilazide (1.0 M solution in THF, 1.2 mL; 1.2 mmol) dropwise with stirring. The temperature of the reaction mixture was slowly allowed to warm to 0 °C for 2 h. The reaction was quenched by satd aq NH_4Cl and the whole was extracted with $CHCl_3$. The product was purified by silica gel column chromatography to give **4** (362 mg; 99%) as a colorless oil. IR (neat) 3034, 1732 (CO), 1273, 1160, 1088, 1064, 751 cm^{-1}; ^1H NMR δ 1.39 (1H, d, *J*=7.4 Hz), 1.57 (3H, s), 2.41 (3H, s), 2.67 (1H, d, *J*=7.3 Hz), 5.19 (1H, d, *J*=12.1 Hz), 5.25 (1H, d, *J*=12.1 Hz), 7.25 (2H, d, *J*=8.2 Hz), 7.34–7.42 (5H, m), 7.46 (2H, d, *J*=8.3 Hz). MS *m*/*z* (%) 362 (M^+, 4), 139 (25), 91 (100), 65 (5). Calcd for $C_{19}H_{19}O_3ClS$: M, 362.0743. Found: *m*/*z* 362.0745.

*3.1.2. 2-Chloro-1-methylcyclopropanecarboxylic acid benzyl ester **5***

To a solution of **4** (72.5 mg; 0.20 mmol) in 2 mL of dry THF at −78 °C was added *i*-PrMgCl (2.0 M solution in THF, 0.3 mL; 0.6 mmol) dropwise with stirring. After 10 min, the reaction was quenched by satd aq NH_4Cl. The whole was extracted with $CHCl_3$. The product was purified by silica gel column chromatography to give **5** (38.6 mg; 86%) as a colorless oil. IR (neat) 2941, 1723 (CO), 1323, 1158, 964, 697 cm^{-1}; ^1H NMR δ 0.95 (1H, t, *J*=5.5 Hz), 1.47 (3H, s), 1.76 (1H, dd, *J*=8.0, 5.8 Hz), 3.60 (1H, dd, *J*=8.0, 5.1 Hz), 5.11 (2H, s), 7.25–7.39 (5H, m). MS *m*/*z* (%) 224 (M^+, 7), 138 (22), 91 (100). Calcd for $C_{12}H_{13}O_2Cl$: M, 224.0604. Found: *m*/*z* 224.0606.

*3.1.3. 2-Chloro-1-methyl-2-(toluene-4-sulfinyl)cyclopropanecarboxylic acid ethyl ester **7a***

Colorless crystals; mp 48.5–49.0 °C (AcOEt–hexane); IR (KBr) 9078, 2997, 1726 (CO), 1273, 1187, 1091, 1050, 807, 742 cm^{-1}; ^1H NMR δ 1.34 (3H, t, *J*=7.2 Hz), 1.38 (1H, d, *J*=7.4 Hz), 1.56 (3H, s), 2.43 (3H, s), 2.66 (1H, d, *J*=7.2 Hz), 4.26 (2H, q, *J*=7.1 Hz), 7.33 (2H, d, *J*=8.1 Hz), 7.55 (2H, d, *J*=8.3 Hz). Anal. Calcd for $C_{14}H_{17}O_3ClS$: C, 55.90; H, 5.70; Cl, 11.79; S, 10.66. Found: C, 55.87; H, 5.28; Cl, 11.68; S, 10.59.

*3.1.4. 1-Butyl-2-chloro-2-(toluene-4-sulfinyl)cyclopropanecarboxylic acid ethyl ester **7b***

Colorless oil; IR (neat) 2959, 1731 (CO), 1466, 1156, 1091, 1063, 811 cm^{-1}; ^1H NMR δ 0.89 (3H, t, *J*=7.1 Hz), 1.33 (3H, t, *J*=7.1 Hz), 1.34 (1H, d, *J*=7.4 Hz), 1.31–1.44 (4H, m), 1.60–1.67 (1H, m), 2.07–2.14 (1H, m), 2.42 (3H, s), 2.57 (1H, dd, *J*=7.3, 1.0 Hz), 4.26 (2H, dq, *J*=7.2, 1.0 Hz), 7.32 (2H, d, *J*=8.0 Hz), 7.60 (2H, d, *J*=8.3 Hz). MS *m*/*z* (%) 342 (M^+, 7), 279 (23), 203 (98), 175 (70), 157 (32), 140 (100), 139 (81). Calcd for $C_{17}H_{23}O_3ClS$: M, 342.1054. Found: *m*/*z* 342.1057.

*3.1.5. [2-Chloro-1-methyl-2-(toluene-4-sulfinyl)cyclopropyl]-phenylmethanone **7c***

To a suspension of sodium hydride (96 mg; 4.0 mmol) in 5 mL of THF at 0 °C was added a solution of dichloromethyl *p*-tolyl sulfoxide (225 mg; 1.0 mmol) in THF (1 mL) followed by a solution of **6c** (175 mg; 1.2 mmol) in THF (0.5 mL) with stirring. The temperature of the reaction mixture was slowly allowed to warm to room temperature and the solution was stirred overnight. The reaction was quenched by satd aq NH_4Cl and the whole was extracted with $CHCl_3$. The product was purified by silica gel column chromatography to give **7c** as colorless crystals (275 mg; 83%). Mp 128–128.5 °C (AcOEt–hexane); IR (KBr) 3056, 1688 (CO), 1451, 1087, 1051, 813, 703 cm^{-1}; ^1H NMR δ 1.19 (1H, d, *J*=7.0 Hz), 1.70 (3H, s), 2.42 (3H, s), 2.54 (1H, d, *J*=7.1 Hz), 7.31 (2H, d, *J*=8.0 Hz), 7.53 (2H, t, *J*=8.0 Hz), 7.60–7.64 (3H, m), 8.03 (2H, d, *J*=8.0 Hz). Anal. Calcd for $C_{18}H_{17}O_2ClS$: C, 64.95; H, 5.15; Cl, 10.65; S, 9.63. Found: C, 64.85; H, 5.04; Cl, 10.59; S, 9.65.

*3.1.6. [2-Chloro-1-propyl-2-(toluene-4-sulfinyl)cyclopropyl]-phenylmethanone **7d***

Colorless oil; IR (neat) 2961, 1682 (CO), 1579, 1449, 1229, 1086, 812 cm^{-1}; ^1H NMR δ 0.85 (3H, t, *J*=7.2 Hz), 1.24 (1H, d, *J*=7.3 Hz),

1.37 (2H, quintet, J=7.4 Hz), 1.80 (1H, ddd, J=14.1, 9.5, 7.4 Hz), 2.15 (1H, dt, J=14.2, 7.4 Hz), 2.42 (3H, s), 2.50 (1H, d, J=7.3 Hz), 7.30 (2H, d, J=8.0 Hz), 7.50–7.67 (5H, m), 8.05 (2H, d, J=8.2 Hz). MS m/z (%) 360 (M^+, 1), 221 (34), 129 (8), 105 (100), 77 (32). Calcd for $C_{20}H_{21}O_2ClS$: M, 360.0950. Found: m/z 360.0950.

3.1.7. 1-[2-Chloro-1-methyl-2-(toluene-4-sulfinyl)cyclopropyl]-4-phenylbutan-1-one **7f**

To a solution of LDA (0.48 mmol) in 4 mL of THF at −78 °C was added a solution of dichloromethyl p-tolyl sulfoxide (90 mg; 0.40 mmol) in THF (0.5 mL) with stirring. The solution was stirred for 5 min, then a solution of **6f** (82 mg; 0.44 mmol) in THF was added. The temperature of the reaction mixture was slowly allowed to warm to room temperature overnight. The reaction was quenched by satd aq NH_4Cl and the whole was extracted with $CHCl_3$. The product was purified by silica gel column chromatography to give **7f** (131 mg; 88%) as a colorless oil. IR (neat) 3025, 2929, 1709 (CO), 1454, 1088, 1062, 750 cm^{-1}; ^1H NMR δ 1.15 (1H, d, J=7.1 Hz), 1.51 (3H, s), 1.95–2.03 (2H, m), 2.42 (3H, s), 2.49 (1H, d, J=7.1 Hz), 2.52–2.77 (4H, m), 7.18–7.21 (3H, m), 7.27–7.31 (4H, m), 7.58 (2H, d, J=8.2 Hz). MS m/z (%) 374 (M^+, 4), 270 (15), 235 (11), 187 (46), 147 (22), 91 (100). Calcd for $C_{21}H_{23}O_2ClS$: M, 374.1107. Found: m/z 374.1116.

3.1.8. 2-Chloro-1,3-dimethyl-2-(toluene-4-sulfinyl)-cyclopropanecarboxylic acid benzyl ester **9**

To a solution of LHMDS (2.68 mmol) in 20 mL of THF at −78 °C was added a solution of dichloromethyl p-tolyl sulfoxide (500 mg; 2.24 mmol) in THF (2 mL) with stirring. The solution was stirred for 5 min, then a solution of **8** (510 mg; 2.68 mmol) in THF was added. The temperature of the reaction mixture was slowly allowed to warm to room temperature for 3 h. The reaction was quenched by satd aq NH_4Cl and the whole was extracted with $CHCl_3$. The product was purified by silica gel column chromatography to give **9** (762 mg; 90%) as a colorless oil (about 1:1 diastereomeric mixture). IR (neat) 2937, 1732 (CO), 1455, 1268, 1088, 1063, 751 cm^{-1}; ^1H NMR δ 1.03 (1.5H, d, J=6.5 Hz), 1.17 (1.5H, d, J=6.5 Hz), 1.37 (1.5H, s), 1.45 (1.5H, s), 2.40 (1.5H, s), 2.42 (1.5H, s), 2.46 (0.5H, q, J=6.5 Hz), 2.80 (0.5H, q, J=6.4 Hz), 5.17–5.34 (2H, m), 7.22–7.54 (9H, m). MS m/z (%) 376 (M^+, 0.1), 140 (11), 139 (12), 91 (100). Calcd for $C_{20}H_{21}O_3ClS$: M, 376.0900. Found: m/z 376.0900.

3.1.9. 2-Chloro-1,3-dimethyl-2-(toluene-4-sulfonyl)-cyclopropanecarboxylic acid benzyl ester **10**

mCPBA (75%; 132 mg; 0.574 mmol) was added to a solution of **9** (108 mg; 0.287 mmol) in 2 mL of CH_2Cl_2 at room temperature. The solution was stirred for 1 h and the reaction was quenched by satd aq $NaHCO_3$ and satd aq Na_2SO_3. The whole was extracted with CH_2Cl_2. The product was purified by silica gel column chromatography to give **10** (109 mg; 96%) as a colorless oil. IR (neat) 3033, 2937, 1738 (CO), 1597, 1455, 1329, 1279, 1168, 1081, 884, 762 cm^{-1}; ^1H NMR δ 1.12 (3H, d, J=6.5 Hz), 1.39 (3H, s), 2.44 (3H, s), 2.77 (1H, q, J=6.5 Hz), 5.20 (1H, d, J=12.2 Hz), 5.26 (1H, d, J=12.2 Hz), 7.30 (2H, d, J=8.1 Hz), 7.35–7.47 (5H, m), 7.83 (2H, d, J=8.3 Hz). MS m/z (%) 392 (M^+, 1), 285 (32), 257 (7), 147 (22), 91 (100), 65 (11). Calcd for $C_{20}H_{21}O_4ClS$: M, 392.0849. Found: m/z 392.0845.

3.1.10. 2-Chloro-1,3-dimethylcyclopropanecarboxylic acid benzyl ester **11**

Colorless oil; IR (neat) 2938, 1722, 1456, 1290, 1246, 1174, 744, 696 cm^{-1}; ^1H NMR δ 1.10 (3H, d, J=6.4 Hz), 1.28 (3H, s), 1.80 (1H, quintet, J=6.8 Hz), 3.71 (1H, d, J=8.1 Hz), 5.10 (2H, s), 7.32–7.38 (5H, m). MS m/z (%) 238 (M^+, 1.2), 203 (1.3), 112 (10), 91 (100), 65 (10), 41 (11). Calcd for $C_{13}H_{15}O_2ClS$: M, 238.0758. Found: m/z 238.0752.

3.1.11. 2-Chloro-1,3-dimethyl-2-(toluene-4-sulfinyl)-cyclopropanecarboxylic acid ethyl ester **13a**

Colorless crystals (about 1:1 mixture of two diastereomers); mp 108–112 °C (AcOEt–hexane); IR (KBr) 2982, 1737, 1263, 1085, 1058, 802 cm^{-1}; ^1H NMR δ 1.03 (1.5H, d, J=6.5 Hz), 1.19 (1.5H, d, J=6.4 Hz), 1.33 (1.5H, t, J=7.2 Hz), 1.36 (1.5H, t, J=7.2 Hz), 1.44 (1.5H, s), 2.42 (3H, s), 2.46 (0.5H, q, J=6.5 Hz), 2.78 (0.5H, q, J=6.5 Hz), 4.25 (1H, q, J=7.2 Hz), 4.25–4.34 (0.5H, m), 4.36 (0.5H, dq, J=10.8, 7.3 Hz), 7.31 (1H, d, J=7.9 Hz), 7.32 (1H, d, J=7.9 Hz), 7.53 (2H, d, J=8.3 Hz). Anal. Calcd for $C_{15}H_{19}O_3ClS$: C, 57.23; H, 6.08; Cl, 11.26; S, 10.18. Found: C, 57.32; H, 5.71; Cl, 11.30; S, 10.28.

3.1.12. 2-Chloro-3-ethyl-1-methyl-2-(toluene-4-sulfinyl)-cyclopropanecarboxylic acid benzyl ester **13b**

Less polar product: Colorless oil; IR (neat) 2968, 1726 (CO), 1455, 1251, 1086, 1061, 751 cm^{-1}; ^1H NMR δ 0.91 (3H, t, J=7.4 Hz), 1.40 (3H, s), 1.35–1.45 (1H, m), 1.53–1.62 (1H, m), 2.40 (3H, s), 2.58 (1H, dd, J=8.2, 6.1 Hz), 5.19 (1H, d, J=12.2 Hz), 5.24 (1H, d, J=12.1 Hz), 7.24 (2H, d, J=8.1 Hz), 7.33–7.43 (5H, m), 7.47 (2H, d, J=8.3 Hz). MS m/z (%) 390 (M^+, 0.1), 299 (0.1), 283 (2), 161 (3), 139 (11), 91 (100). Calcd for $C_{21}H_{23}O_3ClS$: M, 390.1057. Found: m/z 390.1054.

More polar product: Colorless oil; IR (neat) 2970, 1727 (CO), 1455, 1274, 1174, 1089, 751 cm^{-1}; ^1H NMR δ 0.67 (3H, t, J=7.4 Hz), 1.24–1.33 (1H, m), 1.46–1.60 (1H, m), 1.46 (3H, s), 2.26 (1H, dd, J=8.6, 5.8 Hz), 2.42 (3H, s), 5.24 (1H, d, J=12.3 Hz), 5.32 (1H, d, J=12.3 Hz), 7.55 (2H, d, J=8.2 Hz), 7.30–7.44 (7H, m). MS m/z (%) 390 (M^+, 0.1), 299 (0.1), 281 (1), 139 (8), 91 (100). Calcd for $C_{21}H_{23}O_3ClS$: M, 390.1057. Found: m/z 390.1061.

3.1.13. 1-Butyl-2-chloro-3-methyl-2-(toluene-4-sulfinyl)-cyclopropanecarboxylic acid benzyl ester **13c**

Data for the main product is reported: Colorless crystals; mp 123–123.5 °C (AcOEt–hexane); IR (KBr) 2961, 2950, 1723 (CO), 1457, 1169, 1093, 1063, 803, 751 cm^{-1}; ^1H NMR δ 0.81 (3H, t, J=6.9 Hz), 1.03 (3H, d, J=6.5 Hz), 1.17–1.30 (4H, m), 1.46–1.55 (1H, m), 2.12–2.19 (1H, m), 2.37 (1H, q, J=6.5 Hz), 2.42 (3H, s), 5.22 (1H, d, J=12.2 Hz), 5.36 (1H, d, J=12.2 Hz), 7.30 (2H, d, J=8.0 Hz), 7.33–7.40 (3H, m), 7.45 (2H, d, J=8.3 Hz), 7.52 (2H, d, J=8.2 Hz). Anal. Calcd for $C_{23}H_{27}O_3ClS$: C, 65.93; H, 6.50; Cl, 8.46; S, 7.69. Found: C, 65.88; H, 6.35; Cl, 8.31; S, 7.69.

3.1.14. 2-Chloro-1-methyl-3-phenethyl-2-(toluene-4-sulfinyl)-cyclopropanecarboxylic acid ethyl ester **13d**

Colorless crystals; mp 87.5–88.5 °C (AcOEt–hexane); IR (KBr) 2934, 1724 (CO), 1087, 1062, 809, 750 cm^{-1}; ^1H NMR δ 1.27 (3H, s), 1.34 (3H, t, J=7.2 Hz), 1.68–1.87 (2H, m), 2.61–2.69 (2H, m), 2.41 (3H, s), 2.69 (1H, t, J=7.2 Hz), 4.25 (2H, q, J=7.2 Hz), 7.16–7.22 (3H, m), 7.26–7.30 (2H, m), 7.31 (2H, d, J=8.1 Hz), 7.53 (2H, d, J=8.3 Hz). Anal. Calcd for $C_{22}H_{25}O_3ClS$: C, 65.25; H, 6.22; Cl, 8.75; S, 7.92. Found: C, 65.38; H, 5.86; Cl, 8.65; S, 7.91.

3.1.15. [2-Chloro-3-isopropyl-1-methyl-2-(toluene-4-sulfinyl)-cyclopropyl]phenylmethanone **13f**

Colorless crystals; mp 178–178.5 °C (AcOE–hexane); IR (KBr) 2955, 1670 (CO), 1596, 1446, 1092, 1064, 974, 810, 714 cm^{-1}; ^1H NMR δ 0.40 (3H, d, J=6.5 Hz), 1.02 (3H, d, J=6.6 Hz), 1.52 (3H, s), 1.53–1.62 (1H, m), 1.96 (1H, d, J=10.5 Hz), 2.41 (3H, s), 7.31 (2H, d, J=8.0 Hz), 7.52–7.63 (5H, m), 8.02 (2H, d, J=8.6 Hz). Anal. Calcd for $C_{21}H_{23}O_2ClS$: C, 67.27; H, 6.18; Cl, 9.46; S, 8.55. Found: C, 67.24; H, 6.16; Cl, 9.40; S, 8.58.

3.1.16. 1-[2-Chloro-1-methyl-3-phenethyl-2-(toluene-4-sulfinyl)-cyclopropyl]propan-1-one **13g**

Less polar product: Colorless crystals; mp 92.5–93 °C (AcOEt–hexane); IR (KBr) 2940, 2922, 1720 (CO), 1594, 1453, 1086, 1057, 814, 751, 701 cm^{-1}; ^1H NMR δ 1.10 (3H, t, J=7.1 Hz), 1.29 (3H, s), 1.62–1.83

(2H, m), 2.41 (3H, s), 2.38–2.69 (5H, m), 7.13 (2H, d, J=7.2 Hz), 7.19 (1H, t, J=7.3 Hz), 7.25–7.30 (4H, m), 7.56 (2H, d, J=8.2 Hz). Anal. Calcd for $C_{22}H_{25}O_2ClS$: C, 67.94; H, 6.48; Cl, 9.11; S, 8.24. Found: C, 68.02; H, 6.46; Cl, 9.09; S, 8.24.

More polar product: Colorless crystals; mp 129–129.5 °C (AcOEt–hexane); IR (KBr) 3030, 2932, 1704, 1495, 1456, 1130, 1088, 1059, 806, 760 cm^{-1}; ^1H NMR δ 1.18 (3H, t, J=7.2 Hz), 1.36 (3H, s), 1.55–1.73 (2H, m), 2.29 (1H, ddd, J=13.6, 9.5, 6.7 Hz), 2.41 (3H, s), 2.46 (1H, ddd, J=13.8, 9.5, 6.7 Hz), 2.49 (1H, t, J=7.0 Hz), 2.76 (1H, dq, J=18.8, 7.2 Hz), 2.83 (1H, dq, J=18.8, 7.2 Hz), 7.07 (2H, d, J=7.2 Hz), 7.18 (1H, t, J=7.3 Hz), 7.26 (2H, t, J=8.1 Hz), 7.30 (2H, d, J=8.0 Hz), 7.49 (2H, d, J=8.2 Hz). Anal. Calcd for $C_{22}H_{25}O_2ClS$: C, 67.94; H, 6.48; Cl, 9.11; S, 8.24. Found: C, 67.94; H, 6.49; Cl, 8.98; S, 8.17.

3.1.17. 1-[2-Chloro-1-ethyl-3-phenethyl-2-(toluene-4-sulfinyl)-cyclopropyl]butan-1-one **13h**

Colorless oil (about 6:1 mixture of two diastereomers). Data for the main isomer are reported. IR (neat) 2965, 1705 (CO), 1597, 1455, 1090, 1064, 810, 751 cm^{-1}; ^1H NMR δ 0.89 (3H, t, J=7.5 Hz), 1.00 (3H, t, J=7.4 Hz), 1.44–1.54 (1H, m), 1.63–1.95 (4H, m), 2.08 (1H, ddd, J=13.6, 10.8, 5.8 Hz), 2.25–2.47 (3H, m), 2.40 (3H, s), 2.74 (1H, dt, J=18.3, 7.2 Hz), 2.87 (1H, dt, J=18.3, 7.3 Hz), 7.06 (2H, d, J=7.6 Hz), 7.25–7.30 (5H, m), 7.47 (2H, d, J=8.7 Hz). MS m/z (%) 416 (M^+, 0.1), 277 (55), 241 (17), 185 (10), 139 (16), 91 (100). Calcd for $C_{24}H_{29}O_2ClS$: M, 416.1577. Found: m/z 416.1587.

3.1.18. Spirocyclic ketone **13i**

Less polar product: Colorless crystals; mp 202–202.5 °C (AcOEt–hexane); IR (KBr) 3059, 2940, 1671 (CO), 1595, 1445, 1090, 1056, 739, 685 cm^{-1}; ^1H NMR δ 1.11 (3H, d, J=6.5 Hz), 2.22 (1H, dt, J=14.0, 4.3 Hz), 2.32 (1H, ddd, J=14.0, 12.4, 3.9 Hz), 2.42 (3H, s), 2.92 (1H, dt, J=14.1, 3.6 Hz), 2.95 (1H, q, J=6.4 Hz), 3.27 (1H, ddd, J=16.6, 12.4, 4.3 Hz), 7.25 (1H, d, J=7.4 Hz), 7.31 (2H, d, J=7.9 Hz), 7.34 (1H, t, J=7.6 Hz), 7.50 (1H, dt, J=7.5, 1.4 Hz), 7.53 (2H, d, J=8.3 Hz), 8.11 (1H, dd, J=7.8, 1.2 Hz). Anal. Calcd for $C_{20}H_{19}O_2ClS$: C, 66.93; H, 5.34; Cl, 9.88; S, 8.93. Found: C, 66.89; H, 5.27; Cl, 9.83; S, 8.94.

More polar product: Colorless crystals; mp 193–193.5 °C (AcOEt–hexane); IR (KBr) 3051, 2932, 1679 (CO), 1595, 1444, 1277, 1053, 709 cm^{-1}; ^1H NMR δ 1.33 (3H, d, J=6.4 Hz), 2.12 (2H, m), 2.25 (3H, s), 2.48 (1H, ddd, J=16.5, 11.4, 4.8 Hz), 2.75 (1H, dt, J=16.5, 3.9 Hz), 3.26 (1H, q, J=6.4 Hz), 6.91 (2H, d, J=7.9 Hz), 7.14 (2H, d, J=8.3 Hz), 7.15 (1H, d, J=8.4 Hz), 7.39 (1H, t, J=7.5 Hz), 7.52 (1H, dt, J=7.4, 1.3 Hz), 8.12 (1H, dd, J=7.8, 1.2 Hz). Anal. Calcd for $C_{20}H_{19}O_2ClS$: C, 66.93; H, 5.34; Cl, 9.88; S, 8.93. Found: C, 66.51; H, 5.27; Cl, 9.78; S, 8.93.

3.1.19. 1-Chloro-2-phenethyl-1-(toluene-4-sulfinyl)-spiro[2.5]octan-4-one **13j**

Colorless oil; IR (neat) 2938, 1705 (CO), 1454, 1089, 1062, 811, 752 cm^{-1}; ^1H NMR δ 1.50–1.87 (6H, m), 1.98 (1H, ddt, J=14.2, 3.6, 3.1 Hz), 2.12–2.19 (1H, m), 2.29 (1H, ddd, J=13.6, 9.8, 5.8 Hz), 2.41 (3H, s), 2.43–2.49 (1H, m), 2.52 (1H, t, J=7.0 Hz), 2.70–2.73 (2H, m), 7.06 (2H, d, J=7.0 Hz), 7.18 (1H, dd, J=7.2, 2.6 Hz), 7.23–7.27 (2H, m), 7.30 (2H, d, J=8.0 Hz), 7.49 (2H, d, J=8.2 Hz). MS m/z (%) 400 (M^+, trace), 261 (100), 225 (38), 169 (15), 139 (20), 91 (89). Calcd for $C_{23}H_{25}O_2ClS$: M, 400.1264. Found: m/z 400.1265.

3.1.20. 2-Chloro-3-ethyl-1-methylcyclopropanecarboxylic acid benzyl ester **16a**

Colorless oil; IR (neat) 2968, 1721 (CO), 1456, 1296, 1241, 1179, 749, 696 cm^{-1}; ^1H NMR δ 1.01 (3H, t, J=7.4 Hz), 1.32 (3H, s), 1.46 (1H, dq, J=7.4, 6.7 Hz), 1.49 (1H, dq, J=7.5, 6.7 Hz), 1.65 (1H, dt, J=7.9, 6.5 Hz), 3.70 (1H, d, J=8.2 Hz), 5.10 (2H, s), 7.32–7.39 (5H, m). MS m/z (%) 252 (M^+, 1), 217 (5), 175 (5), 126 (12), 91 (100), 65 (7). Calcd for $C_{14}H_{17}O_2Cl$: M, 252.0917. Found: m/z 252.0920.

3.1.21. 2-Butyl-3-chloro-1-methylcyclopropanecarboxylic acid benzyl ester **16b**

Colorless oil; IR (neat) 2960, 1723 (CO), 1455, 1210, 1172, 748, 696 cm^{-1}; ^1H NMR δ 0.88 (3H, t, J=7.2 Hz), 1.15 (3H, d, J=6.4 Hz), 1.30–1.41 (3H, m), 1.49–1.55 (1H, m), 1.61–1.70 (2H, m), 1.75 (1H, dq, J=8.3, 6.8 Hz), 3.68 (1H, d, J=7.9 Hz), 5.11 (2H, s), 7.32–7.38 (5H, m). MS m/z (%) 280 (M^+, 1), 245 (3), 189 (2), 154 (11), 138 (4), 91 (100). Calcd for $C_{16}H_{21}O_2Cl$: M, 280.1230. Found: m/z 280.1225.

3.1.22. 1-(2-Chloro-1-methylcyclopropyl)-4-phenylbutan-1-one **16c**

To a solution of LDA (0.20 mmol) in 1 mL of THF at −78 °C was added a solution of **7f** (37.4 mg; 0.1 mmol) in THF (0.5 mL) with stirring. After 10 min, EtMgCl (2.0 M solution in THF, 0.5 mL; 1.0 mmol) was added to the reaction mixture dropwise with stirring. After 10 min, the reaction was quenched by satd aq NH_4Cl. The whole was extracted with $CHCl_3$. The product was purified by silica gel column chromatography to give **16c** (14.8 mg, 63%) as a colorless oil. IR (neat) 2933, 1693 (CO), 1454, 1368, 1309, 1107, 959, 745, 699 cm^{-1}; ^1H NMR δ 0.88 (1H, t, J=5.3 Hz), 1.52 (3H, s), 1.76 (1H, dd, J=7.8, 5.5 Hz), 1.89 (2H, quintet, J=7.3 Hz), 2.58 (2H, t, J=7.2 Hz), 2.62 (2H, t, J=7.4 Hz), 3.43 (1H, dd, J=7.7, 5.1 Hz), 7.17 (2H, d, J=7.0 Hz), 7.20 (1H, t, J=7.3 Hz), 7.29 (2H, t, J=7.4 Hz). MS m/z (%) 236 (M^+, 12), 132 (18), 117 (13), 104 (100), 98 (63), 91 (80). Calcd for $C_{14}H_{17}OCl$: M, 236.0967. Found: m/z 236.0968.

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References and notes

1. Some recent reviews concerning chemistry, synthesis, and synthetic uses of cyclopropanes: (a) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C.; Tanko, J.; Hudlick, T. *Chem. Rev.* **1989**, *89*, 165; (b) Salaun, J. *Chem. Rev.* **1989**, *89*, 1247; (c) Sonawane, H. R.; Bellur, N. S.; Kulkarni, D.; Ahuja, J. R. *Synlett* **1993**, 875; (d) Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919; (e) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589; (f) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977; (g) Pietruszka, J. *Chem. Rev.* **2003**, *103*, 1051; (h) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151; (i) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597; (j) Halton, B.; Harvey, J. *Synlett* **2006**, 1975.
2. (a) Li, J. J. *Name Reactions*; Springer: Berlin, 2002; (b) Mundy, B. P.; Ellerd, M. G.; Favaloro, F. G., Jr. *Name Reactions and Reagents in Organic Synthesis*, 2nd ed.; John Wiley and Sons: Hoboken, New Jersey, NJ, 2005; (c) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.
3. Miyagawa, T.; Satoh, T. *Tetrahedron Lett.* **2007**, *48*, 4849.
4. Satoh, T.; Kurihara, T.; Fujita, K. *Tetrahedron* **2001**, *57*, 5369.
5. Mahidol, C.; Reutrakul, V.; Panyachotipun, C.; Turongsomboon, G.; Prapansiri, V.; Bandara, B. M. R. *Chem. Lett.* **1989**, 163.
6. Crystal data for **7c**: $C_{18}H_{17}ClO_2S$, M=332.83, *triclinic*, space group $P\bar{1}$ (#2), a=7.8435(7) Å, b=10.1941(9) Å, c=11.7585(11) Å, α=111.3140(10)°, β=105.8060(10)°, γ=99.038(2)°, V=807.63(13) Å^3, Z=2, F(000)=348, D_{calcd}=1.369 g cm^{-3}, μ(Mo Kα)=3.70 cm^{-1}, T=173 K, radiation=0.71073 Å, R_1=0.0467 for $I>2.0\sigma(I)$, wR_2=0.1343 for all data (3482 reflections), GOF=1.039 (256 parameters), crystal dimensions 0.45×0.32×0.10 mm^3.

   Crystal data for **13f**: $C_{21}H_{23}ClO_2S$, M=374.90, *monoclinic*, space group $P2_1/n$ (#14), a=10.6543(12) Å, b=13.4003(15) Å, c=13.6645(16) Å, β=95.991(2)°, V=1940.2(4) Å^3, Z=4, F(000)=792, D_{calcd}=1.283 g cm^{-3}, μ(Mo Kα)=3.16 cm^{-1}, T=173 K, radiation=0.71073 Å, R_1=0.0440 for $I>2.0\sigma(I)$, wR_2=0.1092 for all data (8300 reflections), GOF=0.916 (613 parameters), crystal dimensions 0.42×0.41×0.26 mm^3. The single crystals of **7c** and **13f** were mounted on glass fibers. Diffraction data were measured on a Bruker APEX CCD-Detector X-ray diffractometer with monochromated Mo Kα radiation from a rotating anode source apparatus. The data reduction, structure solution, and refinement, and all the necessary computational data processes were performed using APEX, SAINT, SHELXTL programs. Crystallographic data excluding structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 673248 for **7c** and CCDC 673249 for **13f**, respectively. A copy of the data can be obtained free of charge from CCDC, 12 Union road, Cambridge CB2 1EZ, UK [direct line: +44 1223 762910, fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.