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The suitability of anion-accelerated oxy-Cope rearrangement as a probe to study π-facial selectivity. An experimental study with (6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-en-7-yl)(allyl)methanols †

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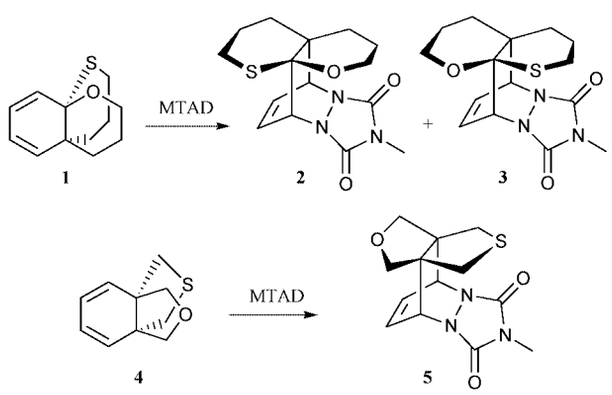
[(6-Methyl-1-oxa-4-thiaspiro[4.5]dec-6-en-7-yl)(allyl)methanols were subjected to anion-accelerated oxy-Cope rearrangement in solvents such as THF, benzene and DME to assess the π-facial selectivity caused by the acetal function. The diastereomeric pairs **17a** and **17b** (R = Ph) furnished the same two diastereomeric products **18a** and **18b**, differing only in the relative preponderance. The reaction of **17a** turned from mostly *syn* to oxygen (**18a** : **18b** = 1 : 4) in THF to moderately *syn* to sulfur (**18a** : **18b** = 2.2 : 1) in DME. The reaction was completely nonselective in benzene. The effect of solvent on the reaction of **17b** was even more interesting. The reaction turned from completely nonselective (**18a** : **18b** = 1 : 1) in THF to highly *syn* to sulfur (**18a** : **18b** = 5.4 : 1) in DME. The selectivity in benzene was somewhere in between (**18a** : **18b** = 2.7 : 1). Likewise, the reaction of **17b** (R = H) turned from moderately *syn* to oxygen in THF (**18a** : **18b** = 1 : 2) to nearly nonselective in DME (**18a** : **18b** = 1 : 1.1). The rotation around the bond between the methanol carbon and the adjacent ring-carbon is restricted to allow rearrangement only *syn* to sulfur in **17a** and *syn* to oxygen in **17b**. The considerable erosion in the observed diastereoselectivity is due to a radical and/or ionic retroaldol–recombination process. The radical pathway, however, is more prevalent than the ionic alternative. The recombination favors somewhat the addition of the allyl radical to the cogenerated 7-benzoyl-6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-ene on the face *syn* to the sulfur. As a result of such dissociation and recombination, the oxy-Cope rearrangement does not appear suitable as a probe for the study of diastereofacial selectivity.

Introduction

The study of diastereofacial selectivity due to a strategically located heteroatom is of much current interest.[1,2] The selection caused by both the oxygen and sulfur on the same carbon has received relatively less attention compared to the single heteroatom examples.[3] Moreover, the bulk of the available reports have focussed primarily on intermolecular Diels–Alder additions wherein the electrostatic effects[4] may be considered to interfere significantly with the through-bond effects of the heteroatom(s). Paquette *et al.*[5] have studied the intermolecular Diels–Alder reaction of a cyclohexadiene containing an allylic hemithioacetal, **1** with reactive dienophiles such as *N*-methyltriazoline-2,5-dione (MTAD) and *N*-phenyltriazoline-2,5-dione (PTAD) and they observed a 20 : 1 preponderance for addition *syn* to the oxygen (**2** : **3** = 20 : 1). Gleiter and Ginsburg[6] have reported the formation of only **5** from the cycloaddition of MTAD to the oxygen- and sulfur-bridged [4.3.3]propellane **4**. The reaction had proceeded exclusively *syn* to the sulfur. However, the homoallylic location of both the heteroatoms in **4** should be noted. Furthermore, both MTAD and PTAD are highly reactive dienophiles that are likely to exhibit selectivities opposite to those observed with the less reactive dienophiles.[7] The reactions of **1** and **4** are collected in Scheme 1.

In examples of 1,2-diastereoselection in 1,4-additions, Sonoda *et al.*[8] have observed addition of Grignard reagents to **6** predominantly *anti* to sulfur in the presence of $CuBr{\cdot}SMe_2$. As high a selectivity as **7** : **8** = 96 : 4 was noted for the addition of PhMgBr. Frye and Eliel[9] have noted addition exclusively *anti* to sulfur that led to the transformation of **9** into **10**. Isobe *et al.*[10] have discovered that the acetal **11** undergoes a 1,4-addition of nucleophiles predominantly *anti* to sulfur to furnish **12**. The reactions of **6**, **9** and **11** are collected in Scheme 2. In reactions involving nucleophiles, cation-chelation effects[11] are likely to influence the net diastereoselectivity and, thus, the true through-bond and through-space electronic effects of the heteroatoms may be undermined.

In view of the intermolecular electrostatic interactions, the difficulty arising from the differential selectivities from highly reactive and less highly reactive dienophiles, and the very limited number of results available, we investigated selected 3,3-sigmatropic processes that avoid some or all of the above



Scheme 1 Literature examples of the study of diastereofacial selection through Diels–Alder cycloadditions.

† ^{1}H and ^{13}C NMR spectra of **17a**,**b**, ^{1}H spectra of **18**,**b** and related compounds, ROESY spectra of **18a**,**b** and COSY spectra of **18a** are available as supplementary data from BLDSC (SUPPL. NO. 57697, 46 pp.) or the RSC Library. See Instructions for Authors available *via* the RSC web page (http://www.rsc.org/authors).
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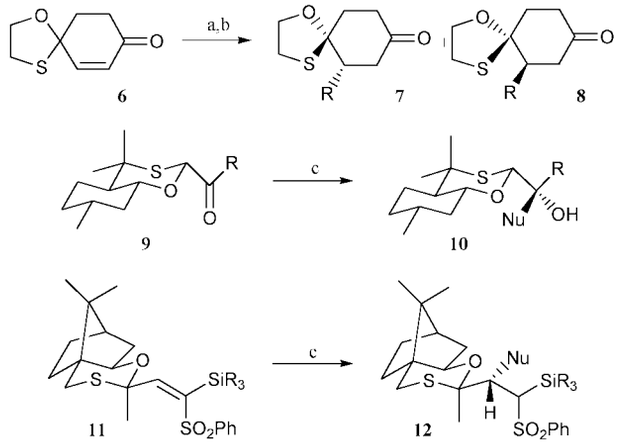
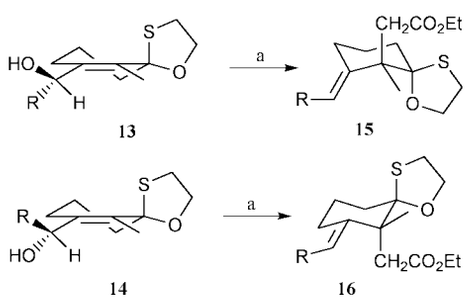


Scheme 2 Literature examples of the study of diastereofacial selection through 1,2- and 1,4-nucleophilic additions. *Reagents*: a, RMgX, $CuBr{\cdot}SMe_2$, TMSCl, HMPA; b, KF; c, Nu^-.

anomalies. We have already reported the Johnson orthoester Claisen rearrangement of **13** (R = H) and its derivatives **13** and **14** (R = Me, Ph), and observed exclusive diastereoselection (Scheme 3).[12] The rearrangement proceeded only *syn* to sulfur

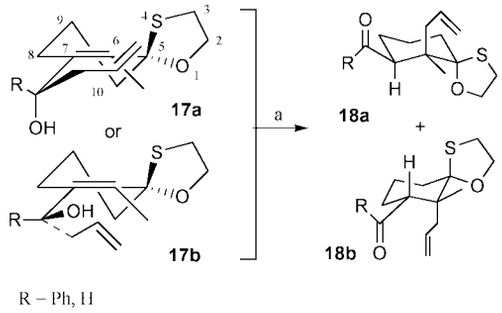


R = H, Ph, Me

Scheme 3 Literature examples of the study of diastereofacial selection through Johnson orthoester Claisen rearrangement. *Reagents and conditions*: a, $MeC(OEt)_3$, toluene, reflux.

or oxygen depending upon whether the methanol function was disposed, respectively, *syn* to sulfur or oxygen across the cyclohexene mean plane. The species **13** (R = Me, Ph) rearranged *syn* to sulfur to give **15**, and **14** (R = Me, Ph) rearranged *syn* to oxygen to give **16**. These results were interpreted as a consequence of (a) restricted rotation around the bond between C7 and the methanol carbon in **13** and **14** (R = Me, Ph), (b) an energetically allowed ring flip from one half chair to the other half chair, and (c) stereoelectronically preferred axial carbon–carbon bond formation on a pre-existing cyclohexene ring. The rearrangement of **13** (R = H) (exclusively *syn* to oxygen) into **16** (R = H) was considered a consequence of the facial effect of the acetal function. Note that **13** (R = H) can undergo both the above rotation and the ring flip under the rearrangement conditions. It can, therefore, rearrange both *syn* to the sulfur and syn to the oxygen.

In this manuscript, we report our results on the anion-accelerated oxy-Cope rearrangement of (6-methyl-1-oxa-4-thia-spiro[4.5]dec-6-en-7-yl)(allyl)methanols, **17**, and demonstrate that a significant portion, if not all, of the process takes place through a radical and/or ionic (preferably radical) retroaldol–recombination pathway (Scheme 4). We show further that the reaction solvent has profound effects on the overall result, so much so that the sense of facial selectivity is even reversed. Due caution, therefore, must be exercised in the application of this rearrangement to the study of facial selectivity. Very recently, le Noble and co-workers[13] have used this rearrangement to assess facial selection in substituted 2-adamantanones, and



R = Ph, H

Scheme 4 Substrates **17** (R = Ph, H) and their rearrangement products. *Reagents and conditions*: a, KH, 18-crown-6, solvent, reflux (30 min).

Paquette[14] and Lee[15] and their co-workers have used it to study oxy-anion effects.

The choice of the substrates **17** was based largely on the fact that the bond formation between the termini of the hexa-1,5-diene unit takes place in the immediate vicinity of the acetal function to allow for maximum possible facial control from the latter. Furthermore, other than acting as a marker in the facial determination of the rearrangement products, the *Me* substituent restricts the rotation around the carbon–carbon bond between the methanol carbon and the adjacent six-ring position. If the rearrangement were truly 3,3-sigmatropic, this rotational constraint would lead the substrate to rearrange exclusively *syn* to either sulfur or oxygen, depending upon whether the disposition of the allyl function across the cyclohexene mean plane was, respectively, *syn* to the sulfur or oxygen.

It is conceivable that such a rotation in **17** (R = H) will be much less restricted due to the very small size of the hydrogen atom in comparison to the size of the Ph group in **17** (R = Ph). This allows both the rotamers to rearrange individually in strict 3,3-sigmatropic fashion to generate a mixture of both the possible products. Such a prospect is, however, somewhat diminished when one considers the preferred conformation of allylic alcohols. The C–O bond is parallel to the π orbitals of the carbon–carbon double bond due to stereoelectronic effects.[16] Any departure from such a geometrical setup through rotation amounts to acting against stereoelectronic effects and, thus, to an energetically demanding maneuver.

The syntheses of **17** (R = H, Ph) are described elsewhere.[17] It is worth noting that the substrates in the present series that had the OH oriented *syn* to the acetal oxygen were more polar to silica gel than those that possessed the OH groups *anti* to the acetal oxygen. We have previously observed such behavior as well.[18]

Results and discussion

The alcohols **17a** and **17b** (R = Ph) were treated with KH and 18-crown-6 in three different solvents at 0 °C to room temperature followed by reflux for 30 min. A mixture of the same two products **18a** and **18b** (R = Ph) was obtained from each. Although there were two distinct *Me* signals at δ 1.43 and 0.94 to allow the diastereoselectivity to be determined (as expected from above), the calculation of the ratio from their integrals was somewhat difficult due to the appearance of other signals in the close vicinity. Fortunately, the ratios were determined rather more accurately from the integrals of the internal vinylic hydrogens that appeared as multiplets at δ 5.85–5.71 and 6.00–5.87, respectively, for **18a** and **18b**.[19] The products were separated by radial chromatography for individual characterization.

2D ^{1}H NMR helped to secure various characteristic hydrogen assignments and ROESY established the relationships of the stereogenic centers in the products. Accordingly, we

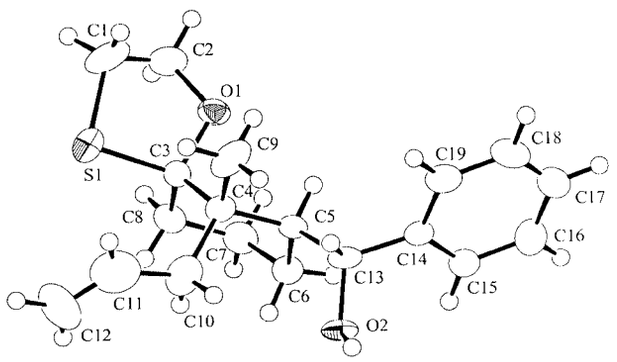


Fig. 1 ORTEP plot of the product of LAH reduction of **18a** (R = Ph). Selected bond lengths (Å), bond angles (°), and torsion angles (°): S1–C1 1.804(5), S1–C3 1.870(4), O1–C2 1.421(5), O1–C3 1.433(4), O2–C13 1.442(4), C10–C11 1.433(7), C11–C12 1.313(8), C1–S1–C3 92.2(2), C2–O1–C3 111.5(3), S1–C3–O1 105.0(2), C4–C10–C11 119.2(4), C10–C11–C12 126.1(6), S1–C3–C4–C5 178.1(2), O1–C3–C4–C10 178.1(3), O2–C13–C5–C4 92.5(4), O2–C13–C14–C15 40.5(5).

have assigned structures **18a** and **18b** (R = Ph), respectively, to the products emanating from reactions *syn* to the sulfur and the oxygen. The signal due to C7-*H* appeared as a dd in **18a** (δ 3.93–3.89, J = 10 and 3 Hz) and **18b** (δ 3.70–3.65, J = 12.6 and 3.3 Hz), the larger J value clearly indicating this hydrogen to be axial in both isomers. In experiments in which the lithium enolates of **18a** and **18b** were separately quenched with MeOH at −80 °C, only the starting materials were isolated. This result is remarkable as it indicates the very high stereospecificity with which the enolates formed from rearrangement were quenched by H^+ from the axial direction during work up. The ROESY of both **18a** and **18b** showed interaction between C7-*H* and a hydrogen that is *ortho* on the phenyl ring. This interaction translates into an arrangement in which the $\sigma_{C=O}$ bond is both antiplanar to C7-*H* and in plane with the phenyl ring. The unusual downfield appearance of C7-*H* (δ 3.93–3.89) must, therefore, be due to the anisotropic effects of both the phenyl ring and the carbonyl group in this specific geometrical setup.

The other characteristic NOEs observed for **18b** (R = Ph) were between (a) the C7-*H* and the *Me*, which showed the latter to be equatorial, and (b) the C*H*$_2$S and the *Me*, which placed the sulfur axial. Compound **18a** (R = Ph) showed no direct NOE for any of the two acetal CH$_2$'s with either of the substituents on C6. The relative stereochemistry was discerned from the single crystal X-ray structure[20] of the predominant product from LAH reduction (Fig. 1). The crucial carbon–carbon bond was formed axial after the ring flip in **17a**. The change in the axial and equatorial orientations of the acetal sulfur and oxygen in **17a** to, respectively, equatorial and axial in **18a** must be noted.

The rearrangement of **17b** (R = H) also furnished a mixture of two diasteroisomers that were inseparable by routine chromatographic techniques. Calculation of the ratio from the ^{1}H integrals of the internal vinylic hydrogens was difficult because their absorptions at 300 MHz overlapped. The ratios, however, were conveniently calculated from the relative ^{1}H integrals of the C*H*O absorptions that appeared at δ 9.98 (s) and 9.84 (s). The stereochemical characterization as a mixture of **18a** and **18b** (R = H) was made possible by its conversion into a mixture of **18a** and **18b** (R = Ph).

The reaction of the mixture of **18a** and **18b** (R = H) above with PhMgBr furnished a mixture of only two alcohols. This shows that the conformation around the carbonyl carbon and the adjacent ring-carbon is fixed, and that the nucleophilic attack of PhMgBr proceeded with very high selectivity. The two alcohols, therefore, must differ from each other only in the relative stereochemistries at C5 and C6 of the spiro system. The ratio of these alcohols (calculated from the ^{1}H integrals of the internal vinylic hydrogens that appeared at δ 6.40–6.20 (m) and 6.13–6.00 (m)) was approximately the same as that of **18a** to **18b** (R = H). Separation of these alcohols was not attempted. Oxidation with pyridinium dichromate furnished a mixture of **18a** and **18b** (R = Ph) and the ratio was determined, as before, from the ^{1}H integrals of the internal vinylic hydrogens. Once again, this ratio was approximately the same as the ratio for the above two alcohols. The species **17a** (R = H) was not studied. The **18a** : **18b** ratios from the reactions of **17** in different solvents and their combined yields are collected in Table 1.

Table 1 Diastereomeric ratios **18a** : **18b** and yields in different solvents[a]

Substrate	Solvent	**18a** : **18b**	Yield (%)
17a, R = Ph	THF	1 : 4	68
17b, R = Ph	THF	1 : 1	67
17a, R = Ph	C_6H_6	1 : 1	65
17b, R = Ph	C_6H_6	2.7 : 1	65
17a, R = Ph	DME	2.2 : 1	70
17b, R = Ph	DME	5.4 : 1	70
17b, R = H	THF	1 : 2	65
17b, R = H	DME	1 : 1.1	70

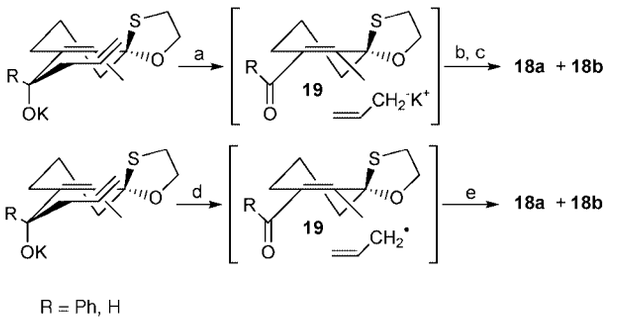
[a] Reaction conditions: reflux for 30 min.

The change in facial selectivity with the change in solvent is remarkable. The reaction of **17a** (R = Ph) turned from predominantly *syn* to oxygen (**18a** : **18b** = 1 : 4) in THF to moderately *syn* to sulfur in DME (**18a** : **18b** = 2.2 : 1). This rearrangement was nonselective (**18a** : **18b** = 1 : 1) in benzene. Interestingly, while the reaction of **17b** (R = Ph) was non-selective in THF (**18a** : **18b** = 1 : 1), it turned highly *syn* to sulfur (**18a** : **18b** = 5.4 : 1) in DME. In benzene, the selectivity was in between (**18a** : **18b** = 2.7 : 1). Likewise, **17b** (R = H) turned from moderately *syn* to oxygen (**18a** : **18b** = 1 : 2) in THF to almost nonselective in DME (**18a** : **18b** = 1 : 1.1). However, a clear trend emerged that shows increasingly favored rearrangement *syn* to sulfur for both **17a** and **17b** as the solvent was changed from THF to benzene to DME.

Rotation around the bond between the methanol carbon and the adjacent ring carbon in **17a** and **17b** (R = Ph) is restricted because of significant steric interactions between the C6-*Me* and the substituents on the methanol carbon. This, in turn, must restrict these species to rearrange only *syn* to sulfur and oxygen, respectively, in accord with our recent findings from the Johnson orthoester Claisen rearrangement.[12] Likewise, **17b** (R = H) must also rearrange predominantly *syn* to oxygen to give **18b**. However, each substrate furnished two products, **18a** and **18b**.

The formation of two products from each methanol may be considered *a priori* possible if a significant portion of the alkoxide, formed on reaction of **17a** or **17b** with KH, dissociated into 7-benzoyl-6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-ene, **19**, and an allyl anion (Scheme 5, top). Other combinations such as allyl phenyl ketone and cyclohexenyl anion or allyl cyclohexenyl ketone and phenyl anion are also possible. Both these processes would, however, be expected to be energetically more demanding than the process leading to the formation of a cyclohexenyl phenyl ketone and an allyl anion, because both the species formed from the alternative pathways are less stable than the species formed by the cleavage of the allyl C–C bond.

The allyl anion will recombine with the ketone in a 1,2-manner to generate a 1 : 1 mixture[17] of the two isomeric alkoxides that may then rearrange in a true 3,3-sigmatropic fashion to yield a 1 : 1 mixture of the products. The product distribution, however, is far from 1 : 1. If the anionic cleavage were the only pathway other than the direct 3,3-sigmatropic rearrangement of the starting alcohol isomer, **17a** and **17b** would always have led to **18a** and **18b**, respectively, as the major products. This, however, contrasts our findings: the species **17a** and **17b** rearranged into **18b** and **18a**, respectively, as the

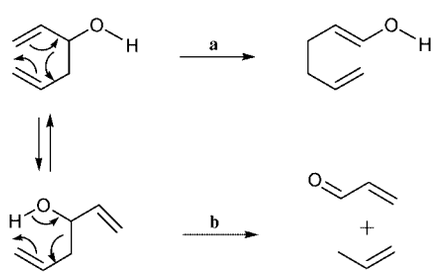


Scheme 5 Anionic and radical cleavage of **17a**. a, Anionic cleavage; b, 1,2-addition; c, oxy-Cope rearrangement; d, radical cleavage; e, conjugate addition.

major products. A pathway other than anionic cleavage must, therefore, be considered.

We considered a radical cleavage of the alkoxide and, hence, the formation of 7-benzoyl-6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-ene, **19**, and an allyl radical (Scheme 5, bottom). The participation of a radical route was confirmed by the detection of a radical ($g = 2.0076$) in the mixture of **17a**, KH and 18-crown-6 in THF. The allyl radical reacts with **19** in a manner that appears to be an overall oxy-Cope rearrangement through conjugate addition to furnish the observed products. This is in keeping with the known reluctance of simple alkyl radicals to react with ketones in a 1,2-manner.[21] The allyl radicals are even less reactive due to resonance stabilization. The 1,4-addition, *syn* to sulfur, of the allyl radical to **19** appears to be favored over the addition *syn* to oxygen.

Viola *et al.*[22] have studied the high temperature (340–390 °C) vapor phase thermolysis of a series of methyl substituted 3-hydroxyhexa-1,5-dienes and noted the formation of some cleavage products along with the products from a normal Cope rearrangement. This was interpreted on the basis of two competing concerted bond reorganizations, both of which proceeded through cyclic six-membered ring transition states as shown in Scheme 6. Path **b** that involves cleavage of



Scheme 6 Mechanistic rationale for the formation of cleavage products according to Viola *et al.*

β-hydroxyolefins[23] was suggested as the sole alternative to account for the cleavage. The radical cleavage of the 3,3-bond was not favored because of the lack of products formed from (a) radical coupling of like fragments and (b) radical inversion. Clearly, we disagree with these observations because our results are best explained by a radical cleavage. In support of this, we have never isolated 7-benzoyl- and 7-formyl-6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-enes from the reactions of **17**. These products would be expected to form if the above concerted cleavage of β-hydroxyolefins were involved. Furthermore, we have also detected radical(s).

Gajewski and Gee[24] have studied the anion-accelerated oxy-Cope rearrangement of 3-methylhexa-1,5-dien-3-ol in THF, in THF in the presence of 18-crown-6, and in DMSO. These authors have indicated a highly dissociative transition state with substantial bond breaking between C3 and C4 and little bond formation between the termini C1 and C6, determined from the secondary deuterium kinetic isotope effects at the bond breaking and bond forming sites in the rearrangement of the potassium alkoxide.

Even with the use of potassium and sodium salts of alkoxides in appropriate solvents Evans *et al.*[25] observed little dissociation–recombination of the type that Viola *et al.*[22] have reported, despite the fact that metal alkoxides of homoallylic alcohols have been documented to undergo cleavage to ketones and allylic organometallics.[26] Exceptions to this were, however, found in those cases where a quaternary center was generated as a consequence of the Cope process and enones were isolated as the predominant products. We generated quaternary centers in the products from **17a**,**b**. In line with the observations of Evans *et al.*, we witnessed extensive dissociation but we did not isolate 7-benzoyl- and 7-formyl-6-methyl-1-oxa-4-thiaspiro-[4.5]dec-6-enes; the enone equivalents. In studies of facial selectivity of 5-substituted 2-adamantanones through the application of anion-accelerated oxy-Cope rearrangement, le Noble and co-workers[13] have generated quaternary centers. Lee *et al.*[15] have also produced quaternary centers in their studies on the oxy-anion effects on the course of this rearrangement.

Conclusions

Evidence exists to show that the anion-accelerated oxy-Cope rearrangement of (6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-en-7-yl)(allyl)methanols takes a predominantly non-concerted route *via* radical cleavage. The allyl radical adds to 7-benzoyl- and 7-formyl-6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-enes, **19**, in a 1,4-fashion and preferably *syn* to the sulfur to generate what eventually appear to be the products of 3,3-sigmatropic shift. Caution must therefore be exercised in the use of anion-accelerated oxy-Cope rearrangement for the study of facial selectivity. The favored 1,4-addition of the allyl radical *syn* to sulfur to give **19**, the *in situ* generated enone, is of significance and requires further attention. The different counterion complexation, alkoxide aggregation and cleavage rates in various solvents may be responsible for the observed changes in selectivity in different solvents.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker DRX-300 and Bruker DPX-200 instruments in $CDCl_3$. Signal positions are reported in ppm relative to TMS for ^1H and $CDCl_3$ for ^{13}C (δ scale). The elemental analyses were performed using a Perkin-Elmer 240C instrument. The separations of both the starting methanols and their oxy-Cope products were performed on a Chromatotron using plates coated with silica gel 60 PF_{254} (E. Merck). The components were eluted using mixtures of petroleum ether (bp 60–80 °C) and EtOAc. All reactions were carried out in an atmosphere of dry argon. KH was obtained from Aldrich Chemical Company and used after it had been washed with the solvent of the reaction. Other experimental details have been reported elsewhere.[27]

Oxy-Cope precursors 17a and 17b

A solution of 7-bromo-6-methyl-1-oxa-4-thiaspiro[4.5]dec-6-ene[17] (0.498 g, 2.0 mmol) in dry THF (10 mL) was cooled to −80 °C and mixed with *n*-BuLi (1.38 mL of a 1.6 M solution in hexane, 2.2 mmol) following a literature protocol.[28] After stirring for 10 min, a solution of allyl phenyl ketone[29] (0.292 g, 2.0 mmol) for the preparation of **17** (R = Ph) or but-3-enal (0.140 g, 2.0 mmol) for the preparation of **17** (R = H) in THF (2 mL) was added. The reaction mixture was stirred for a further 30 min at −80 °C, quenched with MeOH (164 μL, 4.0 mmol), and allowed to warm up to 20 °C. The reaction mixture was diluted with Et_2O (20 mL), mixed with saturated aqueous NH_4Cl (10 mL), and stirred for 10 min. The layers

were separated and the aqueous layer extracted with Et_2O (2 × 10 mL). The combined extracts were washed with water (1 × 10 mL) and brine (1 × 10 mL), dried, and concentrated. The residue obtained on solvent removal was separated into the component alcohols, **17a** and **17b** (combined yield 80–85%) that were formed in almost equal amounts, by radial chromatography.

17a (R = Ph, liquid). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.23 (5H, m), 5.87–5.73 (1H, m), 5.22–5.17 (2H, m), 4.40–4.33 (1H, m), 4.10–4.02 (1H, m), 3.08–3.03 (2H, m), 2.96–2.89 (1H, dd, J = 13.8, 7.2 Hz), 2.79–2.72 (1H, dd, J = 13.8, 7.5 Hz), 2.40–1.57 (7H, m), 1.56 (3H, s). ^{13}C NMR (50 MHz, $CDCl_3$) δ 147.15, 140.78, 134.18, 133.48, 128.63, 127.35, 126.14, 119.86, 98.08, 78.59, 71.50, 45.35, 38.76, 35.18, 29.11, 21.12, 15.37. IR ($CHCl_3$) ν 3440, 1650, 1210 cm^{-1}. Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.12; H, 7.65. Found C, 71.94; H, 7.78%.

17b (R = Ph, liquid). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.23 (5H, m), 5.85–5.74 (1H, m), 5.23–5.17 (2H, m), 4.40–4.34 (1H, m), 4.10–4.00 (1H, m), 3.08–3.04 (2H, m), 2.99–2.89 (1H, m), 2.83–2.72 (1H, m), 2.50–1.55 (7H, m), 1.53 (3H, s). ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.50, 141.62, 134.29, 133.65, 128.61, 127.38, 126.29, 119.86, 97.81, 78.55, 71.37, 45.59, 38.81, 35.29, 29.20, 21.22, 15.55. IR ($CHCl_3$) ν 3450, 1650, 1215 cm^{-1}. Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.12; H, 7.65. Found C, 71.90; H, 7.76%.

17a (R = H, liquid). ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.90–5.70 (1H, m), 5.18–5.09 (2H, m), 4.65–4.58 (1H, m), 4.42–4.35 (1H, m), 4.12–4.04 (1H, m), 3.14–3.05 (2H, m), 1.75 (3H, t, J = 1.8 Hz), 2.40–1.58 (9H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 134.6, 130.3, 117.7, 96.3, 71.0, 70.3, 39.4, 38.8, 34.8, 23.1, 20.5, 12.4. IR (film) ν 3400, 1630, 1430, 1165, 905, 750 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_2S$: C, 64.97; H, 8.39. Found C, 64.82; H, 8.45%.

17b (R = H, liquid). ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.88–5.67 (1H, m), 5.18–5.08 (2H, m), 4.64–4.57 (1H, m), 4.44–4.35 (1H, m), 4.13–4.01 (1H, m), 3.16–3.02 (2H, m), 2.40–1.60 (10H, m), 1.76 (3H, t, J = 2.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 134.7, 130.6, 117.7, 96.6, 71.0, 70.1, 39.4, 38.8, 34.8, 22.8, 20.5, 12.5. Anal. Calcd for $C_{13}H_{20}O_2S$: C, 64.97; H, 8.39. Found C, 64.86; H, 8.50%.

Formation of 18a and 18b (oxy-Cope rearrangement)

A solution of the alcohol **17** (R = Ph, H) (0.3 mmol) in the appropriate solvent (2 mL) was added slowly to a suspension of KH (0.6 mmol) in the same solvent (2 mL) at 0 °C. This was mixed with a solution (1 mL) of 18-crown-6 (0.3 mmol) in the same solvent and the resultant reaction mixture was allowed to warm up to room temperature. The contents were heated to reflux for 30 min when TLC indicated complete disappearance of the reactant alcohol. The contents were cooled to room temperature, the reaction quenched with MeOH (2 equiv.) and stirred with saturated aqueous NH_4Cl for 5 min. The products were extracted into Et_2O (3 × 6 mL) and the combined extracts washed with brine, dried, and filtered. The evaporation of the solvents furnished the crude material which was separated into **18a** and **18b** (R = Ph, H); combined yield 65–70%. The remainder of the material was polymer.

18a (R = Ph, liquid). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94–7.91 (2H, d, J = 7.2 Hz), 7.55–7.50 (1H, t, J = 7.2 Hz), 7.45–7.40 (2H, t, J = 7.2 Hz), 5.85–5.71 (1H, m), 4.62–4.57 (2H, m), 4.46–4.42 (1H, br t, J = 6.9 Hz), 4.04–3.96 (1H, dt, J = 9.6, 5.1 Hz), 3.93–3.89 (1H, br d, J = 9.9 Hz), 3.00–2.95 (1H, m), 2.93–2.84 (1H, dt, J = 9.9, 6.0 Hz), 2.48–2.45 (2H, d, J = 7.5 Hz), 2.10–2.08 (2H, br d, J = 5.4 Hz), 1.80–1.60 (4H, m), 1.43 (3H, s). Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.12; H, 7.65. Found C, 71.96; H, 7.80%.

18b (R = Ph, liquid). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00–7.97 (2H, m), 7.56–7.53 (1H, m), 7.49–7.44 (2H, m), 6.00–5.87 (1H, m), 4.96–4.85 (2H, m), 4.45–4.40 (1H, m), 4.04–3.96 (1H, m), 3.70–3.65 (1H, dd, J = 12.6, 3.3 Hz), 2.94–2.85 (2H, m), 2.70–2.62 (2H, m), 2.21–2.17 (1H, m), 2.15–1.90 (3H, m), 1.84–1.40 (2H, m), 0.94 (3H, s). Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.12; H, 7.65. Found C, 71.90; H, 7.72%.

LAH reduction of 18a (R = Ph)

A solution of **18a**, R = Ph, (0.016 g, 0.05 mmol) in Et_2O (1 mL) was added by a syringe to a stirred ice-cooled suspension of LAH (5 mg) in Et_2O (2 mL). The resultant solution was stirred for 30 min when the reaction was quenched by the addition of saturated aqueous NH_4Cl (0.5 mL) under vigorous stirring. The Et_2O layer was decanted from the semisolid mass. The semisolid material in the reaction vessel was stirred with Et_2O (2 × 2 mL) and the ether solution decanted. The solvent was removed from the combined Et_2O solution and the residue purified by chromatography over silica gel to give the single predominant product. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.39–7.16 (5H, m), 6.41–6.20 (1H, m), 5.32 (1H, br s), 5.21–5.05 (2H, m), 4.40–4.32 (1H, m), 3.98–3.84 (1H, m), 2.97–2.89 (3H, m), 2.60–2.48 (1H, dd, J = 15.6, 8.5), 2.18–2.12 (1H, br d, J = 10.6), 2.02–1.94 (2H, m), 1.75–1.2 (4H, m), 1.32 (3H, s). Calcd mass for $C_{19}H_{26}O_2S$ = 318.1652, observed mass = 318.1640.

Stereochemical characterization of 18a and 18b (R = H) obtained from 17b (R = H)

A solution of PhMgBr (1.0 mmol) was prepared in Et_2O (3 mL) and cooled by an ice-water bath. This was mixed with a solution of **18a** and **18b** (R = H) (0.120 g, 0.5 mmol) in Et_2O (2 mL). The reaction mixture was stirred for 30 min and then quenched by adding saturated aqueous NH_4Cl (5 mL). The contents were diluted with more ether (5 mL) and the layers separated. The aqueous layer was extracted with Et_2O (2 × 5 mL). The combined extracts were dried and concentrated to furnish a residue that was filtered through a small silica gel column to isolate a mixture of two alcohols, 0.152 g, 95%.

Chromium trioxide (0.140 g, 1.4 mmol) was added to a solution of dry pyridine (0.23 mL, 2.9 mmol) in CH_2Cl_2 (2.5 mL). After stirring at 20 °C for 15 min, a solution of a mixture of the above alcohols (0.077 g, 0.24 mmol) in CH_2Cl_2 (1 mL) was added in one portion and stirred for a further 10 min. The solution was decanted from the residue and the solvent evaporated to leave a black residue. This was dissolved in Et_2O (10 mL) and filtered through a silica gel column. The column was washed with Et_2O. The solvent was removed to isolate a mixture of the ketones **18a** and **18b**, 0.053 g, 70%. The ^{1}H spectrum of this ketone mixture was identical, but for the relative proportions, with that of the rearranged products obtained directly from **17a** and **17b** (R = Ph).

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