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Enantiocontrol in intermolecular cyclopropanations: use of diazosulfonate esters

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Received (in Montpellier, France) 9th August 2004, Accepted 7th June 2005
First published as an Advance Article on the web 8th July 2005

The novel use of α-diazosulfonate esters as alternative cyclopropanating agents to diazoacetates is investigated. The effects of structure of both substrate and ligand on diastereo- and enantioselectivity are studied, and the catalytic ability of different metals is compared.

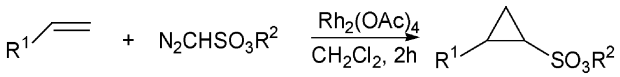
Introduction

Catalytic carbon–carbon bond-forming reactions have been a major area of research for some time with advances in these reactions occurring at pace in the areas of oxidation, reduction and addition. A versatile source of such reactions is transformations involving metal-carbenes derived from diazocarbonyl compounds, and we have been involved with their chemistry for more than a decade.[1] The metal-carbenes undergo a range of insertion and cycloaddition reactions, governed in some part by the metal involved.[1–3] Much work has been published on systems utilising ethyl diazoacetate for cyclopropanation reactions, with both rhodium[4] and copper catalysts,[1–3] and this reaction is seen as the benchmark system for testing catalyst design. The copper catalysts have proven to be more effective at inducing asymmetry in this reaction, with particularly high selectivity achieved by the bisoxazoline (BOX) ligands.[5] Despite a plethora of papers on diazoacetate insertions, few have mentioned work with heteroatom esters. To the best of our knowledge, the only papers mentioning the reaction of α-diazosulfonates have been under photolysis[6] or thermolysis conditions.[7] Here we discuss our findings on metal catalysed cyclopropanation reactions involving α-diazosulfonate esters.

Results and discussion

A range of diazosulfonates was produced following Danheiser's method,[8] and these were initially reacted with a series of alkenes in the presence of dirhodium tetraacetate (Scheme 1). This catalyst readily effected the decomposition of the diazosulfonate, and the corresponding cyclopropane–sulfonic acid derivative was isolated in good to excellent yield (Table 1). Although the yields for these reactions were generally good, the *syn*/*anti* selectivity[9] exhibited by the catalyst was modest. The general trend was for the *anti* product to be favoured, although the best selectivity for this was only 2.9 : 1 (entry 11). Entries 1–5 suggest that the reagent has considerably less influence on the diastereoselectivity than the structure of the substrate, with each of the reagents giving a similar ratio of *anti* : *syn* products with styrene. The non-aromatic substituted alkenes showed a wide difference in the selectivity in this reaction: ethyl vinyl ether showed only a slight preference for the *anti* product (entry 10), whereas the tertiary butyl vinyl ether showed the highest proportion of *anti* product (entry 11).

Having observed only a modest diastereoselectivity in the reaction, we investigated the enantioselectivity by using homochiral dirhodium catalysts. We decided to choose the reaction between styrene and diazosulfonate **1** (Scheme 2), since this had given the most promising *anti*/*syn* ratio of products in the rhodium acetate catalysed reactions, and the results are presented in Table 2. Doyle's catalyst,[10] $Rh_2(MEPY)_4$ gave a lower yield than the carboxylate-based catalyst previously employed, but it did give a satisfactory *anti*/*syn* ratio of product (entry 2). However, although the diastereoselectivity was promising, the products, either *syn* or *anti*, were formed as a racemic mixture. A racemic product was also obtained when the prolinate ligand[11] was used, but this system did not show any differentiation between *syn* and *anti* products (entry 3). Use of the catalyst $Rh_2(PTTL)_4$[12] showed a slight preference for the *syn* product and also a moderate degree of asymmetric induction in each product (entry 4). When the axially-chiral ligands based on the biphenyl structure[13] were used, the preference for the *syn* isomer was again seen, with varying amounts of asymmetric induction observed.[14] The methyl (entry 5), *tert*-butyl (entry 6) and benzyl (entry 7) monoesters of (*S*)-4,4′,5,5′,6,6′-hexamethoxy-2,2′-diphenic acid were all employed as ligands for the dirhodium catalysts. The best results, in terms of both diastereo- and enantioselectivity, were



Scheme 1

Table 1 Cyclopropanation of various alkenes

Entry	R^1	R^2	Yield/%	Anti : Syn
1	Ph	CH_3CH_2	67	1.5 : 1
2	Ph	$PhCH_2CH_2$	81	1.6 : 1
3	Ph	Me_2CHCH_2	91	1.6 : 1
4	Ph	$(Me_2CH)_2CH$	62	1.9 : 1
5	Ph	Me_3CCH_2	83	1.5 : 1
6	*p*-OMe-Ph	Me_3CCH_2	85	1.2 : 1
7	*p*-Me-Ph	Me_3CCH_2	89	1.4 : 1
8	*p*-Cl-Ph	Me_3CCH_2	86	1.5 : 1
9	*m*-NO_2-Ph	Me_3CCH_2	69	2.4 : 1
10	EtO	Me_3CCH_2	86	1.1 : 1
11	Me_3CO	Me_3CCH_2	83	2.9 : 1
12	$MeCO_2CH_2$	Me_3CCH_2	42	2.1 : 1

DOI: 10.1039/b412285b

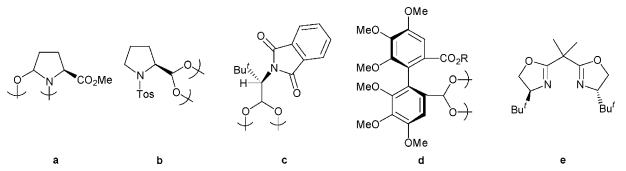
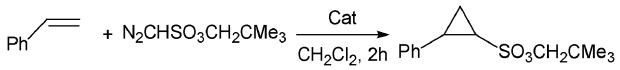


Fig. 1



Scheme 2

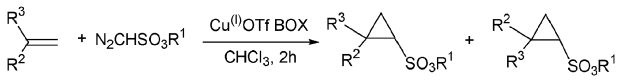
Table 2 Cyclopropanations using different catalysts

Entry	Catalyst	Yield/%	*anti* : *syn*	*anti* (ee%)	Syn (ee%)
1	$Rh_2(OAc)_4$	83	1.5 : 1	—	—
2	a	44	2.8 : 1	0	0
3	b	82	1.0 : 1	0	0
4	c	85	1 : 1.3	29	25
5	**d** (R = Me)	80	1 : 1.2	15	4
6	**d** (R = Bu^t)	84	1 : 1.2	20	7
7	**d** (R = Bn)	60	1 : 2.0	38	15
8	e	90	6.1 : 1	92	79

obtained when the benzyl ester was used, but the selectivity was still disappointingly moderate on each count.

Moving from rhodium to copper, using the Cu$^{(I)}$BOX catalyst (entry 8), the preference for the *anti* product was quite marked, and on analysing the product (chiral HPLC),[14] the *anti* cyclopropane was found to have an ee of 92%. Encouragingly, the minor *syn* isomer was found to have an ee of 79%, and the combined yield of 90% emphasised that this catalyst was by far the best performer of those tried.

Given these encouraging results, we decided to use the Cu$^{(I)}$BOX catalyst for some of the earlier transformations and the results are shown in Table 3. In each case, the copper catalyst showed a greater selectivity for the *anti* isomer over the *syn* isomer. More importantly, the enantioselectivity shown was very high. The examples with *para*-substituted styrenes (entries 2–4) gave moderate to good diastereoselectivity, and very good enantioselectivities in both the *syn* and *anti* isomers, while *meta*-nitrostyrene (entries 5 and 6) showed almost total selectivity in both isomers, albeit at the expense of overall yield. Reaction of the sulfonate with 1,1-diphenylethene (entry 7) proceeded to give the cyclopropanesulfonate ester almost enantio-specifically. Cyclopropanation of *tert*-butyl vinyl ether proceeded to give a moderate preference for the *anti* isomer



Scheme 3

Table 3 Cyclopropanations mediated by Cu$^{(I)}$(BOX)

Entry	R^1	R^2	R^3	Yield%	*anti* : *syn*	*anti* (ee%)	*syn* (ee%)
1	Me_3CCH_2	Ph	H	90	6.1 : 1	92	79
2	Me_3CCH_2	*p*-Me-C_6H_4	H	87	5.1 : 1	90	90
3	Me_3CCH_2	*p*-MeO-C_6H_4	H	92	4.1 : 1	89	85
4	Me_3CCH_2	*p*-Cl-C_6H_4	H	85	5.9 : 1	90	88
5	Me_3CCH_2	*m*-NO_2-C_6H_4	H	69	9.2 : 1	>99	97
6	$(Me_2CH)_2CH$	*m*-NO_2-C_6H_4	H	65	11.4 : 1	>99	—
7	Me_3CCH_2	Ph	Ph	43	—	>99	—
8	Me_3CCH_2	Me_3CO	H	81	3.1 : 1	77	91
9	Me_3CCH_2	$MeCO_2CH_2$	H	34	4.5 : 1	>99	—

and reduced enantioselectivity for each of the product isomers (entry 8). Vinyl acetate gave a higher proportion of *anti* product, and gave this product in greater than 99% ee (entry 9).[14] Examining the preference for a particular isomer and relating this to reactant structure readily explains the selectivity shown in these reactions. In terms of the substrate, an electron-deficient alkene has exhibited the best *anti* : *syn* ratio. This is probably due to the electrophilic carbene species reacting less readily with it, and therefore being more sensitive to steric factors. In contrast, the electron-rich vinyl ether (Table 1, entry 10) showed virtually no selectivity in terms of product geometry. A bulky substituent on the alkene also encourages more *anti* product to form, but the selectivity was relatively low.

Conclusion

We have shown that α-diazosulfonates may be used as versatile alternatives to diazoacetates. The behaviour of the diazosulfonates is similar to the diazoacetates insofar as the *anti* product is generally favoured, although this is somewhat influenced by the catalyst employed for the decompositions. The reactions proceed much more favourably with the copper catalyst than the rhodium ones and again, this mirrors the results of the analogous acetates. Rhodium catalysed reactions showed moderate selectivity, but when copper was employed as the catalyst far superior selectivities were observed, in terms of both relative and absolute stereochemistry. The BOX ligands, which have proven to be very versatile and effective ligands in a range of different metal-mediated reactions, have proven to be so again in this reaction.

Experimental

General procedure for preparation of alkyl α-diazomethanesulfonate

To a solution of alkyl methanesulfonate (15 mmol) in dry THF (50 mL) was added a 1 M LiHMDS solution in hexane (18 mL, 18 mmol) at −78 °C. After stirring the reaction mixture for 30 min at this temperature, 2,2,2-trifluoroethyl trifluoroacetate (2.4 mL, 18 mmol) was added rapidly in one portion *via* syringe (over about 5 s.). After 10 min, the reaction mixture was poured into a solution of diethyl ether (20 mL) and 5% hydrochloric acid (40 mL). The mixture was extracted with diethyl ether (200 mL), washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure using a rotary evaporator to give a yellow oil. This yellow oil was immediately dissolved in CH_3CN (30 mL). To this solution was added 4-acetamidobenzenesulfonyl azide (4.32 g, 18 mmol), Et_3N (2.5 ml, 18 mmol), and water (0.27 mL, 15 mmol). After stirring the reaction mixture overnight at rt, the solvent was removed under reduced pressure using a rotary evaporator. The residue was filtered on short silica gel and washed with a mixture of ethyl acetate (100 mL) and hexane (100 mL). The filtrate was concentrated under vacuum and the residue was purified by flash chromatography on silica gel to afford the desired product.

2,2-Dimethylpropyl α-diazomethanesulfonate. This compound was obtained as a yellow oil (60%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.96(s, 9H), 3.79(s, 2H), 5.26(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 79.9, 51.9, 31.5, 25.8. IR (neat) 3096, 2967, 2106, 1468, 1367, 1273, 1145, 956, 829

2-Methylpropyl α-diazomethanesulfonate. This compound was obtained as a yellow oil (48%). ^{1}H NMR (270 MHz, $CDCl_3$) δ_H 1.00(d, 6H, J = 6.9 Hz), 2.02(m, 1H), 3.95(d, 2H, J = 6.6 Hz), 5.29(s, 1H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ_C.76.7, 52.1, 27.8, 18.5. IR(neat) 2966, 2117, 1472, 1355, 1170, 975. MS (EI): 150($M^+ - N_2$, 8). HRMS (EI): calcd for $C_5H_{10}O_3S$ 150.0350, found 150.0346.

Ethyl α-diazomethanesulfonate. This compound was obtained as a yellow oil (40%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.42(t, 3H, J = 7.2 Hz), 4.26(q, 2H, J = 7.2 Hz), 5.30(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 67.3, 52.1, 14.4. IR(neat) 3102, 2988, 2114, 1346, 1178, 997, 916. MS (EI): 122($M^+ - N_2$, 100), 92(10), 65(25). HRMS (EI): calcd for $C_3H_6O_3S$ 122.0037, found 122.0037.

2,4-Dimethyl-3-pentyl α-diazomethanesulfonate. This compound was obtained as a yellow oil (63%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.97(d, 6H, J = 4.2 Hz), 1.01(d, 6H, J = 4.2 Hz), 2.03(m, 2H), 4.32(t, 1H, J = 5.7 Hz), 5.30(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 96.6, 54.8, 30.0, 19.8, 17.5. IR(neat) 2924, 2111, 1375, 1260, 1092.

2-Phenylethyl α-diazomethanesulfonate. This compound was obtained as a yellow oil (42%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.01(t, 2H, J = 6.8 Hz), 4.33(t, 2H, J = 6.8 Hz), 5.04(s, 1H), 7.10–7.33(m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 136.1, 128.7, 128.5, 126.8, 71.1, 51.9, 34.9. IR(neat) 3082, 2106, 1446, 1360, 1259, 1165, 956, 754, 694. MS (EI): 198($M^+ - N_2$, 5), 122(22), 104(100). HRMS (EI): calcd for $C_9H_{10}O_3S$ 198.0350, found 198.0345.

General procedure for dirhodium(II) complexes catalyzed cyclopropanation with alkyl α-diazomethanesulfonates

To a solution of rhodium catalyst (2 mol%) and styrene (5 equiv) in CH_2Cl_2 was added a solution of α-diazomethanesulfonate in CH_2Cl_2 by syringe pump over a 2 h period. The reaction mixture was stirred for an additional 1 h. The solvent and excess styrene were removed under reduced pressure and the residue was purified by flash chromatography on silica gel to afford the desired product.

General procedure for Cu(I)OTf/bisoxazoline catalyzed cyclopropanation with alkyl α-diazomethanesulfonates

In an inert-atmosphere box, copper triflate benzene complex (0.011 g, and 0.0393 mmol of copper) and chiral bisoxazoline (0.0118 g, 0.0401 mmol) were added to a 10 mL round bottom flask. After the addition of 3.0 mL of dry chloroform, the solution was stirred at r.t. for 1 h. The blue-green solution was then transferred by filter cannula into a flask containing the styrene in chloroform under nitrogen. A solution of diazosulfonate in chloroform was added to the solution of copper complex and styrene by syringe pump over 2 h. The reaction mixture was stirred for an additional 1 h, and solvent and styrene were removed by rotary evaporation. The crude oil was purified by flash chromatography on silica gel to afford the desired product.

Ethyl 2-phenylcyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.41(t, 3H, J = 7.1 Hz), 1.51(ddd, 1H, J = 8.5, 6.6, 5.6 Hz), 1.80(dt, 1H, 9.8, 5.6 Hz), 2.67(ddd, 1H, J = 8.5, 5.6, 4.5 Hz), 2.80(ddd, 1H, J = 9.8, 6.6, 4.5 Hz), 4.34(q, 2H, J = 7.1 Hz), 7.12–7.36(m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 137.1, 128.7, 127.3, 126.5, 66.7, 36.3, 23.3, 15.1, 13.8. IR (neat) 2922, 1351, 1168, 1004, 916. MS (EI): 226(M^+, 2), 117(100). HRMS (EI): calcd for $C_{11}H_{14}O_3S$ 226.0663, found 226.0656. ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.27(t, 3H, J = 7.1 Hz), 1.64(td, 1H, J = 8.6, 5.6 Hz), 1.97(dt, 1H, J = 8.0, 5.6 Hz), 2.73(q, 1H, J = 8.5 Hz), 2.81(td, 1H, J = 8.6, 5.6 Hz), 4.06(dq, 2H, J = 7.1, 1.2 Hz), 7.24–7.38(m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 133.3, 129.5, 128.0, 127.4, 65.9, 35.1, 23.7, 15.0, 10.6. IR (neat) 2919, 1350, 1167, 1003, 899. MS (EI): 226(M^+, 3), 160(4), 117(100). HRMS (EI): calcd for $C_{11}H_{14}O_3S$, 226.0663, found 226.0664.

2-Phenylethyl 2-phenylcyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.42(dt, 1H, J = 8.5, 6.7 Hz), 1.72(dt, 1H, J = 10.7, 5.6 Hz), 2.52(dt, 1H, J = 8.5, 5.6 Hz), 2.73(ddd, 1H, J = 10.7, 6.7, 4.5 Hz), 3.04(t, 2H, J = 6.9 Hz), 4.45(t, 2H, J = 6.9 Hz), 7.03–7.32(m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 137.0, 136.3, 128.9, 128.7, 128.6, 127.2, 126.9, 126.4, 70.5, 36.2, 35.6, 23.3, 13.7. IR (neat) 3010, 2950, 1358, 1168, 958, 696. MS (EI): 302(M^+, 2), 117(100), 104(73). HRMS (EI): calcd for $C_{17}H_{18}O_3S$ 302.0977, found 302.0974. ***syn*-isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.52(td, 1H, J = 8.6, 6.1 Hz), 1.91(q, 1H, J = 6.1 Hz), 2.67(dd, 2H, J = 8.6, 6.7 Hz), 2.91(t, 2H, J = 7.2 Hz), 4.18(dt, 2H, J = 7.2, 2.0 Hz), 7.12–7.34(m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 136.4, 133.2, 129.5, 128.9, 128.5, 128.0, 127.4, 126.9, 69.8, 35.5, 35.0, 23.7, 10.6. IR (neat) 3030, 2959, 1350, 1167, 958, 775, 696. MS (EI): 302(M^+, 2), 153(9), 117(100), 104(90). HRMS (EI): calcd for $C_{17}H_{18}O_3S$ 302.0977, found 302.0985.

2-Methylpropyl 2-phenylcyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (270 MHz, $CDCl_3$) δ_H 0.96(d, 6H, J = 7.0 Hz), 1.53(ddd, 1H, J = 8.3, 6.6, 5.6 Hz), 1.80(dt, 1H, J = 9.9, 5.6 Hz), 2.04(m, 1H), 2.67(ddd, 1H, J = 8.3, 5.6, 4.6 Hz), 2.78(ddd, 1H, J = 9.9, 6.6, 4.6 Hz), 4.03(d, 1H, J = 6.6 Hz), 7.12–7.34(m, 5H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ_C, 137.1, 1287.8, 127.3, 126.5, 76.2, 36.2, 28.2, 23.3, 18.6, 13.7. IR (neat) 2962, 1349, 1160, 968, 829. MS (EI): 254(M^+, 3), 153(11), 136(17), 117(100). HRMS (EI): calcd for $C_{13}H_{18}O_3S$ 254.0977, found 254.0976. ***syn*-isomer**: ^{1}H NMR (270 MHz, $CDCl_3$) δ_H 0.89(d, 6H, J = 6.6 Hz), 1.62(td, 1H, J = 8.5, 5.6 Hz), 1.89(m, 1H), 2.00(dt, 1H, J = 7.9, 5.6 Hz), 2.74(q, 1H, J = 8.5 Hz), 2.82(td, 1H, J = 8.5, 5.6 Hz), 3.75(d, 1H, J = 6.6 Hz), 7.25–7.39(m, 5H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ_C, 133.4, 129.5, 128.0, 127.4, 75.4, 35.1, 28.1, 23.7, 18.6, 10.5. IR (neat) 2965, 1359, 1171, 978. MS (EI): 254(M^+, 50), 205(16), 181(24), 153(100), 107(23). HRMS (EI): calcd for $C_{13}H_{18}O_3S$ 254.0977, found 254.0971.

2,2-Dimethylpropyl 2-ethoxycyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.98(s, 9H), 1.23(t, 3H, J = 7.0 Hz), 1.45–1.54(m, 2H), 2.54(ddd, 1H, J = 9.3, 6.4, 2.1 Hz), 3.61–3.71(m, 2H), 3.82(ddd, 1H, J = 6.4, 4.6, 2.1 Hz), 3.89(s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 79.1, 67.1, 57.2, 33.4, 31.7, 26.0, 14.8, 13.8. IR (neat) 2971, 1344, 1161, 964, 827. MS (EI): ($M^+ - OC_5H_{11}$, 100), 133(45). HRMS (EI): calcd for $C_5H_9O_3S$ 149.0272, found 149.0249. ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.02(s, 9H), 1.27(t, 3H, J = 7.1 Hz), 1.41(dt, 1H, J = 9.3, 6.8 Hz), 1.78(td, 1H, J = 6.8, 5.0 Hz), 2.44(dt, 1H, J = 9.3, 5.0 Hz), 3.62–3.74(m, 2H), 3.80(m, 1H), 3.91(d, 1H, J = 9.2 Hz), 3.97(d, 1H, J = 9.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 79.3, 67.4, 56.6, 33.7, 31.7, 26.1, 14.9, 13.4. IR (neat) 2974, 1357, 1220, 1172, 969, 836. MS (EI): ($M^+ - OC_5H_{11}$, 60), 80(100). HRMS (EI): calcd for $C_5H_9O_3S$ 149.0272, found 149.0249.

2,4-Dimethyl-3-pentyl 2-phenylcyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.99(m, 12H), 1.49(d*t*, 1H, J = 8.5, 6.6 Hz), 1.80(d*t*, 1H, J = 10.8, 5.4 Hz), 2.01(m, 2H), 2.71(ddd, 1H, J = 8.5, 5.4, 4.4 Hz), 2.79(ddd, 1H, J = 10.8, 6.6, 4.4 Hz), 4.36(*t*, 1H, J = 5.7 Hz), 7.12–7.32(m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 137.8, 128.8, 127.3, 126.6, 94.8, 37.8, 30.2, 30.1, 23.5, 20.1, 17.9, 17.7, 14.5. IR (neat) 2915, 1200, 1159. MS (EI): 296(M^+, 3), 181(46), 153(100), 136(57), 117(55), 108(24). HRMS (EI): calcd for $C_{16}H_{24}O_3S$ 296.1446, found 296.1457. ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.87(2d, 6H, J = 6.8 Hz), 0.98(2d, 6H, J = 6.8 Hz), 1.62(td, 1H, J = 8.5, 5.6 Hz), 1.87–1.98(m, 3H), 2.68(q, 1H, J = 8.5 Hz), 2.85(td, 1H, J = 8.5, 5.6 Hz), 4.26(*t*, 1H, J = 5.6 Hz), 7.22–7.40(m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 133.6, 129.6, 127.9, 127.3, 93.5, 36.2, 30.1, 30.0, 23.9, 20.0, 19.8, 17.8, 17.5, 11.0. IR (neat) 2965, 1350, 1167, 893. MS (EI): 296(M^+, 4), 181(53), 117(100). HRMS (EI): calcd for $C_{16}H_{24}O_3S$ 296.1446, found 296.1449.

2,2-Dimethylpropyl 2-phenylcyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.98(s, 9H), 1.45(d*t*, 1H, J = 8.5, 6.7 Hz), 1.73(d*t*, 1H, J = 10.1, 5.3 Hz), 2.59(ddd, 1H, J = 8.5, 5.3, 4.5 Hz), 2.72(ddd, 1H, J = 10.1, 6.7, 4.5 Hz), 3.84(s, 2H), 7.05–7.26(m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 137.1, 128.7, 127.3, 126.5, 79.4, 36.0, 31.7, 26.0, 23.2, 13.6. IR (neat) 2951, 1344, 1153, 958, 819. MS (EI): 268(M^+, 2), 153(6), 117(100). HRMS (EI): calcd for $C_{14}H_{20}O_3S$ 268.1133, found 268.1139. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 7.95 and 8.58) ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.89(s, 9H), 1.62(td, 1H, J = 8.6, 5.6 Hz), 1.96(d*t*, 1H, J = 8.0, 5.6 Hz), 2.68(q, 1H, J = 8.6 Hz), 2.82(td, 1H, J = 8.6, 5.6 Hz), 3.70(d, 1H, J = 9.2 Hz), 3.73(d, 1H, J = 9.2 Hz), 7.23–7.38(m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 133.3, 129.5, 128.0, 127.3, 78.6, 34.9, 31.5, 25.9, 23.7, 10.5. IR (neat) 2962, 1353, 1168, 969, 839. MS (EI): 268(M^+, 2), 181(3), 117(100). HRMS (EI): calcd for $C_{14}H_{20}O_3S$ 268.1133, found 268.1120. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 7.53 and 8.15).

2,2-Dimethylpropyl 2-(2-methoxyphenyl)cyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.99(s, 9H), 1.47(ddd, 1H, J = 8.4, 6.6, 5.5 Hz), 1.76(d*t*, 1H, J = 9.9, 5.5 Hz), 2.59(ddd, 1H, J = 8.4, 5.5, 4.5 HzHz), 2.75(ddd, 1H, J = 9.9, 6.6, 4.5 Hz), 3.79(s, 3H), 3.91(s, 2H), 6.84(d, 2H, J = 8.6 Hz), 7.06(d, 2H, J = 8.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 158.9, 129.0, 127.7, 114.1, 79.3, 55.3, 35.9, 31.7, 26.0, 22.7, 13.4. IR (neat) 2965, 1514, 1344, 1238, 1167, 1030, 958, 827. MS (EI): 298(M^+, 4), 153(10), 147(100). HRMS (EI): calcd for $C_{15}H_{22}O_4S$ 298.1239, found 298.1234. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 11.1 and 12.0) ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.91(s, 9H), 1.60(td, 1H, J = 8.5, 5.7 Hz), 1.91(d*t*, 1H, J = 7.9, 5.7 Hz), 2.66(q, 1H, J = 8.5 Hz), 2.75(td, 1H, J = 8.5, 5.7 Hz), 3.67(d, 1H, J = 9.2 Hz), 3.70(d, 1H, J = 9.2 Hz), 3.77(s, 3H), 6.84(d, 2H, J = 8.8 Hz), 7.30(d, 2H, J = 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 158.9, 130.6, 125.3, 113.5, 78.6, 55.2, 34.8, 31.6, 26.0, 23.0, 10.7. IR (neat) 2960, 1516, 1348, 1246, 1173, 964, 829. MS (EI): 298(M^+, 3), 147(100). HRMS (EI): calcd for $C_{15}H_{22}O_4S$ 298.1239, found 298.1239. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 7.37 and 8.95).

2,2-Dimethylpropyl 2-(4-methylphenyl)cyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.98(s, 9H), 1.49(d*t*, 1H, J = 8.5, 6.2 Hz), 1.78(d*t*, 1H, J = 9.8, 5.3 Hz), 2.33(s, 3H), 2.63(d*t*, 1H, J = 8.5, 5.3 Hz), 2.75(ddd, 1H, J = 9.8, 6.2, 4.5 Hz), 3.90(s, 2H), 7.01(d, 2H, J = 8.0 Hz), 7.13(d, 2H, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 137.0, 134.1, 129.4, 126.4, 79.4, 36.0, 31.8, 26.0, 23.0, 21.0, 13.6. IR (neat) 2965, 1343, 1170, 963, 812. MS (EI): 282(M^+, 5), 212(19), 195(7), 131(100), 129(5). HRMS (EI): calcd for $C_{15}H_{22}O_3S$ 282.1290, found 282.1293. The enantiomeric excess of this isomer was determined by analysis of ^{1}H NMR spectra of samples containing increasing amounts of the chiral shift reagent (Eu(hfc)$_3$). ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.91(s, 9H), 1.59(td, 1H, J = 8.5, 5.7 Hz), 1.94(d*t*, 1H, J = 7.9, 5.7 Hz), 2.32(s, 3H), 2.68(q, 1H, J = 8.5 Hz), 2.77(td, 1H, J = 8.5, 5.7 Hz), 3.66(d, 1H, J = 9.2 Hz), 3.69(d, 1H, J = 9.2 Hz), 7.11(d, 2H, J = 8.0 Hz), 7.27(d, 2H, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 137.0, 130.2, 129.4, 128.7, 78.6, 34.8, 31.5, 25.9, 23.3, 21.1, 10.5. IR (neat) 2959, 1352, 1169, 971, 850. MS (EI): 282(M^+, 3), 131(100). HRMS (EI): calcd for $C_{15}H_{22}O_3S$ 282.1289, found 282.1282. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 9.96 and 10.7).

2,2-Dimethylpropyl 2-(4-chlorophenyl)cyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.98(s, 9H), 1.50(d*t*, 1H, J = 8.5, 6.6 Hz), 1.82(d*t*, 1H, J = 10.0, 5.4 Hz), 2.65(ddd, 1H, J = 8.5, 5.4, 4.5 Hz), 2.76(ddd, 1H, J = 10.0, 6.6, 4.5 Hz), 3.91(s, 2H), 7.06(d, 2H, J = 8.5 Hz), 7.30(d, 2H, J = 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 135.6, 133.1, 128.9, 127.9, 79.4, 36.1, 31.7, 26.0, 22.6, 13.7. IR (neat) 2959, 1342, 1168, 959, 820. MS (EI): 302(M^+, 5), 215(4), 151(100), 115(11). HRMS (EI): calcd for $C_{14}H_{19}O_3SCl$ 302.0743, found 302.0743. The enantiomeric excess of this isomer was determined by analysis of ^{1}H NMR spectra of samples containing increasing amounts of the chiral shift reagent (Eu(hfc)$_3$). ***syn*-isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92(s, 9H), 1.65(td, 1H, J = 8.5, 5.7 Hz), 1.9(d*t*, 1H, J = 7.9, 5.7 Hz), 2.68(q, 1H, J = 8.5 Hz), 2.82(td, 1H, J = 8.5, 5.7 Hz), 3.70(d, 1H, J = 9.2 Hz), 3.73(d, 1H, J = 9.2 Hz), 7.29(m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 133.3, 131.9, 130.9, 128.2, 78.7, 34.8, 31.6, 26.0, 23.0, 10.7. IR (neat) 2961, 1355, 1171, 967, 833. MS (EI): 302(M^+, 5), 151(100). HRMS (EI): calcd for $C_{14}H_{19}O_3SCl$ 302.0743, found 302.0740. The enantiomeric excess of this isomer was determined by analysis of ^{1}H NMR spectra of samples containing increasing amounts of the chiral shift reagent (Eu(hfc)$_3$).

2,2-Dimethylpropyl 2-(2-nitrophenyl)cyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.98(s, 9H), 1.62(d*t*, 1H, J = 8.6, 6.6 Hz), 1.92(d*t*, 1H, J = 10.0, 5.5 Hz), 2.78(ddd, 1H, J = 8.6, 5.5, 4.5 Hz), 2.90(ddd, 1H, J = 10.0, 6.6, 4.5 Hz), 3.94(s, 2H), 7.50–7.54(m, 2H), 7.97(S, 1H), 8.13(d*t*, 1H, J = 7.1, 2.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 148.5, 139.4, 133.1, 129.7, 122.3, 121.1, 79.6, 36.3, 31.7, 25.9, 22.6, 14.0. IR (neat) 2965, 1520, 1336, 1167, 964, 833. MS (EI): 313(M^+, 1), 298(10), 162(73), 145(11), 116(100). HRMS (EI): calcd for $C_{14}H_{19}O_5NS$ 313.0983, found 313.0985. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 9.15 and 11.62) ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.95(s, 9H), 1.75(td, 1H, J = 8.5, 5.6 Hz), 2.03(d*t*, 1H, J = 8.0, 5.6 Hz), 2.81(q, 1H, J = 8.5 Hz), 2.92(td, 1H, J = 8.5, 5.6 Hz), 3.75(d, 1H, J = 9.2 Hz), 3.78(d, 1H, J = 9.2 Hz), 7.49(*t*, 1H, J = 8.2 Hz), 7.73(d*t*, 1H, J = 8.2, 0.8 Hz), 8.14(dd, 1H, J = 8.2, 2.2 Hz), 8.24(s,1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 148.0, 135.8, 135.7, 128.9, 124.7, 122.5, 79.0, 34.8, 31.6, 25.9, 22.9, 10.7. IR (neat) 2953, 1531, 1349, 1172, 955. MS (EI): 313(M^+, 6), 298(31), 263(23),

162(58), 149(26), 116(100). HRMS (EI): calcd for $C_{14}H_{19}O_5NS$ 313.0983, found 313.0980. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 7.5 and 8.7).

2,2-Dimethylpropyl 2-(1,1-dimethylethoxy)cyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.99(s, 9H), 1.30(s, 9H), 1.37(ddd, 1H, J = 9.5, 6.7, 4.4 Hz), 1.46(q, 1H, J = 6.7 Hz), 2.48(ddd, 1H, J = 9.5, 6.1, 2.3 Hz), 3.80(ddd, 1H, J = 9.5, 4.4, 2.3 Hz), 3.88(s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 78.8, 76.3, 51.0, 34.3, 31.7, 27.8, 26.0, 13.0. IR (neat) 2973, 1356, 1169, 976, 837. MS (EI): 249(M^+ − Me, 13), 179(26), 127(28), 121(57), 113(100). HRMS (EI): calcd for $C_{11}H_{21}O_4S$ 249.1161, found 249.1172. The enantiomeric excess of this isomer was determined by analysis of ^{1}H NMR spectra of samples containing increasing amounts of the chiral shift reagent (Eu(hfc)$_3$). ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.99(s, 9H), 1.30(s, 9H), 1.37(d*t*, 1H, J = 9.3, 6.5 Hz), 1.65(td, 1H, J = 6.5, 5.4 Hz), 2.40(d*t*, 1H, J = 9.3, 6.5 Hz), 3.58(q, 1H, J = 5.4 Hz), 3.86(d, 1H, J = 9.3 Hz), 3.99(d, 1H, J = 9.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 79.3, 76.2, 50.7, 33.0, 31.7, 27.8, 26.0, 14.4. IR (neat) 2978, 1369, 1176, 976, 837. MS (EI): (M^+ − Me, 2), 209(15), 179(54), 153(35), 121(67), 113(100). HRMS (EI): calcd for $C_{11}H_{21}O_4S$ 249.1161, found 249.1157. The enantiomeric excess of this isomer was determined by analysis of ^{1}H NMR spectra of samples containing increasing amounts of the chiral shift reagent (Eu(hfc)$_3$).

2,2-Dimethylpropyl 2-(acetyloxy)methylcyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.00(s, 9H), 1.14(d*t*, 1H, J = 8.4, 6.1 Hz), 1.51(d*t*, 1H, J = 9.6, 5.6 Hz), 2.00(m, 1H), 2.08(s, 3H), 2.49(d*t*, 1H, J = 9.6, 6.1 Hz), 3.89(s, 2H), 3.90(dd, 1H, J = 11.8, 7.7 Hz), 4.21(dd, 1H, J = 11.8, 5.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 170.6, 79.4, 64.0, 32.0, 31.7, 26.0, 20.7, 18.1, 10.1. IR (neat) 2963, 1744, 1362, 1244, 1173, 1036, 978, 854. MS (EI): 249(M^+ − Me, 5), 209(32), 195(31), 149(10), 113(100). HRMS (EI): calcd for $C_{10}H_{17}SO_5$ 249.0797, found 249.0809. The enantiomeric excess of this isomer was determined by analysis of ^{1}H NMR spectra of samples containing increasing amounts of the chiral shift reagent (Eu(hfc)$_3$). ***syn*-isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.01(s, 9H), 1.39–1.46(m, 2H), 1.80(q, 1H, J = 8.1 Hz), 2.09(s, 3H), 2.59(td, 1H, J = 8.1, 6.1 Hz), 3.91(d, 1H, J = 9.2 Hz), 3.95(d, 1H, J = 9.2 Hz), 4.34(dd, 1H, J = 11.9, 7.9 Hz), 4.52(dd, 1H, J = 11.9, 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 170.8, 79.2, 61.8, 32.1, 31.7, 26.0, 20.8, 18.3, 11.0. IR (neat) 2961, 1744, 1354, 1233, 1167, 1034, 968. MS (EI): 249(M^+ − Me, 2), 209(28), 195(32), 149(12), 113(100). HRMS (EI): calcd for $C_{10}H_{17}SO_5$ 249.0797, found 29.0795.

2,4-Dimethyl-3-pentyl 2-(2-nitrophenyl)cyclopropanesulfonate. *anti*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.00(m, 12H), 1.58(ddd, 1H, J = 8.5, 6.5, 5.4 Hz), 1.91(d*t*, 1H, J = 10.8, 5.4 Hz), 2.04(m, 2H), 2.79(d*t*, 1H, J = 8.5, 5.4 Hz), 2.89(ddd, 1H, J = 10.8, 6.5, 4.5 Hz), 4.40(*t*, 1H, J = 5.7 Hz), 7.48–7.54(m, 2H), 7.97(s, 1H), 8.12(d*t*, 1H, J = 7.0, 2.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 148.4, 139.8, 133.1, 129.7, 122.2, 121.1, 95.2, 37.9, 30.15, 30.11, 23.0, 20.00, 19.98, 17.78, 17.6, 14.5. IR (neat) 2970, 1536, 1351, 1167, 892. MS (EI): 341(M^+, 3), 298(100), 162(51), 116(48). HRMS (EI): calcd for $C_{16}H_{23}NSO_5$ 341.1296, found 341.1287. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 9.5 and 11.2).

2,2-Dimethylpropyl 2,2-diphenylcyclopropanesulfonate. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.96(s, 9H), 1.85(dd, 1H, J = 8.7, 5.6 Hz), 2.34(*t*,1H, J = 5.6 Hz), 3.24(dd, 1H, J = 8.7, 5.6 Hz), 3.79(d, 1H, J = 9.1 Hz), 3.81(d, 1H, J = 9.1 Hz), 7.17–7.53(m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C, 143.4, 137.7, 129.7, 128.8, 128.3, 127.8, 127.6, 127.2, 79.0, 40.7, 38.7, 31.7, 26.0, 19.0. IR (neat) 2963, 1362, 1167, 970, 837, 702. MS (EI): 176(M^+, 1), 192(100), 115(16). HRMS (EI): calcd for $C_{20}H_{24}O_3S$ 344.1446, found 344.1431. The enantiomeric excess of this isomer was determined by chiral HPLC analysis (Column: Daicel OD; Mobile phase: hexane/isopropanol, Retention time (minutes): 7.5 and 8.7).

Acknowledgements

We acknowledge financial support from the Hong Kong Research Grants Council (Project: HKU 7125/00P) and The University of Hong Kong. CYZ would like to thank Dr W. Y. Yu (HKU) for some helpful suggestions.

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