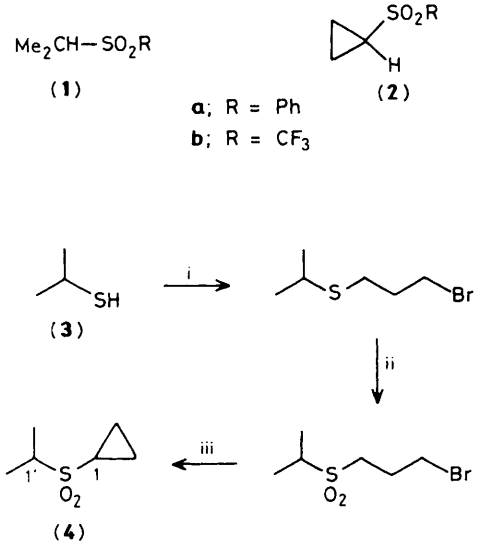
Kinetic Acidity of Cyclopropyl Sulphones

Wolfgang Kirmse* and Uwe Mrotzeck

Facultät für Chemie, Ruhr-Universität Bochum, D-4630 Bochum, F.R.G.

Base-catalysed exchange of 2-H and 4-H in 3-thiatricyclo[2.2.1.$0^{2,6}$]heptane 3,3-dioxide (**9**) proceeds faster than the exchange of analogous hydrogens in cyclopropyl isopropyl sulphone (**4**), despite enforced pyramidalisation of the carbanion intermediates derived from (**9**).

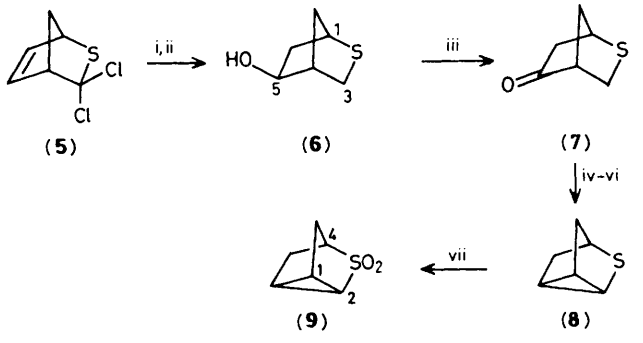
The geometry of α-sulphonyl carbanions is currently under active investigation, both theoretically[1] and experimentally.[2] The acidity of cyclopropyl sulphones may be expected to provide some insight into the problem.[3] If the sulphonyl group demands p character of the cyclopropyl anion, cyclopropyl sulphones should be less acidic than their acyclic analogues, owing to the additional strain introduced by rehybridising a cyclopropane carbon from sp^3 to sp^2. In the case of pyramidal α-sulphonyl carbanions, the intrinsically greater acidity of cyclopropyl hydrogens should prevail.



Scheme 1. *Reagents:* i, $Br[CH_2]_3Br$, MeONa, MeOH; ii, *meta*-choroperbenzoic acid, $CHCl_3$; iii, NaH, tetrahydrofuran.

Application of these criteria has been complicated by conflicting experimental results. Zimmerman[4] and Cram[5] reported that the equilibrium acidities of isopropyl phenyl sulphone (**1a**) and of cyclopropyl phenyl sulphone (**2a**) are approximately equal. Hydrogen–deuterium exchange (CH_3OD, 0.22 M NaOMe, 53 °C) proceeded *ca.* 34 times faster with (**2a**) than with (**1a**).[6] On the other hand, the SO_2CF_3 group was found to have a larger acidifying effect in (**1b**) (p*K* 21.8) than in (**2b**) (p*K* 26.6 in dimethyl sulphoxide).[7] Our approach to the problem was to prepare cyclopropyl isopropyl sulphone (**4**) and 3-thiatricyclo[2.1.1.$0^{2,6}$]heptane 3,3-dioxide (**9**). Both cyclopropyl and isopropyl hydrogens are positioned α to the sulphonyl groups of these compounds. In contrast to (**4**), the rigid tricyclic structure of (**9**) does not permit the intervention of planar α-sulphonyl carbanions.

Cyclopropyl isopropyl sulphone (**4**) was obtained from propane-2-thiol (**3**) and 1,3-dibromopropane as shown in Scheme 1. Hydrogen–deuterium exchange in D_2O–DONa



Scheme 2. *Reagents:* i, B_2H_6; ii, H_2O_2, NaOH; iii, Bu^tOCrO_2OH, CCl_4, pyridine; iv, *p*-$MeC_6H_4SO_2NHNH_2$; v, NaH; vi, heat; vii, $NaBO_3{\cdot}4H_2O$, NaOH, MeOH.

Table 1. Rates of H–D exchange (D_2O, 0.5 M NaOD).[a]

Compound	Hydrogen	Temp./°C	k/s^{-1}
(**4**)	1-H	74	$2.58 \pm 0.05 \times 10^{-4}$
(**4**)	1′-H	74	$1.21 \pm 0.03 \times 10^{-6}$
(**4**)	1-H	35	$4.27 \pm 0.08 \times 10^{-6}$
(**9**)	2-H	35	$1.47 \pm 0.02 \times 10^{-4}$
(**9**)	4-H	35	$1.01 \pm 0.02 \times 10^{-6}$

[a] Samples were thermostatted (±0.2 °C) in sealed n.m.r. tubes, and the exchange was monitored by ^1H n.m.r. spectroscopy. Aliquots were extracted with diethyl ether to obtain samples for ^2H n.m.r. spectra.

was monitored by ^1H- and ^2H-n.m.r. spectroscopy. The relative rates of exchange for the cyclopropyl hydrogen (1-H, δ 2.28) and the isopropyl hydrogen (1′-H, δ 3.13) were 47 : 1 (Table 1), in good agreement with De Boer's data for (**1a**) and (**2a**).

The synthesis of (**9**) (m.p. 148 °C) started from (**5**), the adduct of cyclopentadiene to thiocarbonyl chloride.[8] A salient feature was the hydroboration–reduction of (**5**) to give (**6**) (m.p. 141 °C) regioselectively (5-OH : 6-OH 98 : 2), albeit in low yield (14%). Lithium aluminium hydride reduction of (**5**),[9] followed by hydroboration, afforded the isomeric alcohol (6-OH, 54%)[9] exclusively. Selective oxidation of (**6**) to give the ketone (**7**) (m.p. 133 °C) was achieved with t-butyl chromate. Intramolecular carbene insertion, leading to (**8**), and sodium perborate oxidation of (**8**) proceeded smoothly (Scheme 2). Again, the cyclopropyl hydrogen (2-H, δ 2.4) of (**9**) exchanged faster than the 'isopropyl hydrogen' (4-H, δ 2.88) (Table 1). Moreover, the kinetic acidity of 2-H in (**9**) was enhanced over that of 1-H in (**4**) by a factor of 34.

Our data indicate that enforced pyramidalisation, as in (**9**), does not inhibit the formation of α-sulphonyl carbanions. Intramolecular competition clearly attributes greater kinetic acidity to cyclopropyl sulphones as compared with isopropyl sulphones. Our observations are compatible with recent theoretical studies.[1] Although the anion of dimethyl sulphone prefers a planar structure, the energetic demand for pyramidalisation is very small (0.57 kcal mol^{-1} for 20° out-of-plane bending).†[1] The rigid skeleton of (**9**) provides exactly the *gauche* configuration of $>CH–SO_2–$ required for optimal stabilisation of the incipient carbanion, and may thus account for the enhanced acidity.

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† 1 kcal = 4.184 kJ.