Tetrahedron: *Asymmetry* 20 (2009) 754–757

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Catalytic enantioselective tandem carbonyl ylide formation—intramolecular cycloaddition with unsaturated α-diazo-β,ε-diketo sulfones

David M. Hodgson [a,*], Rebecca Glen [a], Alison J. Redgrave [b]

[a] *Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, UK*
[b] *GlaxoSmithKline Medicines Research Centre, Gunnels Wood Road, Stevenage SG1 2NY, UK*

ARTICLE INFO

Article history:
Received 26 January 2009
Accepted 23 February 2009
Available online 1 April 2009

This paper is dedicated to Professor George Fleet, on the occasion of his 65th birthday

ABSTRACT

The synthesis and 1,3-dipolar cycloaddition reactions of unsaturated α-diazo-β,ε-diketo sulfones **7** using chiral rhodium catalysts (up to 71.5:28.5 er) are described.

1. Introduction

Transition-metal-catalysed tandem carbonyl ylide formation—1,3-dipolar cycloadditions using diazo compounds (e.g., Scheme 1) were originally developed by Ibata and Padwa for the synthesis of oxapolycycles;[1] they are of interest due to the opportunities for rapid generation of molecular complexity in a single operation. Over the last decade, encouraging levels of asymmetric induction have been obtained in such transformations using chiral catalysts with certain classes of achiral diazo substrates and dipolarophiles.[2] As the catalyst-free carbonyl ylide intermediate in these reactions would be achiral, the chiral catalyst is likely associated with the carbonyl ylide (e.g., **2**, Scheme 1) to influence enantiofacial selectivity in the cycloaddition; however, the origins of asymmetric induction remain unclear.[3] So as to assess the scope and determine the factors influencing enantioselectivity in this asymmetric process, part of our research programme in this area involves variation of electronic (and steric) effects within the dipole (e.g., R = ester, aryl).[4]

Herein, we report on the enantioselective tandem carbonyl ylide formation—intramolecular cycloaddition employing sulfonyl functionality as a different type of electron-withdrawing group at the ylidic carbon, specifically using unsaturated α-diazo-β,ε-diketo sulfones **1** (R = sulfonyl group). The sulfonyl functionality was examined partly due to its subsequent potential utility in the cycloadduct,[5] but of principal interest was the effect of its presence on the viability of the cycloaddition and especially on asymmetric induction in the cycloadduct **3**, since in substrate **1** (R = sulfonyl group) there would be two rather different electron-withdrawing groups spanning the diazo functionality, compared with the two similar carbonyl groups present in precursor **1** (R = ester). In contrast to α-diazo-β-keto esters, there are significantly fewer studies concerning the use of α-diazo sulfones in typical (asymmetric) transition-metal-catalysed transformations of diazo compounds [σ-bond (e.g., C–H, O–H) insertion and cyclopropanation][1a,g,6] and only one isolated report of an α-diazo sulfone in (acyclic and non asymmetric) carbonyl ylide formation—cycloaddition.[7]

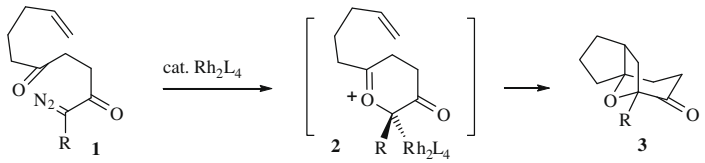
2. Results and discussion

Cycloaddition substrate **7a** was readily accessed (Scheme 2) by α-sulfonyl carbanion acylation[5,8] with known ketal ester **5** (itself prepared in 3 steps via lithiation–alkylation of 2,3-dihydrofuran **4**),[4] followed by diazo transfer using 4-acetamidobenzenesulfonyl azide (ABSA).[9]

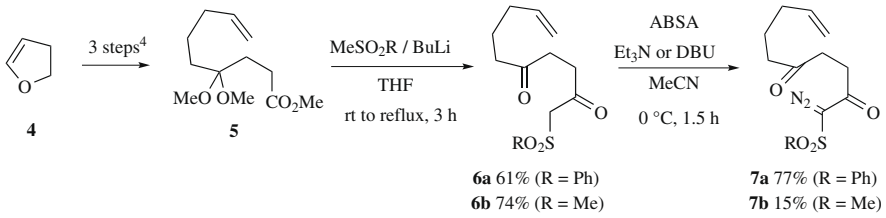
Although hexane is the preferred solvent for the (asymmetric) cycloadditions with α-diazo-β,ε-diketo esters **1** (R = ester),[4] phenyl sulfone substrate **7a** proved insoluble in hexane. However, another hydrocarbon solvent toluene gave improved solubility. Initial studies examining the viability of the cycloaddition process in toluene with achiral rhodium catalysts commenced with $Rh_2(OAc)_4$, which gave cycloadduct **8a** in 12% yield (Scheme 3 and Table 1, entry 1). The more electron-deficient catalyst $Rh_2(tfa)_4$ gave an improved 39% yield (Table 1, entry 2), whereas $Rh_2(cap)_4$ (cap = caprolactamate) failed to decompose phenyl sulfone substrate **7a**, even after 20 h (Table 1, entry 3). $Rh_2(oct)_4$, which is electronically very similar to $Rh_2(OAc)_4$ but with higher solubility in non-polar solvents, gave cycloadduct **8a** in 72% yield (Table 1, entry 4). This last result indicated the viability of tandem carbonyl ylide formation—intramolecular cycloaddition with this class of α-diazo sulfone and set the stage for an examination of chiral rhodium catalysts previously shown to deliver good enantiomeric ratios[10] in carbonyl ylide cycloadditions.

* Corresponding author.
E-mail address: david.hodgson@chem.ox.ac.uk (D.M. Hodgson).

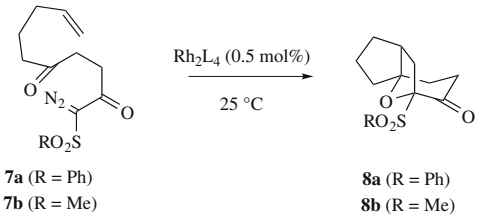
0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.02.031



Scheme 1. Metal-catalysed carbonyl ylide formation—1,3-dipolar cycloaddition using diazocarbonyl compounds.



Scheme 2. Synthesis of cycloaddition substrates **7a**,**b**.



Scheme 3. Cycloaddition of substrates **7a**,**b**.

Table 1

Entry	Catalyst	Solvent	Yield **8a** (%)	er[a]	$[\alpha]_D^{25}$[b]
1	$Rh_2(OAc)_4$	Toluene	12	—	—
2	$Rh_2(tfa)_4$	Toluene	39	—	—
3	$Rh_2(cap)_4$	Toluene	0[c]	—	—
4	$Rh_2(oct)_4$	Toluene	72	—	—
5	$Rh_2[(S)\text{-DOSP}]_4$	Toluene	67	52:48	−0.8
6	$Rh_2[(R)\text{-DDBNP}]_4$	Toluene	67	54.5:45.5	−2.9
7	$Rh_2[(S)\text{-PTPA}]_4$	$PhCF_3$	37	63.5:36.5	+6.4
8	$Rh_2[(S)\text{-PTTL}]_4$	$PhCF_3$	80	67:33	+9.6
9	$Rh_2[(S)\text{-BPTV}]_4$	$PhCF_3$	75	71.5:28.5	+13.6

[a] Determined by chiral HPLC.
[b] All *c* 1, in CH_2Cl_2.
[c] No reaction observed after 20 h at rt.

The asymmetric process was first studied with $Rh_2[(S)\text{-DOSP}]_4$ and $Rh_2[(R)\text{-DDBNP}]_4$ (Fig. 1): two hydrocarbon soluble catalysts (due to the presence of the dodecyl chains) which have previously provided useful levels of asymmetric induction in cycloadditions with α-diazo-β,ε-diketo esters.[4a] Reaction of phenyl sulfone substrate **7a** with proline-derived $Rh_2[(S)\text{-DOSP}]_4$ and binaphthyl-based $Rh_2[(R)\text{-DDBNP}]_4$ was reasonably efficient (67% yield in both cases, Table 1 entries 5 and 6), but only low levels of asymmetric induction were observed.

Recently, Hashimoto et al. reported the efficient asymmetric intermolecular cycloaddition of cyclic carbonyl ylides derived from α-diazo-β,ε-diketo esters, using *N*-phthaloyl-amino acid-based rhodium catalysts in $PhCF_3$.[2c] In the present case with phenyl sulfone substrate **7a**, improved levels of asymmetric induction were observed using such catalysts compared with $Rh_2[(S)\text{-DOSP}]_4$ and $Rh_2[(R)\text{-DDBNP}]_4$. Thus, a gradual rise in er for cycloadduct **8a** was found on moving from phenyl alanine-derived catalyst $Rh_2[(S)\text{-PTPA}]_4$ (63.5:36.5, Table 1, entry 7) to the slightly more hindered *tert*-leucine-based $Rh_2[(S)\text{-PTTL}]_4$ (67:33), to the benzene-fused phthaloyl valine derivative $Rh_2[(S)\text{-BPTV}]_4$ (71.5:28.5). As with the intramolecular cycloaddition of unsaturated α-diazo-β,ε-diketoesters **1** (R = ester),[4a] catalysts $Rh_2[(S)\text{-DOSP}]_4$ and $Rh_2[(R)\text{-DDBNP}]_4$ gave the opposite sense of asymmetric induction compared to catalysts $Rh_2[(S)\text{-PTPA}]_4$, $Rh_2[(S)\text{-PTTL}]_4$ and $Rh_2[(S)\text{-BPTV}]_4$. An attempt to improve the er with $Rh_2[(S)\text{-BPTV}]_4$ by reducing the reaction temperature to 0 °C simply led to the recovery of phenyl sulfone substrate **7a**. We also briefly examined variation of the sulfone substituent with methyl sulfone **7b**: compared with phenyl sulfone substrate **7a**, achiral catalysts $Rh_2(OAc)_4$ and $Rh_2(oct)_4$ in toluene were both less effective with methyl sulfone **7b** (20% and 43% yield of cycloadduct **8b**, respectively), whereas catalysis by $Rh_2(S\text{-BPTV})_4$ in $PhCF_3$ was of comparable efficiency (80% yield) but the er for cycloadduct **8b** {$[\alpha]_D^{25} = +3.1$ (*c* 1.05, CH_2Cl_2)} was lowered (from 71.5:28.5 for **8a** to 66.5:33.5 for **8b**).

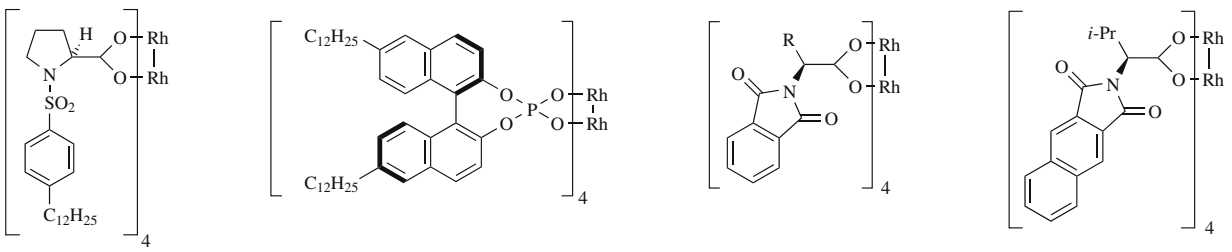


Figure 1.

3. Conclusion

In conclusion, a route to unsaturated α-diazo-β,ε-diketo sulfones **7** has been developed and such substrates have been shown to undergo efficient tandem cyclic ylide formation—intramolecular cycloaddition. Using these substrates, the first asymmetric induction in the cycloadditions of sulfone-substituted carbonyl ylides has been observed, with the *N*-phthaloyl-amino acid-based rhodium catalysts giving the best enantioselectivities (up to 71.5:28.5 er for phenyl sulfone **8a**) and extending their usefulness.[2c] Aside from further catalyst and intermolecular cycloaddition studies, as the level of asymmetric induction has been shown to be sensitive to the sulfone group (phenyl, methyl) then variation at this position[11] could be a productive avenue to pursue.

4. Experimental

4.1. General

All reactions requiring anhydrous conditions were conducted in flame- or oven-dried apparatus under an argon atmosphere. Syringes and needles for the transfer of reagents were oven-dried and allowed to cool in a desiccator over self-indicating silica gel or P_2O_5 prior to use. All solvents were distilled before use. Ethers were distilled from sodium/benzophenone ketyl; (halogenated) hydrocarbons and MeCN from CaH_2. 'Petrol' refers to the fraction of light petroleum ether boiling between 40 and 60 °C. Degassing in the Rh(II)-catalysed reactions was performed by purging the reaction mixture with argon. Reactions were monitored by TLC using commercially available aluminium- or glass-backed plates pre-coated with silica (0.25 mm, Merck 60 F_{254}), which were developed using standard visualising techniques: UV fluorescence (254 nm) and/or potassium permanganate or vanillin solution, followed by heating. Flash chromatography was performed on Kieselgel 60 (40–63 μm). Solvents were removed using a Büchi rotary evaporator under reduced pressure and residual solvent was removed with a static oil pump (~1 mmHg). Melting points were determined using a Griffin melting point apparatus and are uncorrected. IR spectra were recorded as thin films on NaCl discs or as KBr discs on a Perkin–Elmer Paragon 1000 Fourier transform spectrometer. Selected absorbances (ν_{max}) are reported. Peak intensities are specified as strong (s), medium (m) or weak (w). ^{1}H and ^{13}C NMR spectra were recorded using Bruker DPX400 (400 MHz), AM500 (500 MHz) or AMX500 (500 MHz) spectrometers. Chemical shifts (δ_H) are quoted in parts per million (ppm), referenced to the appropriate solvent peak ($CHCl_3$, 7.27). Coupling constants (*J*) are reported to the nearest 0.5 Hz; multiplicities are given as multiplet (m), singlet (s), doublet (d), triplet (t), quartet (q) and quin (quintet). Chemical shifts (δ_C) are quoted in ppm, referenced to the appropriate residual solvent peak ($CDCl_3$, central line of triplet, 77.0). Mass Spectra were obtained from the EPSRC Mass Spectrometry Service Centre, Swansea using a Micromass Quattro II low resolution triple quadrupole mass spectrometer for EI or CI. Alternatively they were recorded on an Open Linx Micromass Platform 1 using APCI. Accurate masses were obtained by the EPSCR Mass Spectrometry Service Centre, Swansea using a Finnigan MAT 900 XLT high resolution double focusing mass spectrometer with tandem ion trap. Microanalyses were performed by Elemental Microanalysis Limited, Okehampton, Devon. Chiral stationary phase HPLC was performed using a Daicel Chiralpak OD column (4.6 mm × 250 mm) on a Gilson System with 712 Controller Software and a 118 UV–vis detector set at 254 nm. Chiral GC was performed using a ThermoQuest CE Instruments TRACE GC, running Chrom-Card for TRACE software, fitted with a CYDEX-β column at 180 °C. Retention times (t_R) are given in min. Optical rotations $[\alpha]_D^T$ were measured using a Perkin–Elmer 241 polarimeter with a cell of path length either 1.0 dm or 0.1 dm, at *T* °C and are given in 10^{-1} deg cm^2 g^{-1}. Concentrations (*c*) are given in grams per 100 cm^3.

4.2. 1-(Phenylsulfonyl)dec-9-ene-2,5-dione 6a

n-BuLi (2.5 M in hexanes, 17.9 cm^3, 44.8 mmol) was added to a stirred solution of methylphenyl sulfone (7.00 g, 44.8 mmol) in THF (100 cm^3) at 0 °C. The reaction mixture was warmed to room temperature for 30 min, then methyl 4,4-dimethoxynon-8-enoate[4] **5** (3.43 g, 14.9 mmol) in THF (15 cm^3) was added via cannula. The mixture was stirred at room temperature for 20 min, then heated at reflux for 3 h. After being allowed to cool, aq HCl (2 M, 100 cm^3) was added and the mixture was extracted with Et_2O (3 × 250 cm^3). The combined organic layers were washed successively with H_2O (300 cm^3), saturated aq. $NaHCO_3$ (150 cm^3), brine (200 cm^3), then dried over $MgSO_4$ and evaporated under reduced pressure. Purification of the residue by column chromatography (SiO_2, 3:2 petrol/Et_2O) gave a colourless oil, which solidified upon standing, β-ketophenyl sulfone **6a** (2.82 g, 61%): mp 44–45 °C (petrol–EtOAc); R_f 0.15 (1:1 petrol/Et_2O); ($C_{16}H_{20}O_4S$ requires C, 62.3; H, 6.5. Found: C, 62.6; H, 6.7); ν_{max} (KBr disc)/cm^{-1} 2929 m (CH), 1713s (C=O), 1448 m, 1388 m, 1309s (SO_2) and 1149s (SO_2); δ_H (400 MHz; $CDCl_3$) 7.89-7.86 (2H, m, 2 × aromatic H), 7.67–7.62 (1H, m, aromatic H), 7.56-–7.52 (2H, m, 2 × aromatic H), 5.70 (1H, ddt, *J* 17, 10 and 7, =CH), 4.99–4.91 (2H, m, CH_2=), 4.22 (2H, s, CH_2SO_2), 2.93–2.90 (2H, m, $COCH_2CH_2CO$), 2.68–2.66 (2H, m, $COCH_2CH_2$-CO), 2.40 (2H, t, *J* 7.5, =$CH(CH_2)_2CH_2$), 1.99 (2H, q, *J* 7, =$CHCH_2$) and 1.61 (2H, quin, *J* 7.5, $CH_2CH_2CH_2$); δ_C (100 MHz; $CDCl_3$) 208.5 (C=O), 197.1 (C=O), 138.6 (aromatic C), 137.8 (=CH), 134.2 (aromatic CH), 129.3 (2 × aromatic CH), 128.2 (2 × aromatic CH), 115.3 (CH_2=), 67.0 (CH_2SO_2), 41.5 (CH_2), 37.8 (CH_2), 36.3 (CH_2), 32.9 (CH_2) and 22.7 (CH_2); *m*/*z* (APCI) 331 (M+Na$^+$, 42%), 309 (M+H$^+$, 76), 291 (35), 149 (100) and 122 (50).

4.3. 1-Diazo-1-(phenylsulfonyl)dec-9-ene-2,5-dione 7a

Et_3N (1.0 cm^3, 7.2 mmol) was added dropwise to a stirred solution of β-ketophenyl sulfone **6a** (2.00 g, 6.49 mmol) and 4-acetamidobenzenesulfonyl azide (1.72 g, 7.16 mmol) in MeCN (50 cm^3) at 0 °C. After 1.5 h, the mixture was filtered through Celite, saturated aq NH_4Cl (100 cm^3) was added and the mixture was extracted with Et_2O (3 × 100 cm^3). The combined organic layers were washed with brine (250 cm^3), dried over $MgSO_4$ and evaporated under reduced pressure. Purification of the residue by column chromatography (SiO_2, 2:1 petrol/Et_2O) gave a pale yellow oil, which solidified on standing, α-diazo-β-ketophenyl sulfone **7a** (1.66 g, 77%): mp 28–29 °C (Et_2O); R_f 0.45 (1:1 petrol/Et_2O); ($C_{16}H_{18}N_2O_4S$ requires C, 57.5; H, 5.4; N, 8.4. Found: C, 57.35; H, 5.5; N, 8.2); ν_{max} (thin film)/cm^{-1} 2934w (CH), 2117s (CN_2), 1714s (C=O), 1667s (C=O), 1448m, 1336s (SO_2) and 1155s (SO_2); δ_H (400 MHz; $CDCl_3$) 8.06–7.98 (2H, m, 2 × aromatic H), 7.69–7.65 (1H, m, aromatic H), 7.61–7.57 (2H, m, 2 × aromatic H), 5.73 (1H, ddt, *J* 17, 10 and 7, =CH), 5.01–4.95 (2H, m, CH_2=), 2.84–2.81 (2H, m, $COCH_2CH_2CO$), 2.73–2.70 (2H, m, $COCH_2CH_2CO$), 2.41 (2H, t, *J* 7.5, =$CH(CH_2)_2CH_2$), 2.01 (2H, q, *J* 7, =$CHCH_2$) and 1.63 (2H, quin, *J* 7.5, $CH_2CH_2CH_2$); δ_C (100 MHz; $CDCl_3$) 208.4 (C=O), 187.2 (C=O), 141.8 (aromatic C), 137.8 (=CH), 134.1 (aromatic CH), 129.5 (2 × aromatic CH), 127.3 (2 × aromatic CH), 115.3 (CH_2=), 41.6 (CH_2), 35.9 (CH_2), 32.9 (CH_2), 32.9 (CH_2) and 22.6 (CH_2) (CN_2 not observed); *m*/*z* (CI, NH_3) 352 M+(NH_4^+, 100%), 335 (M+H$^+$, 25) and 326 (59) ($C_{16}H_{19}N_2O_4S$ requires *M*, 335.1066. Found: M+H$^+$, 335.1064).

4.4. General procedure for cycloadditions

A Rh(II) catalyst (0.5 mol%) was added to α-diazo-β-keto sulfone **7a** or **7b** (~0.2 mmol) in the desired solvent (3 cm^3) and the mixture was stirred until the substrate was consumed (typically within 2 h, by TLC monitoring). The reaction mixture was then evaporated under reduced pressure and the residue was purified by column chromatography (SiO_2, 1:1 petrol/Et_2O).

4.5. 7-(Phenylsulfonyl)-11-oxatricyclo[5.3.1.$0^{1,5}$]undecan-8-one 8a

Following the General Procedure for the cycloadditions using α-diazo-β-ketophenyl sulfone **7a** gave white crystals, cycloadduct **8a**: mp (racemate) 196–198 °C (petrol–CH_2Cl_2); R_f 0.10 (1:2 petrol/Et_2O); ($C_{16}H_{18}O_4S$ requires C, 62.7; H, 5.9. Found: C, 62.4; H, 5.95); ν_{max} (KBr disc)/cm^{-1} 2931w (CH), 1732s (C=O), 1448m, 1323s (SO_2), 1310s, 1168s and 1145s (SO_2); δ_H (400 MHz; $CDCl_3$) 7.99–7.97 (2H, m, 2 × aromatic H), 7.67–7.62 (1H, m, aromatic H), 7.55–7.51 (2H, m, 2 × aromatic H), 2.60 (1H, dd, *J* 13.5 and 9, C*H*H), 2.49–2.43 (3H, m, CH and CH_2), 2.35–2.30 (1H, m, C*H*H), 2.22 (1H, dd, *J* 13.5 and 5.5, C*H*H), 2.05-2.00 (1H, m, C*H*H), 1.88–1.77 (2H, m, 2 × C*H*H), 1.66–1.58 (2H, m, 2 × C*H*H), 1.53–1.45 (1H, m, C*H*H) and 1.41–1.36 (1H, m, C*H*H); δ_C (100 MHz; $CDCl_3$) 201.7 (C=O), 136.0 (aromatic C), 134.1 (aromatic CH), 130.6 (2 × aromatic CH), 128.5 (2 × aromatic CH), 99.8 (C–O), 96.5 (C–O), 45.4 (CH), 39.8 (CH_2), 36.9 (CH_2), 35.2 (CH_2), 33.8 (CH_2), 32.5 (CH_2) and 24.7 (CH_2); *m*/*z* (APCI) 329 (M+Na^+, 50%), 307 (M+H^+, 75), 143 (82), 135 (100) and 122 (78) ($C_{16}H_{22}NO_4S$ requires *M*, 324.1270. Found: M+NH_4^+, 324.1271). ees were determined by HPLC (Daicel Chiralpak OD, 60:40 heptane/EtOH, 1 cm^3 min^{-1}) t_R 11.8 and 13.8 (major enantiomer elutes first when specific rotation is positive).

4.6. 1-(Methylsulfonyl)dec-9-ene-2,5-dione 6b

Following the procedure for ketophenyl sulfone **6a**, but using *n*-BuLi (2.5 M in hexanes, 13.0 cm^3, 32.5 mmol), dimethylsulfone (3.08 g, 32.7 mmol) and methyl 4,4-dimethoxynon-8-enoate[4] **5** (2.51 g, 10.9 mmol) gave, after purification of the residue by column chromatography (SiO_2, CH_2Cl_2), a colourless oil which solidified upon standing, β-ketomethyl sulfone **6b** (1.99 g, 74%): mp 43–44 °C (petrol-Et_2O); R_f 0.20 (1:2 petrol/Et_2O); ($C_{11}H_{18}O_4S$ requires C, 53.6; H, 7.4. Found: C, 53.7; H, 7.7); ν_{max} (KBr disc)/cm^{-1} 3004w, 2940m (CH), 1718s (C=O), 1644w, 1388m, 1310s (SO_2) and 1144s (SO_2); δ_H (400 MHz; $CDCl_3$) 5.75 (1H, ddt, *J* 17, 10 and 7, =CH), 5.04–4.96 (2H, m, CH_2=), 4.13 (2H, s, CH_2SO_2), 3.04 (3H, s, Me), 2.93–2.90 (2H, m, COC$H_2$$CH_2$CO), 2.77–2.74 (2H, m, $COCH_2CH_2$CO), 2.46 (2H, t, *J* 7.5, =CH$(CH_2)_2$CH_2), 2.04 (2H, q, *J* 7, =CHCH_2) and 1.67 (2H, quin, *J* 7.5, $CH_2CH_2CH_2$); δ_C (100 MHz; $CDCl_3$) 208.6 (C=O), 198.5 (C=O), 137.8 (=CH), 115.3 (CH_2=), 65.0 (CH_2SO_2), 41.5 (CH_2), 41.4 (Me), 37.8 (CH_2), 36.3 (CH_2), 32.9 (CH_2) and 22.7 (CH_2); *m*/*z* (CI, NH_3) 264 M+(NH_4^+, 100%) and 246 (M^+, 47) ($C_{11}H_{22}NO_4S$ requires *M*, 264.1270. Found: M+NH_4^+, 264.1268).

4.7. 1-Diazo-1-(methylsulfonyl)dec-9-ene-2,5-dione 7b

Following the procedure for α-diazo-β-ketophenyl sulfone **7a**, but using DBU (1.1 cm^3, 7.36 mmol), β-ketomethyl sulfone **6b** (1.50 g, 6.10 mmol) and 4-acetamidobenzenesulfonyl azide (1.76 g, 7.33 mmol) gave, after purification of the residue by column chromatography (SiO_2, 1:2 petrol/Et_2O), a pale yellow oil which solidified on standing, α-diazo-β-ketomethyl sulfone **7b** (249 mg, 15%): mp 32–33 °C (Et_2O); R_f 0.60 (1:3 petrol/Et_2O); ($C_{11}H_{16}N_2O_4S$ requires C, 48.5; H, 5.9; N, 10.3. Found: C, 48.6; H, 6.0; N, 10.2); ν_{max} (thin film)/cm^{-1} 2928w (CH), 2122 (CN_2), 1712m (C=O), 1663s (C=O), 1330s (SO_2) and 1147s (SO_2); δ_H (400 MHz; $CDCl_3$) 5.74 (1H, ddt, *J* 17, 10 and 7, =CH), 5.03–4.95 (2H, m, CH_2=), 3.35 (3H, s, Me), 2.87–2.80 (4H, m, $COCH_2CH_2CO$), 2.46 (2H, t, *J* 7.5, =CH$(CH_2)_2$CH_2), 2.04 (2H, q, *J* 7, =CHCH_2) and 1.67 (2H, quin, *J* 7.5, $CH_2CH_2CH_2$); δ_C (100 MHz; $CDCl_3$) 209.1 (C=O), 187.9 (C=O), 137.7 (=CH), 115.4 (CH_2=), 84.2 (CN_2), 45.6 (Me), 41.5 (CH_2), 36.6 (CH_2), 32.9 (CH_2), 32.6 (CH_2) and 22.7 (CH_2); *m*/*z* (CI, NH_3) 290 M+(NH_4^+, 100%), 273 (M+H^+, 14), 264 (40) and 246 (46) ($C_{11}H_{17}N_2O_4S$ requires *M*, 273.0909. Found: M+H^+, 273.0902).

4.8. 7-(Methylsulfonyl)-11-oxatricyclo[5.3.1.$0^{1,5}$]undecan-8-one 8b

Following the General Procedure for cycloadditions using α-diazo-β-ketomethyl sulfone **7b** gave a white solid, cycloadduct **8b**: mp (racemate) 120–121 °C (EtOAc); R_f 0.30 (1:3 petrol/Et_2O); ($C_{11}H_{16}O_4S$ requires C, 54.1; H, 6.6. Found: C, 54.0; H, 6.95); ν_{max} (KBr disc)/cm^{-1} 2936w (CH), 1728s (C=O), 1444w, 1312s (SO_2), 1165m and 1142m (SO_2); δ_H (500 MHz; $CDCl_3$) 3.02 (3H, s, Me), 2.67–2.62 (3H, m, CH and CH_2), 2.57 (1H, dd, *J* 13.5 and 9, C*H*H), 2.50–2.41 (2H, m, 2 × C*H*H), 2.16–2.12 (1H, m, C*H*H), 2.04–1.96 (3H, m, 3 × C*H*H) and 1.78–1.59 (3H, m, 3 × C*H*H); δ_C (125 MHz; $CDCl_3$) 201.7 (C=O), 99.2 (C–O), 98.3 (C–O), 45.8 (CH), 38.6 (Me), 38.2 (CH_2), 36.9 (CH_2), 35.7 (CH_2), 34.5 (CH_2), 34.4 (CH_2) and 25.7 (CH_2); *m*/*z* (CI, NH_3) 262 M+(NH_4^+, 100%) and 184 (8) ($C_{11}H_{20}NO_4S$ requires *M*, 262.1113. Found: M+NH_4^+, 262.1117). ee was determined by GC (CYDEX-β, 180 °C) t_R 31.6 and 33.0.

Acknowledgements

We thank the EPSRC and GlaxoSmithKline for a CASE award (to R.G.), Dr. B. Odell for NMR experiments and the EPSRC National Mass Spectrometry Service Centre for mass spectra.

References

1. (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998;; (b) Hodgson, D. M.; Stupple, P. A.; Forbes, D. C. In *Rodd's Chemistry of Carbon Compounds*; Sainsbury, M., Ed.; Topical Volume, Asymmetric Catalysis; Elsevier: Oxford, 2001; pp 65–99; (c) McMills, M. C.; Wright, D. In *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; Padwa, A., Pearson, W. H., Eds.; John Wiley & Sons: New York, 2002; pp 253–314; (d) Clark, J. S. *Nitrogen, Oxygen and Sulfur Ylide Chemistry*; Oxford University Press: Oxford, 2002;; (e) Mehta, G.; Muthusamy, S. *Tetrahedron* **2002**, *58*, 9477–9504; (f) Selden, D. A.; Hodgson, D. M.. In *Comprehensive Organic Functional Group Transformations II*; Jones, K., Ed.; Elsevier: Oxford, 2004; Vol. 3, pp 309–353; (g) Zhang, Z.; Wang, J. *Tetrahedron* **2008**, *64*, 6577–6605.
2. For the first report: (a) Hodgson, D. M.; Stupple, P. A.; Johnstone, C. *Tetrahedron Lett.* **1997**, *38*, 6471–6472; For more recent examples, see: (b) Hodgson, D. M.; Brückl, T.; Glen, R.; Labande, A. H.; Selden, D. A.; Dossetter, A. G.; Redgrave, A. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5450–5454; (c) Shimada, N.; Anada, M.; Nakamura, S.; Nambu, H.; Tsutsui, H.; Hashimoto, S. *Org. Lett.* **2008**, *10*, 3603–3606.
3. Hodgson, D. M.; Pierard, F. Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50–61.
4. (a) Hodgson, D. M.; Stupple, P. A.; Pierard, F. Y. T. M.; Labande, A. H.; Johnstone, C. *Chem. Eur. J.* **2001**, *7*, 4465–4476; (b) Hodgson, D. M.; Glen, R.; Grant, G. H.; Redgrave, A. J. *J. Org. Chem.* **2003**, *68*, 581–586.
5. Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993.
6. For recent examples, see: (a) Watanabe, H.; Nakada, M. *Tetrahedron Lett.* **2008**, *49*, 1518–1522; (b) Gomes, L. F. R.; Trindade, A. F.; Candeias, N. R.; Gois, P. M. P.; Afonso, C. A. M. *Tetrahedron Lett.* **2008**, *49*, 7372–7375.
7. Johnson, T.; Cheshire, D. R.; Stocks, M. J.; Thurston, V. T. *Synlett* **2001**, 647–648; For isomünchnone formation—intermolecular cycloaddition from diazosulfones, see: Padwa, A.; Sheehan, S. M.; Straub, C. S. *J. Org. Chem.* **1999**, *64*, 8648–8659.
8. House, H. O.; Larson, J. R. *J. Org. Chem.* **1968**, *33*, 61–65.
9. Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709–1716.
10. Gawley, R. E. *J. Org. Chem.* **2005**, *71*, 2411–2416.
11. Takeda, H.; Nakada, M. *Tetrahedron: Asymmetry* **2006**, *17*, 2896–2906.