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BASE INDUCED REARRANGEMENTS OF α-HALOSULFONES α-SULFONYL CARBANIONS WITH BRIDGEHEAD ELECTROFUGAL[a] CENTRE

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Abstract—The KOtBu-induced Ramberg–Bäcklund reaction of the *trans* bicyclic halosulfones **1** and **2** is studied in DME and DMSO. Strong indications are obtained that the reaction proceeds *via* the intermediate Z-episulfone with retention-inversion (involving *exo*-S-geometry).† Base induced epimerization at the nucleofugal centre (from axial to equatorial halogen) is demonstrated in DMSO.

The susceptibility of α-halosulfones for base-initiated 1,3-elimination to give alkenes, the Ramberg–Bäcklund (RB) reaction is in strong contrast with the non reactivity in intermolecular displacements. Both this intriguing fact and the value of the reaction for synthesis of many olefins, cyclic and acyclic, which would be difficult to prepare by other methods,[1] explain the increasing attention for the title reactions.[2]

Several mechanistic details have been revealed in the literature. The anion formation is rapid and reversible in many examples.[3] Anion asymmetry in acyclic systems is maintained by a high rotational barrier and a low inversion barrier, making the anion effectively planar. The intramolecular S_N2 displacement of the halide ion gives an intermediate episulfone, which decomposes in many cases with stereospecificity to the olefin.[4]

The conformational requirements are more pronounced in cyclic sulfones[5] as a result of restricted rotational freedom and have been formulated as an easily obtainable *semi*-W-conformation[6] for the transition state leading to the episulfone.

More recently a double inversion mechanism (W-transition state) has been presented independently by two groups[7] for the transannular double bond formation in bridgehead α-halo-sulfones. The concerted character of the reaction, however, has been challenged.[2b,4]

We have previously reported[8] the KOH/CCl_4-induced rearrangement of *cis* bicyclic α-halosulfones. In the present communication we wish to report our observations on the rearrangement of *trans* bicyclic α-halosulfones **1** and **2**[9] as a function of solvent polarity and the relative configuration at the nucleofugal centre.

The reaction products are given in Scheme 1, reaction conditions and yields in Table 1.

DISCUSSION

Table 1 shows that the RB-reaction can compete efficiently with the 1,2-elimination of HCl, leading to the corresponding vinyl sulfones. The 1,2-elimination dominates in the weakly dissociating DME, while DMSO favours the RB-reaction.

Reactions 1–10 undoubtedly involve rapid and reversible anion formation.[2,3] For this reason we ascribe the higher proportion of RB-reaction in DMSO compared with DME to the higher steady state concentration of the initial tertiary α-sulfonyl carbanion in DMSO. The observation that sulfone **2** (X = Y = H) exhibits a markedly faster H/D exchange at the tertiary position than the corresponding sulfone **1** (R = X = Y = H)‡ also points in this direction. The enhanced stability of the tertiary anion derived from **2** affects all reactions that proceed *via* this anion. Consequently reaction of **2a** in DME leads predominantly to the olefins **5** and **6**, while **1a** is converted exclusively to the 1,2-elimination product, under the same circumstances (runs 4 and 1, respectively). The greater dissociating power of DMSO raises the steady state concentration of the tertiary anion derived from **1a** sufficiently to give exclusive RB-reaction (*cf* runs 1 and 3).

Unfortunately no data are available on the relative stability of the anion derived from **1c**. The lower ratio 1,3/1,2-elimination of **1c** compared with **2a** in DME (runs 4 and 8) might be a result of steric hindrance in proton abstraction by the second acetal function at C6 in **1c**. Comparison of runs 1 and 2 shows that the presence of tBuOH in the base system affects the conversion adversely. However, we have not been able thus far to achieve higher conversion by the use of base systems capable of irreversible proton abstraction.

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[a] The terms electrofugal and nucleofugal are used as defined in Ref 4.

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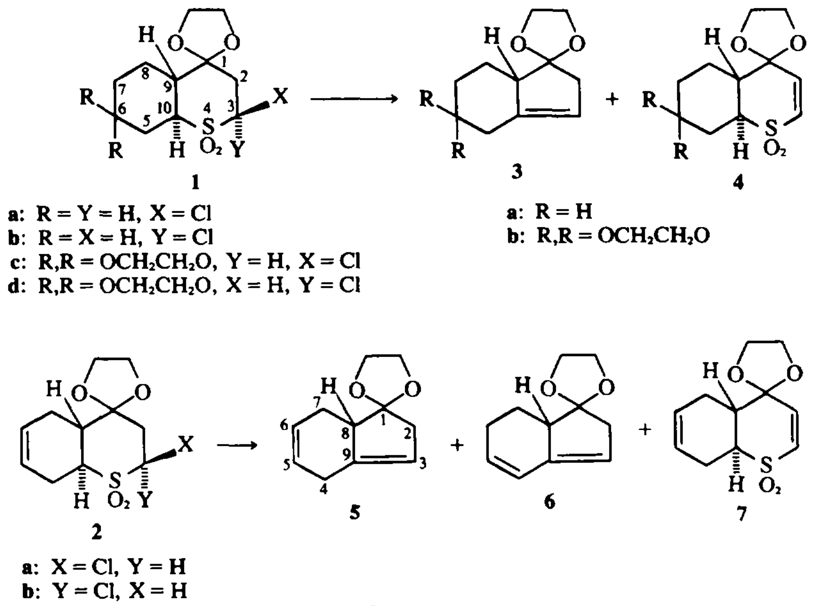
†The geometry descriptions have been taken from Ref 6 and are used as in Ref 4.

‡J. Kattenberg, unpublished results.



SCHEME 1.

Table 1. Base induced rearrangement of 1 and 2 at r.t. with 1·2 eq. base[a]

Reaction	Compound	Basesystem	Products (% yield)	Recovered sulfone (% yield)
1	**1a**	KOtBu/DME	**3a** (trace), **4a** (32)	**1a** (43)
2	**1a**	KOtBu/DME[b]	**3a** (18), **4a** (35)	**1a** (19)
3	**1a**	KOtBu/DMSO	**3a** (62)	**1a** (21)
4	**2a**	KOtBu/DME	**5** (48), **6** (25)	**2a** (18)
5	**2b**	KOtBu/DME	**7** (55)	—
6	**1a**	NaOAc/DMSO[c]	**4a** (10)	**1a** (80)
7	**2b**	NaOAc/DMSO[c]	**7** (20), **2a** (50)	**2b** (20)
8	**1c**	KOtBu/DME[b]	**3b** (18), **4b** (8)[d]	**1c** (49)
9	**1c**	KOtBu/DMSO[b]	**3b** (42)	**1c** (44)
10	**1d**	KOtBu/DMSO	**3b** (20), **1c** (55)	—

[a] Freshly sublimated KOtBu was used unless otherwise stated.

[b] KOtBu was sublimated three times, to remove last traces of tBuOH.

[c] 100° overnight, excess dried NaOAc.

[d] **4b** was obtained as a 2:1 mixture with the corresponding Michael adduct (4% yield) of tBuOH at the vinyl sulfone moiety.

Stereochemical aspects

Reactions 1–10 enable us to reconstruct the course of the RB-reaction in DME, but do not allow a conclusion for the reaction course in DMSO.

When the reaction is performed in DME, epimerization[10] at the nucleofugal centre can be considered very slow, if occuring at all, for the following reasons: (i) No epimerized α-halosulfone is detected in any of the reactions run in DME, (ii) Under conditions where **2a** reacts smoothly in the RB-reaction (run 4), the epimer **2b** gives the vinyl sulfone **7** (run 5). This indicates that diaxial 1,2-elimination is considerably faster than epimerization.

Scheme 2 gives the conceivable steps for the formation of the episulfones **9** and **13** (the immediate precursors of the olefins) starting from the initial tertiary anion **8**. When the C3-halogen occupies an equatorial position in the initial anion (Scheme 2, X = Cl, Y = H), only path *a*, involving *exo*-S-geometry and leading to the Z-episulfone,* will be followed during olefin formation. The alternative sequences *bcd* and *bcef* would involve inversion at the electrofugal centre C10, followed by conformational change of the resulting anion **10** to **11**, with U-type geometry, unfavourable for 1,3-elimination (step *d*).† Step *e*, leading to **12**, geometrically favourable for conversion to the E-episulfone **13**,

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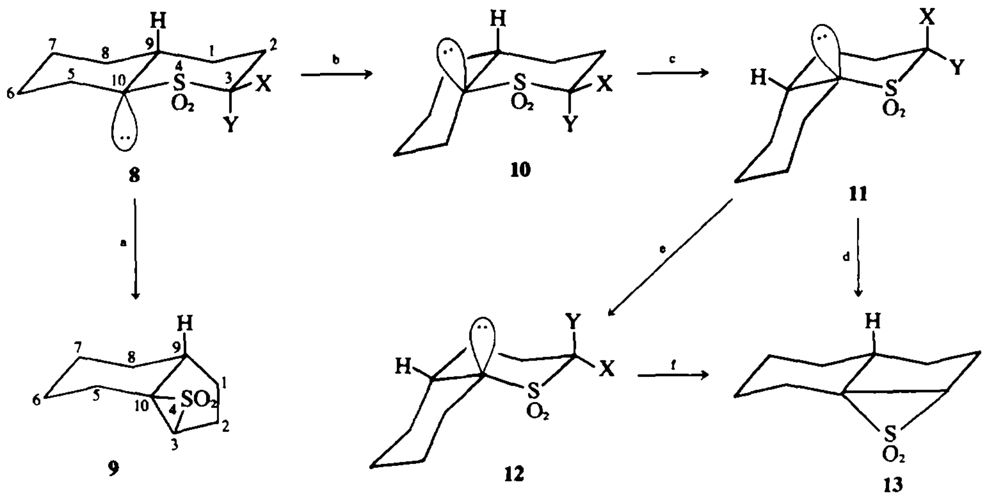
*The notations Z and E refer to the relative position of C9H and the SO_2 group.

†The failure of **2b** in giving 1,3-elimination excludes the overall U-type process *via* path *a*; This is in agreement with abundant data in the literature.[4]



Scheme 2.

can be excluded, since it requires epimerization at C3.

An axial position of the C3-halogen (Scheme 2, X = H, Y=Cl) leads to 1,2-elimination in DME (run 5). Evidently the sequence *bcd*, though geometrically favoured, cannot compete with 1,2-elimination.

The behaviour of the α-sulfonyl carbanions in DMSO differs strongly from that in DME. Treatment of **2b** with acetate ions in DMSO or **1d** with butoxide (runs 7 and 10, respectively) leads to substantial epimerization. Moreover, the equilibrium between the C3-epimers lies almost completely at the side of the equatorial halogen (*cf* runs 6 and 7).[10,11] The latter factor works in favour of the RB-reaction, since it suppresses 1,2-elimination. However, the fact that the relative configuration at C3 cannot be followed during the reaction prevents any assignement of a preferred reaction course in DMSO.

Comparison of the results described in the present paper with the high yield of RB-product **3a** and **5** on treatment of the nonhalogenated *cis* fused sulfones corresponding to **1** and **2** with KOH/CCl_4, described in an earlier communication,[8] indicate that in the latter medium no inversion at the electrofugal centre takes place and that *cis* ring fusion constitutes optimal geometry for RB-reaction.

In all cases the episulfones lose SO_2 to form the olefinic products, with the possible exception of the episulfone formed from **2a**, which might undergo an allylic rearrangement prior to loss of SO_2, although prototropic interconversion to **5** to **6** cannot be excluded.

In a forthcoming paper we will describe the application of RB-reactions on the preparation of estrone derivatives, starting from tetracyclic α-halosulfones.

EXPERIMENTAL

KOtBu (K&K, Plainview, NY) was resublimed prior to use. DMSO and DME were freshly distilled from CaH_2. M.ps were determined on a Leitz apparatus and are uncorrected. Satisfactory elemental analyses, performed by Mr. H. Pieters from the Microanalytical Department of this laboratory, were obtained for all new compounds. IR and NMR (TMS, $\delta = 0$) were recorded on a Unicam SP 200 spectrometer and a Varian Associates Model HA-100 instrument, respectively.

RB-rearrangement (*general procedure in DME*). Reactions 1, 2, 4, 5, and 8 were performed by dropwise addition of a soln of KOtBu (1·22 mmol) in DME (10 ml) to a well-stirred soln of **1a**, **2a**, **2b** or **1c** (1 mmol), respectively, in DME (20 ml), followed by stirring at r.t. during 15 h. The precipitated KCl was filtered off and the solvent evaporated *in vacuo*. Addition of ether (30 ml) resulted in complete precipitation of unconverted α-halosulfone in a pure state. The residue remaining after evaporation of the mother liquor was worked up as described below for the individual runs. *Run* 1 *and* 2. Vinyl sulfone **4a**[9] (m.p. 158–160°) was obtained by fractional crystallization of the residue in ether/hexane. Evaporation of the mother liquor and GLC (Carbowax 5%, 2M, 150°) furnished the pure olefin **3a**[8] as a colourless oil. *Run* 4. GLC separation of the residue (Carbowax 5%, 2M, 145°) gave pure **5**[8] and **6**. **6**, IR ($CHCl_3$): 1640, 1610 (C=C), 1140 and 1040 cm^{-1} (acetal), NMR ($CDCl_3$): 6·20 (C5-H, d, J 10 Hz); 5·78 (C4-H, m); 5·42 (C3-H, narrow m); 3·98 (acetal, s); 2·9 – 2·5 (C2 and C8-H, m); 2·20 (C6-H, m); 1·7 (C7-H, m). Irradiation of the signal at 2·2 in multiple resonance leads to an AB-pattern (J_{AB} 10 Hz) at 6·2 and 5·7 for C4 and C5-H, respectively, excluding a homoannular isomer. *Run* 5. Vinyl sulfone **7** (m.p. 135–137°) was obtained by partial crystallization of the residue in $CHCl_3$/ether. **7**, IR(KBr): 1620 (C=C), 1300, 1280 and 1120 cm^{-1} (SO_2), NMR ($CDCl_3$): 6·40 (C3-H, AB-pattern, J_{AB} 11 Hz); 6·15 (C2-H, d); 5·73 (C6 and C7-H, narrow m); 4·2–3·9 (acetal, m); 3·75–3·45 (C10-H, m); 2·9–2·2 (remaining H). *Run* 8. Extraction of the partially crystalline residue with hexane and GLC separation (Apiezon M 25%, 0·5M, 190°) gave the olefin **3b** as a slightly yellow oil. IR ($CHCl_3$): 1660, 1100, 1070 and 1030 cm^{-1}

(acetal), NMR ($CDCl_3$): 5·32 (C3-H, m, $W_{\frac{1}{2}}$ 6 Hz); 3·95 (acetal, narrow m); 2·55 (C4-H, s, $W_{\frac{1}{2}}$ 8 Hz); 2·45–2·2 (C2-H, s and C8-H, m); 1·9–1·6 (C6 and C7-H, m). Irradiation at C4-H in multiple resonance produces a singlet ($W_{\frac{1}{2}}$ 3 Hz), irradiation at C2-H a singlet ($W_{\frac{1}{2}}$ 4·5 Hz) for C3-H. The fraction insoluble in hexane was recrystallized from EtOH to give a mixture of **4b** and its corresponding Michael adduct of tBuOH at the vinyl sulfone moiety in a ratio of 2 : 1 (m.p. 145–185°). No further separation was attempted. The vinylic-H appear as an AB-pattern at 6·35 and 6·10 (J_{AB} 11 Hz) in the NMR spectrum of the mixture; 1·45 (OtBu, s).

RB-rearrangement (*general procedure in DMSO*). Reactions 3, 9 and 10 were performed by stirring the corresponding α-halosulfone (1 mmol) with KOtBu (1·2 mmole) in 30 ml DMSO at r.t. during 15, 24 and 5 h, respectively. The DMSO of runs 9 and 10 was evaported (40°, 0·01 mm). The unconverted halosulfones and olefin were isolated and purified following the same procedure as described under DME. In run 3 the olefin was extracted with hexane prior to evaporation of the solvent, on account of its expected volatility.

NaOAc-*induced isomerization* (*run* 7). Sulfone **2b**[9] (0·5 mmol, m.p. 162–166°) and NaOAc (5 mmol) was dissolved in DMSO (10 ml) and heated overnight at 100°. The solvent was removed *in vacuo* and 20 ml water was added. $CHCl_3$ extraction gave a mixture of sulfones which was separated on a Silica column (CH_2Cl_2/EtOAc) into a fraction consisting of **2a**[9] and **2b** (m.p. 155–168°) in a ratio 5 : 2 and a fraction of **7**. Run 6 was performed in an identical manner.

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