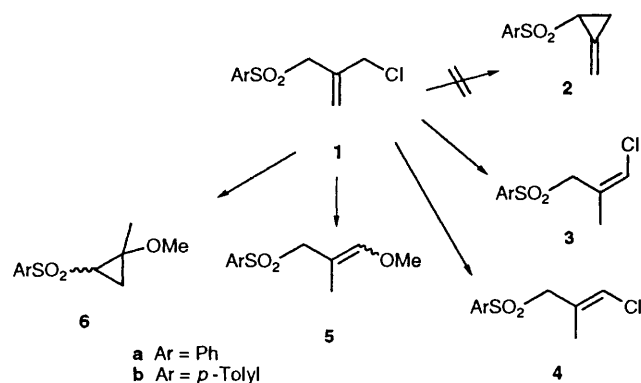# Formation of Cyclopropylsulfones from 1-Arylsulfonyl-2-chloromethyl-prop-2-enes

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Methylenecyclopropyl sulfones are not formed when the title chlorosulfones are treated with methanolic methoxide; instead 1-arylsulfonyl-2-methoxy-2-methylcyclopropanes are formed by an addition–cyclisation sequence involving intramolecular displacement of chloride and not methoxide as suggested by other workers.

As part of an exploration of the limit of excess enthalpy differential (EED) that can be tolerated for intramolecular nucleophilic substitution,[1] we examined the reactions of bases with sulfone 1a. We were mindful of the fact that cyclisation *via* a sulfonyl-stabilised carbanion leading to methylenecyclopropane 2 would involve an EED of 171 kJ mol⁻¹.† In the event, none of 2 was obtained, under a wide variety of conditions (Table 1). When the base was strong but poorly nucleophilic (Bu^{t}OK–Bu^{t}OH) the isomerisation products 3a and 4a were obtained (entry 1) but no cyclisation occurred. When the base was weaker but more nucleophilic (NaOMe–MeOH), the products were initially 3a and 4a (entry 2) which were converted under more vigorous conditions into the cyclopropanes 6a (entries 3 and 4) with small quantities of the ether 5a (entry 6) (Scheme 1).

A reasonably consistent pathway is outlined in Scheme 2. Isomerisation of 1 to the sulfone-conjugated isomer 9, probably

Scheme 1

a Ar = Ph
b Ar = p-Tolyl

Scheme 2

in equilibrium with the much-favoured[3] isomer(s), 3 and 4.‡ Addition–cyclisation involving methoxide (*cf.* 7), then gives the cyclopropanes, 6 formed as a mixture of (*E*) and (*Z*) isomers with the (*E*)-6 favoured. No evidence for formation of methylenecyclopropane, 2, was found. A minor product, however, was ether 5, presumably formed by direct substitution on chloride 9, giving 8, which then isomerises to the more stable, sulfone-deconjugated isomer, 5 (entry 6). By treatment of 2a, prepared separately,[4] with methanolic sodium methoxide we have established that it is not an intermediate in these reaction pathways.

While this work was in progress, reaction of the sulfone 1b with methanolic sodium methoxide was reported[5] to give, in 95% yield, a 1:1 mixture of open chain ether (*E*)-5b and cyclopropane (*E*)-6b. It is implied in this report[5] that this
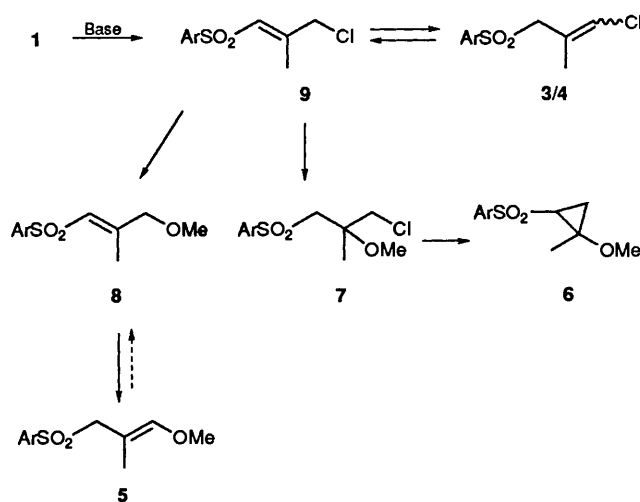
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† Here the EED between methylenecyclopropane (171 kJ mol⁻¹) (see ref. 2) and an 'unstrained' precursor 1a is assumed to equal the strain energy of 2.

‡ Reactions of 1a with MeOD/MeO⁻ affords [²H₆]-3a/4a supporting equilibration of all double bond isomers of the anion of 1a.

Table 1 Product yields from reactions of 1a with base

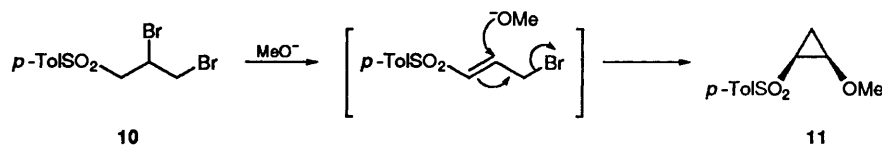| Entry	Substrate	Conditions[a]	Products ratio[b] (%)				Isolated yield (%)			
			1a	3a/4a (ratio)	5	6	1a	3a/4a	5	6
1	1a	1 × KOBu^{t}Bu^{t}OH, 26 °C	—	100 (2:1)	—	—	—	26[c]	—	—
2	1a	3 × MeO⁻/MeOH, 3 h, 22 °C	66	33 (3:1)	—	—	52	25	—	—
3	1a	3 × MeO⁻/MeOH, 18 h, 22 °C	5	85 (4:1)	—	10[d]	—	76	—	—
4	1a	3 × MeO⁻/MeOH, 3 d, 22 °C	—	80 (4:1)	—	20[e]	—	75	—	5[d]
5	1a	3 × MeO⁻/MeOH, 2 d, 65 °C	—	40 (4:1)	—	60[e]	—	—	—	—
6	1a	3 × MeO⁻/MeOH, 4 d, 65 °C	—	—	10[d]	90[f]	—	—	—	81[f]
7	1a	0.5 × MeO⁻/MeOH, 3 d, 65 °C[g]	—	62 (2:1)	9[d]	29[h]	—	—	—	—
8	3a/4a (2:1)	3 × MeO⁻/MeOH, 3 d, 65 °C	—	—	—	—	—	10	—	76[i]
9	5a	3 × MeO⁻/MeOH, 7 d, 65 °C	—	—	75[j]	—	—	—	—	—
10	(*E*)-6a	5 × MeO⁻/MeOH, 7 d, 65 °C	—	—	—	80[j,k]	—	—	—	—

[a] Numbers refer to molar ratios of base to substrate. [b] By ¹H NMR. [c] Single isomer by recrystallisation (petrol–ethyl acetate). [d] Observed/isolated as a single isomer. [e] Isomer ratio 9:1. [f] Isomer ratio 6:1. [g] HPLC yields reported. [h] Isomer ratio 18:1. [i] Isomer ratio 5:1. [j] Product recovery estimated from HPLC analysis. [k] (*E*)-Isomer only recovered.

10 **11**

mixture on prolonged exposure to methanolic sodium methoxide at reflux gives an 84% yield of (E)-**5b** and (E)-**6b** in a 2:98 ratio. The authors suggest that, in contrast to our work, a single methoxycyclopropane **6** is obtained by a pathway involving addition of methoxide ion to **8** and *intramolecular displacement of the distal methoxy-group*.*

In earlier work from our laboratories,[6] formation of cyclopropanes by intramolecular displacement of phenoxide as leaving group was found to be exceedingly slow, with a rate constant of *ca.* 5×10^{-13} dm^{-3} mol^{-1} s^{-1} at 30 °C. Leaving group rank[7] in such reactions was quantified and shown to correlate excellently with the $pK_a^{(Bu^tOH)}$ of the leaving group. We consider it very improbable therefore that this reaction can occur under the reported conditions. The result of reacting chlorides **3a/4a** gives **6a** (entry 8) but we find that *no* cyclopropane, **6a** is obtained when the ethers, **5a** react with methanolic sodium methoxide under our conditions (entry 9). We have also established that the cyclopropane (E)-**6a** appears not to be involved in subsequent reaction to yield **5a** nor indeed (Z)-**6a** over the timescale of these reactions (see Table 1, entry 10). In an analogous situation, the Spanish authors report a timescale of 7 d reflux in 0.4 mol dm^{-3} MeONa/MeOH for reaction of **10** *via* a related species to afford[8] cyclopropane **11**.

In the present situation, the origin of such experimental inconsistencies may lie in differing reaction conditions, with our base concentrations typically at *ca.* 0.5 mol dm^{-3}. Notwithstanding the differing product ratios, the chlorides **3a** and **4a** appear unequivocally to be the source of cyclopropanes **6a**, as indicated by both the present experiments and the relative leaving group ranks for Cl *vs.* OMe.[7]

Experimental

General Directions.—M.p.s are uncorrected. Petrol refers to light petroleum b.p. 40–60 °C. ^{1}H NMR spectra were recorded in CDCl$_3$ at 400 MHz with Me$_4$Si reference; ^{13}C spectra were recorded at 62.9 MHz. Methanol was HPLC grade. *tert*-Butanol was dried (CaH$_2$) and distilled prior to use. HPLC analysis was performed on 5 µ Spherisorbsilica column (25 cm × 4.6 mm i.d.) eluting with petrol–ethyl acetate (80:20) and with UV detection at 254 nm. Semi-preparative HPLC was performed on 5 µ Spherisorbsilica (25 cm × 20 mm i.d.) eluting with petrol–ethyl acetate 85:15, flow rate 15 cm^3 min^{-1}; UV detection at 254 nm. The following retention times (min) were observed using semi-preparative HPLC: **4a** (minor isomer), t_R 8.90; **3a** (major isomer), t_R 11.22; **5a**, t_R 13.54; (Z)-**6a**, t_R 14.57; and (E)-**6a**, t_R 16.38. No unassigned peaks were observed. 3-Phenylsulfonyl-2-chloromethylprop-1-ene **1a** had m.p. 55–56 °C (lit.,[9] 54–55 °C) and 1-methylene-2-phenylsulfonylcyclopropane **2a** had m.p. 46–48 °C (lit.,[10] 47.5–48.5 °C).

Reaction of **1a**.—(a) *With methanolic sodium methoxide*. 1-Phenylsulfonyl-2-methoxymethylcyclopropane **6a**. A stirred solution of **1a** (2.4 g, 0.01 mol) in methanol (50 cm^3) was treated with sodium methoxide (30 cm^3, 0.03 mol; 1 mol dm^{-3} solution in methanol). The whole was refluxed for 4 d under argon, quenched with dil. hydrochloric acid, extracted with dichloromethane, concentrated and chromatographed (petrol–ethyl acetate, 7:3) to yield first (Z)-**6a** (minor isomer) (0.21 g, 9%),

m.p. 85–87 °C; ν_{max}/cm^{-1} 1295 and 1150; δ_H 8.0–7.90 (2 H, m) and 7.60–7.40 (3 H, m, PhSO$_2$), 3.45 (3 H, s, OMe), 2.38 (1 H, dd, J 8 and 6 Hz), 1.98 [1 H, dd appears as t, J 2 × 6 Hz, C(3)Ha], 1.40 (3 H, s, CH$_3$) and 1.25 [1 H, dd, J 8 and 6 Hz, C(3)Hb] [NOE observed between C(2)CH_3 and C(1)H] (Found: C, 58.1; H, 6.1. C$_{11}$H$_{14}$O$_3$S requires C, 58.39; H, 6.24%). Next eluted was (E)-**6a** (major isomer) (1.62 g, 72%), m.p. 42–44 °C; ν_{max}/cm^{-1} 1300 and 1145; δ_H 8.0–7.85 (2 H, m), 7.70–7.50 (3 H, m, PhSO$_2$), 3.24 (3 H, s, OMe), 2.25 (1 H, dd, J 8 and 6 Hz) and 1.65–1.50 (2 H, m) [NOE enhancement observed between OMe and C(1)H] (Found: C, 58.3; H, 6.1; S, 14.15. C$_{11}$H$_{14}$O$_3$S requires: C, 58.39; H, 6.24; S, 14.17%).

(b) *With potassium* tert-*butoxide in* tert-*butanol*. In a similar reaction to that described above in *tert*-butanol with potassium *tert*-butoxide gave **3a/4a**. Major isomer, m.p. 110–112.5 °C (petrol–ethyl acetate), ν_{max}/cm^{-1} 1300 and 1150; δ_H 7.90–7.82 (2 H, m), 7.70–7.62 (1 H, m) and 7.60–7.54 (2 H, m, PhSO$_2$), 5.90–5.88 (1 H, m), 4.89 (2 H, d, J 1 Hz, PhSO$_2$CH_2) and 3.84 (3 H, d, J 2 Hz, CH_3); δ_C 138.24, 133.90, 129.16, 128.36, 127.21, 122.05, 63.28 and 17.22; *m/z* (CI) 250/248 (M + NH$_4^+$, 100%) (Found: C, 52.1; H, 4.6; Cl, 15.4; S, 13.8. C$_{10}$H$_{11}$O$_2$ClS requires: C, 52.06; H, 4.81; Cl, 15.37; S, 13.89%). Minor isomer, m.p. 80–83 °C; δ_H 7.92–7.87 (2 H, m), 7.68–7.62 (1 H, m) and 7.56–7.51 (2 H, m, PhSO$_2$), 5.99–5.97 (1 H, m), 4.04 (2 H, s, PhSO$_2$CH_2) and 2.00 (3 H, d, J 2 Hz, CH_3). (No NOE enhancements observed for either isomer.)

1-*Methoxy-2-methyl-3-phenylsulfonylprop*-1-*ene* **5a**.—This compound was isolated by semi-preparative HPLC separation of reaction products, m.p. 50–53 °C; δ_H 7.95–7.85 (2 H, m), 7.65–7.45 (3 H, m, PhSO$_2$), 5.80 (1 H, br s), 3.90 (2 H, br s), 3.10 (3 H, s, OMe) and 1.70 (3 H, d, J 0.5 Hz, CH$_3$); *m/z* (EI) 226 (M$^+$, 60%) (Found: 226.2902. C$_{11}$H$_{14}$O$_3$S requires 226.2898).

Reaction of 1-*Methylene-2-phenylsulfonylcyclopropane* **2a** *with Methanolic Sodium Methoxide*.—Under conditions similar to those described above for **1a** a sample of **2a** (0.56 g, 2.88 mmol) in methanolic sodium methoxide was heated under reflux for 3 d. The resulting residue (0.36 g) was shown by ^{1}H NMR spectroscopy and HPLC analysis to be recovered **2a**. No evidence for the formation of the ether **5a** or the cyclopropanes **6a** was obtained.

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* *Note added in proof*. Professor Najera tells us in a private communication that the conditions used in her laboratories for the conversion of a 1:1 mixture of compounds **5b** and **6b** into **6b** involved treatment of the mixture with 3 equiv. NaOMe without solvent at 80 °C for 3 days.