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Asymmetric Michael Additions via SAMP-/RAMP-Hydrazones Enantioselective Synthesis of 2-Substituted 4-Oxosulfones

Dieter Enders *, Kyriakos Papadopoulos

Institut für Organische Chemie, Rheinisch-Westfälische Technische Hochschule, Professor-Pirlet-Str.1, D-5100 Aachen, Germany

Eberhardt Herdtweck

Anorganisch-chemisches Institut der Technischen Universitat, Lichtenbergstraße 4, D-8046 Garching, Germany

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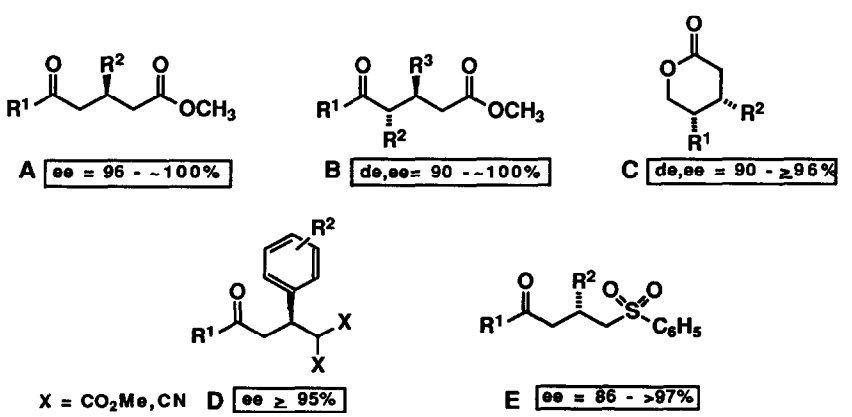
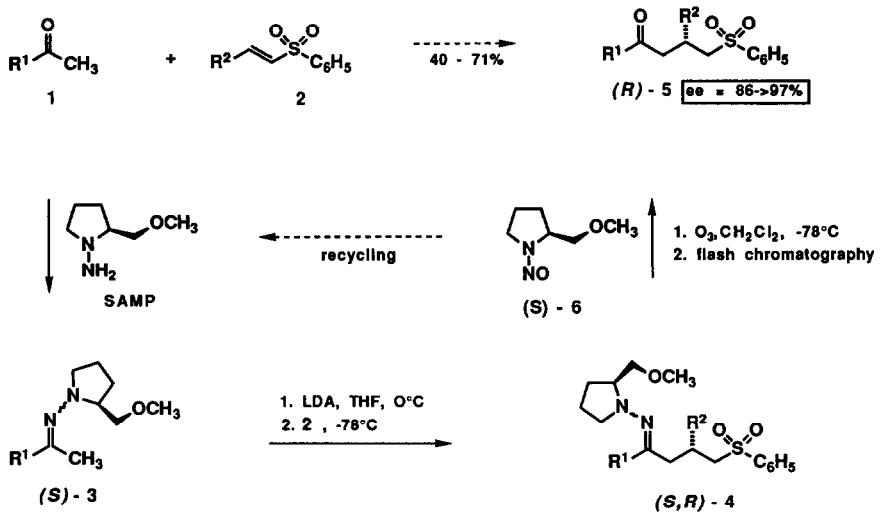
Dedicated to Professor Shun-ichi Yamada on the occasion of his 77th birthday ("ki-ju"), a pioneer in the field of asymmetric synthesis, who inspired our own work a lot

Abstract: A simple and efficient enantioselective synthesis of 2-substituted 4-oxosulfones **5** in 40 - 71% overall chemical yield and enantiomeric excesses of 86->97% is described. The key step is an asymmetric Michael-addition of lithiated methylketone -SAMP-/ RAMP-hydrazones **3** to α,β-unsaturated phenylsulfones **2**. The absolute configuration is determined by X-ray structure analysis of a crystalline hydrazone Michael adduct (**4k**) and through chemical correlation by polarimetry.

Alkenylsulfones are known to be excellent Michael acceptors for more than half of a century[1] and a variety of organometallic nucleophiles, such as organolithium, organocopper and Grignard reagents, enolates, azaenolates, tin and sulfur nucleophiles[2], as well as enamines[3], have been added by 1.4-addition. Whereas diastereoselective Michael additions of organometallic reagents to chiral alkenylsulfones have been studied extensively by Fuchs et al.[4] and Isobe et al.[5], it was only recently that efficient asymmetric Michael additions to alkenylsulfones have been carried out [6,7]. Employing our SAMP-/RAMP-hydrazone method [8,9], we previously reported efficient diastereo- and enantioselective syntheses of substituted 5-oxoesters **A**[10,11] and **B**[12-14], δ-lactones **C**[11,14],oxo diesters and -dinitriles **D**[15] and heterocyclic systems[16,17] via 1.4-addition.

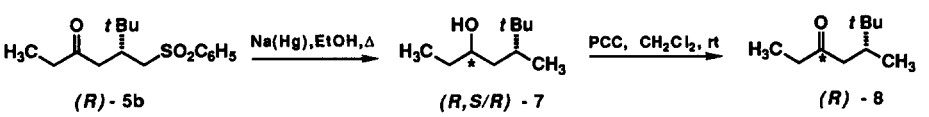




We now wish to describe a useful extension of these methods leading to 2-substituted 4-oxosulfones **E** in good overall yields and excellent enantiomeric purities. As is depicted in the scheme, the methylketones **1** are transformed into their corresponding SAMP-hydrazones (*S*) -**3**, which are metalated with lithium diisopropylamide in tetrahydrofuran followed by treatment with the alkenylsulfones **2** at -78°C. The resulting crude Michael adducts (*S,R*) -**4** are oxidatively cleaved by ozonolysis in methylene chloride at -78°C. Separation of (*S*) -**6** by chromatography (recycling of the auxiliary by LAH-reduction)[18] affords the oxosulfones (*R*) -**5** in overall yields for the three step procedure of 40 - 71% and enantiomeric excesses of 86 ->97% (s. Table). The enantiomeric title compounds (*S*) -**5** can be prepared in the same manner by simply using RAMP instead of SAMP as chiral auxiliary as was demonstrated in the case of (*R*) -and (*S*) -**5a**.

The ee-values of the final products **5** were determined by ^{1}H NMR shift experiments with Eu(hfc)$_3$. For comparison, the racemic oxosulfones *rac* - **5a-j** were prepared in the same way via the corresponding dimethylhydrazone homocuprate 1.4-additions [19,20].

The configurations given are based on a chemical correlation of (*R*) -**5b** with the ketone (*R*) -**8**, of known absolute configuration[21], easily prepared by desulfonation[22] with sodium amalgam in ethanol to form the alcohol (*R,S/R*) -**7**, followed by oxidation with pyridinium chlorochromate[23] (see experimental).



In addition, we were able to obtain single crystals of a Michael adduct **4k** (see experimental), which allowed the unambiguous determination of the absolute configuration to (*S,R*) by X-ray structure analysis (Figure 1).

In conclusion, the novel asymmetric Michael Addition described offers an efficient entry to 2-substituted 4-oxosulfones of high enantiomeric purity, useful compounds for further synthetic applications.

Table 1. 2-Substituted 4-Oxosulfones **5** Prepared by Asymmetric Michael Addition of SAMP-/RAMP-Hydrazones **3** to Alkenylphenylsulfones **2**

5 [a]	R^1	R^2	m.p. (°C)	yield [b] (%)	$[\alpha]_D^{23}$ (c, acetone)	ee [c] (%)
(*R*)-**5a**	Me	*t*Bu	d)	58	-42.9 (2.08)	90
(*S*)-**5a**[e]	Me	*t*Bu	d)	69	+43.9 (2.08)	92
(*R*)-**5b**	Et	*t*Bu	82	54	-43.9 (2.30)	86
(*R*)-**5c**	*i*Bu	*t*Bu	d)	53	-44.7 (2.35)	94
(*R*)-**5d**	*n*Pe	*t*Bu	d)	49	-41.4 (1.93)	95
(*R*)-**5e**	Ph	*t*Bu	109.5	40	-88.9 (2.28)	>97
(*R*)-**5f**	Naph	*t*Bu	135	36	-73.6 (1.69)[f]	g)
(*R*)-**5g**	Me	Ph	102	71	+0.68 (2.05)[h]	>97
(*R*)-**5h**	Me	pTol	91	56	-1.66 (0.78)	>97
(*R*)-**5i**	Me	*p*MeOPh	73	68	-44.7 (2.35)	>97
(*R*)-**5j**	Ph	*p*Tol	77	45	-0.50 (1.20)	>97

[a] The absolute configurations of **5** are based on an X-ray structure analysis of the crystalline SAMP-hydrazone of 2-*t*-butyl-4 (3,4,5-trimethoxyphenyl)-4-oxo-phenylsulfone [(*S*,*R*)-**4k**] (Figure 1), on a chemical correlation of (*R*)-**5b** with the ketone (*R*)-**8** of known absolute configuration (polarimetry) and by assuming a uniform reaction mechanism in all cases. - [b] Overall yield of the process **1** → **5** (see Scheme). - [c] Determined by ^{1}H NMR - LIS technique with Eu(hfc)$_3$ (90 MHz, methyl or *t*-butyl singlet). [d] Viscous oil.- [e] RAMP was used as chiral auxiliary. [f] Measured at 28°C. - [g] ee-Value could not be determined.- [h] Benzene was used as solvent.

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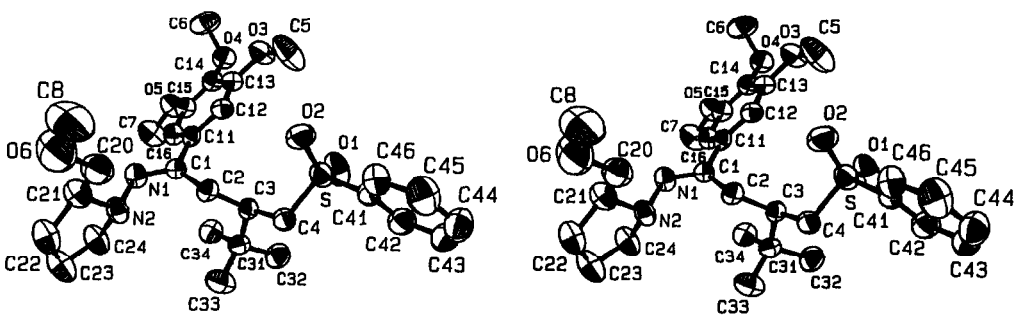

Figure 1. ORTEP stereo representation of the X-ray structure of **4k**. Non-hydrogen atoms have been drawn at the 50% probability level. Hydrogen atoms are omitted for clarity [25-32].

EXPERIMENTAL PART

^1H NMR and ^{13}C NMR spectra were recorded on Varian EM-390 or Varian VXR 300 spectrometers. IR spectra were taken with a Beckman Acculab 4 instrument. Mass spectra were obtained on Kratos MS-30 and Kratos MS-50 spectrometers at an ionization energy of 70 eV. The elemental analyses were carried out with a Heraeus Micro U/D apparatus. Optical rotation values were measured with a Perkin Elmer P 241 polarimeter. Ozonolyses were carried out with a Fischer ozon generator type 502. For analytical TLC Merck TLC-plates silica gel 60 F_{254} were used. All solvents were dried and distilled according to standard procedures. The melting points (Büchi apparatus; system Dr. Tottoli) are uncorrected.

The alkenylsulfones **2** were prepared according to the method described by Shahak and Almog[24] [R^2= *t*Bu: b.p. 116-118°C/0.1 Torr, m.p. 55-56°C; overall yield 53%. R^2= Ph: m.p. 74-75°C (MeOH); overall yield 50%. R^2= pMeOPh: m.p. 123-124°C (MeOH); overall yield 53%].

The methylketone-SAMP-hydrazones *(S)*-**3** were prepared as described earlier from *(S)*-2-methoxymethylpyrrolidine (SAMP) and the corresponding methylketones and were isolated as colourless to bright yellow oils after purification by short-path distillation or as a solid.

(S) - 2 - Methoxymethyl - 1 [1(3,4,5-trimethoxyphenyl) ethylideneamino] pyrrolidine [(S)-3 (R^1=trimethoxyphenyl)]:10.5g (50 mmol) 3,4,5-trimethoxyacetophenone and 6.55g (50 mmol) SAMP yields 12.4g (77%); b.p. 140-150°C/0.1 Torr; $[\alpha]_D^{21}$= 730° (c=2,0, benzene). IR(film): ν= 3100, 2980, 2880, 2840, 2740, 1575, 1510, 1465, 1410, 1360, 1260, 1240, 1190, 1130, 1015, 980, 925, 890, 860, 835, 785, 750, 665 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=1.65 - 2.15 (compl. m, 2H, ß-ring CH_2) 2.22 and 2.26 (2s, E:Z=95:5, 3H, CH_3), 2.55 (dt, 1H, NCHH), 3.35 (m, 2H, NCH, NCHH), 3.37 (s, 3H, OCH_3), 3.52 (m, 2H, OCH_2), 3.85 and 3.90 (2s, 9H, 3 OCH_3), 7.0 (s, 2H, $H_{arom.}$) ppm.

$C_{17}H_{26}N_2O_4$ (322.4) calc. C 63.33 H 8.12 N 8.69
found C 63.01 H 8.30 N 8.35

(S)-2-Methoxymethyl-1[1(2-naphthyl) ethylideneamino] pyrrolidine [(S)-3(R^1=2-naphtyl)]. 8.5g (50 mmol) ß-naphthylmethylketone and 6.5g (50 mmol) SAMP yields 11.4g (80.8%) of a yellow solid, m.p. 67°C (EtOH); $[\alpha]_D^{20}$=+ 1171.8°(c=3.2, benzene). IR (KBr): ν= 3060, 2980-2810, 1600 (CN), 1500, 1480, 1460, 1450, 1370, 1350, 1280, 1200, 1135, 1100, 1070, 1020, 970, 955, 950, 900, 870, 840, 780, 750 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$):δ=1.93 (m, 4H, ß-ring CH_2),, 2.36 (s, 3H, CH_3), 3.38 (s, 3H, OCH_3), 3.56 (m, 5H, NCH_2, NCH, OCH_2), 7.43-8.2 (compl. m, 7H, $H_{arom.}$) ppm. ^{13}C NMR (22.63 MHz, $CDCl_3$):δ=16.6, 22.8, 26.9, 54.8, 59.2, 66.9, 75.9, 123.9, 125.4, 126.1, 126.2, 126.7, 133.5, 137.0, 156.5, 167.6 ppm. MS (70eV); m/z (rel.int.): 283 (1.5, M^++1), 282 (7, M^+), 238 (11), 237 (73), 169 (15), 168 (100), 154 (8), 153 (31), 152(7), 128(12), 127(77), 126(11), 45(5), 41(9).

$C_{18}H_{22}N_2O$ (282.2) calc. C 76.56 H 7.85 N 9.92
found C 76.55 H 7.79 N 9.78

(S,R)-[2-tert-Butyl-4(3,4,5-trimethoxyphenyl)-4-oxo-but-1-yl]phenylsulfone-SAMP-hydrazone[(*S,R*)-**4k**]:
3.22g (10 mmol) trimethoxyacetophenone-SAMP-hydrazone and 2.24g (10 mmol) (3,3-dimethyl-but-1-ene-1-yl)phenylsulfone gave 3.7g (67.7%) colourless crystals, m.p. 121°C (ether); $[\alpha]_D^{21}$= +105.6° (c=1.5, acetone). IR(KBr) : ν=3075, 3005, 2960, 2890, 2840, 2740, 1620, 1585, 1515, 1470, 1450, 1420, 1350, 1310, 1290, 1250, 1190, 1150, 1140, 1090, 1015, 930, 870, 850, 785, 745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$):δ= 0.81 (s, 9H, *t*-Bu), 1.62 - 2.10 (compl. m, 4H, ß-ring CH_2), 2.25 (m, 1H, CH), 2.75 (m, 1H, NCHH), 2.95 - 3.87 (compl. m, 9H, $2CH_2$, NCH_2, NCH, OCH_2), 3.35 (s, 3H, OCH_3), 3.87 and 3.92 (2s, 9H, 3 OCH_3), 7.0 (s, 2H, $H_{arom.}$), 7.47, 7.57 and 7.72 (3m, 5H, $H_{arom.}$) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$):δ= 22.44, 26.85, 27.29, 31,41, 34.48, 40.71, 55.92, 56.30, 58,02, 59.09, 60.87, 66.65, 75.16, 105.15, 127.93, 129.10, 133.47, 133.59, 138.50, 140.05, 153.0, 167.30 ppm. MS (70 eV); m/z (rel.int.): 547 (2.6, M^++1), 503 (10), 502 (31), 501 (100, M^+-CH_2OCH_3), 433 (7), 432 (26.5), 405 (5), 290 (2), 234 (3.5), 168

(3), 115 (2.5), 97 (2), 83 (3), 77 (3), 70 (4), 69 (2.5), 57 (5), 55 (10), 45 (3.5), 43 (2), 41 (7).
$C_{29}H_{42}N_2O_6S$ (546.7) calc. C 63.70 H 7.74 N 5.12
found C 63.83 H 7.90 N 4.93

X-Ray Crystallographic Determination of (S,R) - **4k**
$C_{29}H_{42}N_2O_6S$, M_r=546.7, monoclinic, space group $P2_1$, with a=8.847(1), b=19.037(2), c=9.755(1) Å, ß=114,17(1)°, V=1499 $Å^3$, Z=2, D_x=1.211 Mgm^{-3}, λ(MoK_α) =0.71073 Å, μ=1.4 cm^{-1}, F_{ooo}=588, T=296 K. A well shaped colourless prism of approximate dimensions = 0.2 x0.2x0.3 mm was randomly mounted on a glass fiber. Preliminary examinations and data collection were carried out with MoK_α radiation on an Enraf-Nonius CAD4 diffractometer equipped with a graphite monochromator. The observed extinctions (0k0:k=2n+1) together with the monoclinic crystal system selects the space groups $P2_1/m$ or $P2_1$ of which the latter one was confirmed during the calculations. Final cell constants were obtained by least squares refinement of 50 automatically centered high angle reflections (33.9°<2Θ<40.7°). Data were collected using ω-scans. Each reflection in the hemisphere h:±11; k:±24; l:±12 and $2\Theta_{max}$= 25.0° was measured with a maximum scan speed of 60 s. Orientation control reflections were monitored every 200th reflections. No loss of intensity of three standards, checked every 3600 s during the data collection was observed. No absorption correction was applied. After averaging, 4605 [I>1.0 σ(I)] out of 5830 reflections were used in the refinement. The structure was solved by direct methods and subsequent difference Fourier maps. Full-matrix least-squares refinement was carried out by minimizing $\Sigma w(|Fo|-|Fc|)^2$. Anisotropic thermal parameters were introduced for all non-H atoms. All hydrogen atoms were calculated in ideal positions d_{C-H}=95pm, included with individual isotropic thermal parameters in the parameter set but not refined. Atomic scattering factors were taken from international tables for X-ray Crystallography [25]. Anomalous dispersion was considered [26]. The refinement converged at R=0.045 and Rw=0.036, for 342 parameters and weighting scheme w=1 /σ^2(Fo). The absolute configuration was not checked, but a refinement of the enantiomorphic model gave a slighly higher R-factor R=0.046. Final difference Fourier syntheses showed no significant features (min./max.: +0.81/ -0.49 e $Å^{-3}$). All calculations were performed on a Vax 730 computer with the STRUX-III [27] system including the programmes MULTAN [28] ORTEP [29], PARAM[30], SCHAKAL[31] and SDP [32].

SAMP-Hydrazones (S,R) -**4**, *General Procedure*
A solution of *n*-butyllithium in *n*-hexane (1.1 eq, 1.6 M) was added dropwise via syringe to a solution of diisopropylamine in tetrahydrofuran (1.1 eq, 1.0 M) under argon at 0°C and stirred for 15 min to generate a solution of lithium diisopropylamide (1.1eq). After dropwise addition of (*S*)-**3** (1.1 eq) the mixture was stirred at 0°C for 2-4 h, cooled to -78°C, and a solution of the alkenylsulfone **2** (1.0 eq) was added. Stirring was continued at this temperature for 2 h, after which the mixture was allowed to warm up to 0°C within 8-12 h. The mixture was then poured into a saturated aqueous ammonium chloride solution and extracted three times with ether. After drying the organic layer with sodium sulfate and concentrating in vacuo the crude viscous oily product was oxidatively cleaved with ozone.

Oxidative cleavage of the Hydrazones ***4*** *by Ozonolysis to Form the Oxosulfones* ***5****. General Procedure*
The crude hydrazone Michael adducts were dissolved in dichloromethane (50 ml) and, after cooling to –78°C, a gentle stream of ozone was flushed through the solution until the colour of the solution turned green to blue (indicating excess ozone). Argon was then flushed through the solution as it warmed up to room temperature. The solution was concentrated in vacuo, and the oxosulfones **5** were separated from the nitrosamine (*S*)-**6** by column chromatography (silica gel, ether/ pentane or ethylacetate/ pentane, 1:1).

*(R)-(2-t-Butyl-4-oxo-pent-1-yl) phenylsulfone [(R)-**5a**]*
1.7g (10 mmol) acetone-SAMP-hydrazone and 2.24g (10 mmol) (3,3-dimethyl-but-1-ene-1-yl) phenylsulfone afforded 1.83g (65%) of a bright yellow oil. IR (film): ν= 3080, 2980, 2920, 2880, 1730 (CO), 1595, 1485, 1455, 1430, 1410, 1375, 1310, 1275, 1250, 1230, 1190, 1150, 1090, 1060, 1040, 1010, 970, 940, 910, 880,

810, 760, cm^{-1}. 1H NMR (90 MHz, $CDCl_3$):δ = 0.73 (s, 9H, *t*-Bu), 2.05 (s, 3H, CH_3), 2.50 (m, 1H, CH), 2.66-3.30 (compl. m, 4H, 2 CH_2), 7.63 and 7.86 (2 m, 5H, $H_{arom.}$) ppm. MS (70eV); m/z (rel.int.): 283 (0,8, M^++1), 282 (0,6, M^+), 226 (6.7), 225 (42), 183 (11), 143 (13), 141 (15), 125 (20), 123 (7), 85 (36), 84 (14), 83 (25), 78 (5.5), 77 (15), 69 (3.5), 58 (3.5), 57 (79.5), 55 (12), 51 (7), 43 (100), 41 (25).

$C_{15}H_{22}O_3S$ (282.4) calc. C 63.80 H 7.85
found C 63.71 H 7.95

(S)-(2-t-Butyl-4-oxo-pent-1-yl) phenylsulfone [(S) -5a]
1.7g (10 mmol) acetone-RAMP-hydrazone and 2.24g (10mmol) (3,3-dimethyl-but-1-ene-1-yl) phenylsulfone afforded 2.17g (77%) of a bright yellow oil. The spectroscopic data were identical with those of (*R*) -**5a**.

(R)-(2-t-Butyl-4-oxo-hex-1-yl) phenylsulfone [(R) -**5b**]
1.84g (10 mmol) butane-2-one-SAMP-hydrazone and 2.24g (10mmol) (3,3-dimethyl-but-1-ene-1-yl) phenylsulfone yielded 2.2g (74%) of a colourless solid, m.p. 82°C. IR (KBr): ν= 3090, 2990, 2930, 2900, 1730(CO), 1600, 1480, 1460, 1430, 1415, 1380, 1320, 1250, 1235, 1180, 1160, 1130, 1100, 1040, 1020, 950, 930, 870, 820, 760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$):δ=0.70 (s, 9H, *t*-Bu), 1.07 (t, J=7, 3H, CH_3), 2.38-2.75 (compl. m, 5H, CH_2COCH_2, CH_2), 2.92 (dd, J=14.8, 10.4, 1H, C<u>H</u>HSO_2), 3.20 (dd, J=15.2, 3.2, 1H, CH<u>H</u>SO_2), 7.60 and 7.86 (2 m, 5H, $H_{arom.}$) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$):δ=7.88, 26.74, 33.53, 35.84, 37.10, 43.61, 57.76, 128.41, 129.17, 133.68, 138.65, 209.19 ppm. MS (70eV); m/z (rel.int.): 297 (0.9, M^++1), 296 (2.8, M^+) 268 (7.5), 267 (46.5), 239 (20.5), 183 (4.5), 155 (9.5), 143 (11), 139 (8.5), 125 (9.5), 99 (9), 98(8), 97 (23), 83 (6), 77 (8), 69 (6), 57 (100), 55 (17), 42 (24).

$C_{16}H_{24}O_3S$ (296.4) calc. C 64.83 H 8.16
found C 65.20 H 8.11

(R)-(2-t-Butyl-6-methyl-4-oxo-hept-1-yl) phenylsulfone [(R) -**5c**]
4.24g (20 mmol) 4-methyl-pentane-2-one-SAMP-hydrazone and 4.48g (20 mmol) 3,3-dimethyl-but-1-ene-1-yl) phenylsulfone afforded 4.30g (70%) of a bright yellow oil. IR (film):ν= 3070, 2940, 2860, 1705 (CO), 1580, 1470, 1450, 1410, 1390, 1360, 1300, 1240, 1165, 1140, 1080, 850, 800, 750, 730, 680 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$): δ= 0.7 (s, 9H, *t*-Bu), 0.9 [d, J=6.5, 6H, $(C\underline{H}_3)_2CH$], 2.06-3.26 (compl. m, 8H, 3 CH_2, 2 CH), 7.53 and 7.83 (2m, 5H, $H_{arom.}$) ppm. MS (70eV); m/z (rel.int.): 325 (0.6,M^++1), 324 (1.3, M^+), 282 (7), 268 (6.5), 267 (41), 241 (5.5), 225 (17), 167 (5), 160 (5), 143 (9), 141 (3), 126 (5), 125 (8.5), 97 (9), 86 (5), 85 (100), 77 (9), 69 (7), 57 (82), 55 (14), 43 (8), 41 (31).

$C_{18}H_{28}O_3S$ (324.5) calc. C 66.62 H 8.69
found C 66.49 H 8.81

(R)-(2-t-Butyl-4-oxo-non-1-yl) phenylsulfone [(R) -**5d**]
2.26g (10 mmol) heptane-2-one-SAMP-hydrazone and 2.24g (10mmol) 3,3-dimethyl-but-1-ene-1-yl) phenylsulfone yielded 2.0g (59%) of a bright yellow oil. IR (film):ν= 3080, 2980, 2940, 2880, 1720, (CO), 1590, 1480, 1450, 1420, 1380, 1320, 1230, 1180, 1150, 1090, 1030, 1010, 850, 810, 740 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$):δ= 0.70 (s, 9H, *t*-Bu), 0.83 (t, 3H, J=7, CH_3), 0.84-1.76 [compl. m, 6 H, $(CH_2)_3$], 2.3-3.26 (compl. m, 7H, $CH_2COCH_2CHCH_2$), 7.56 and 7.90 (2 m, 5H, $H_{arom.}$) ppm. MS (70 eV); m/z (rel. int.): 339 (1, M^++1), 338 (2,M^+), 282 (24), 281 (16), 267 (40), 226 (15), 225 (100), 181 (8.5), 161 (6), 143 (23), 140 (14.5), 139 (12.5), 125 (15), 99 (98), 97 (19), 84 (27.5), 83 (28), 77 (12.5), 71 (47), 69 (13), 57 (43), 55 (34), 43 (83), 42 (50).

$C_{19}H_{30}O_3S$ (338.5) calc. C 67.41 H 8.93
found C 67.31 H 8.86

(R)-(2-t-Butyl-4-oxo-4-phenyl-but-1-yl) phenylsulfone [(R) -**5e**]
2.32g (10 mmol) acetophenone-SAMP-hydrazone and 2.24g (10 mmol) 3,3-dimethyl-but-1-ene-1-yl)

phenylsulfone afforded 1.76g (51%) of a colorless solid, m.p. 109.5°C. IR (KBr):ν= 3080, 2980, 2925, 2915, 1680 (CO), 1600, 1585, 1485, 1450, 1420, 1400, 1370, 1310, 1260, 1220, 1190, 1150, 1100, 1080, 1060, 1035, 1010, 1000, 960, 930, 860, 810, 790, 740, 700, 670 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$):δ= 0.73 (s, 9H, *t*-Bu), 2.67 (m, 1H, CH), 3.05 (dd, J= 14.8, 10.7, 1H, CH<u>H</u>CO), 3.25 (m, 3H, C<u>H</u>HCO, CH_2SO_2), 7.45, 7.57 and 7.92 (3m, 10H, $H_{arom.}$) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$):δ= 26.83, 33.77, 37.26, 39.72, 57.77, 127.97, 128.44, 128.52, 129.16, 132.90, 133.68, 136.96, 138.58, 198.14 ppm. MS (70 eV); m/z (rel.int.): 345 (0.15, M^++1), 344 (0.5, M^+), 287 (7), 204 (2), 203 (14), 147 (3), 146 (5), 145 (8), 106 (8), 105 (100), 77 (21), 57 (13), 51 (5), 41 (8.5).

$C_{20}H_{24}O_3S$ (344.5) calc. C 69.73 H 7.02
found C 69.86 H 7.10

*(R)-[2-t-Butyl-4(2-naphthyl)-4-oxo-but-1-yl) phenylsulfone [(R) -***5f***]*

2.82g (10 mmol) ß-naphthylmethylketone-SAMP-hydrazone and 2.24g (10 mmol) 3,3-dimethyl-but-1-ene-1-yl)phenylsulfone gave 1.77g (44.8%) of a bright yellow solid, m.p. 135°C. IR (KBr):ν= 3070, 2980-2880, 1685 (CO), 1630, 1600, 1590, 1480, 1450, 1400, 1370, 1310, 1270, 1260, 1210, 1190, 1170, 1140, 1095, 1085, 1035, 925, 880, 840, 820, 760 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$):δ= 0.73 (s, 9H, *t*-Bu), 2.63-3.46 (compl. m, 5H, CH_2CHCH_2), 7.53 (m, 5H, $H_{arom.}$), 7.9 (m, 6H, $H_{arom.}$), 8.46 (s, 1H, $H_{naphthyl}$) ppm. MS (70 eV); m/z (rel. int.): 394 (0.5, M^+), 337 (4), 235 (3.5), 196 (3), 195 (6.5), 170(14), 156 (12), 155 (100), 128 (5), 127 (32), 77 (5.5), 57 (8.5), 55 (3), 41 (6.5), 29 (3.5).

$C_{24}H_{26}O_3S$ (394.5) calc. C 73.06 H 6.64
found C 73.19 H 6.76

*(R)-(4-Oxo-2-phenyl-pent-1-yl) phenylsulfone [(R) -***5g***]*

1.70g (10 mmol) acetone-SAMP-hydrazone and 2.44g (10 mmol) benzylidenephenylsulfone yielded 2.38g (79%) of a colourless solid, m.p. 102°C. IR (KBr): ν= 3100, 3080, 3040,; 2970-2900, 1720 (CO), 1500, 1450, 1370, 1360, 1350, 1320, 1310, 1290, 1250, 1200, 1170, 1160, 1140, 1050, 1020, 910, 860, 780, 760, 750, 700, 680, cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$):δ= 1.95 (s, 3H, CH_3), 2.80 (dd, J= 17.5, 8.5, 1H, CH<u>H</u>CO), 3.14 (dd, J= 17.5, 6.0, 1H, C<u>H</u>HCO), 3.30 (dd, J= 16.0, 5.0, 1H, CH<u>H</u>SO_2), 3.50 (dd, J= 16.0, 8.1, 1H, C<u>H</u>HSO_2), 3.73 (m, 1H, CH), 7.05 (m, 5H, $H_{arom.}$), 7.45 and 7.72 (2 m, 5H, $H_{arom.}$) ppm. MS (70 eV); m/z (rel. int.): 303 (0.1, M^++1), 161 (21), 145 (8), 118 (4), 91 (3), 77 (10), 43 (100).

$C_{17}H_{18}O_3S$ (302.4) calc. C 67.54 H 6.00
found C 67.91 H 5.97

*(R)-(4-Oxo-2-p-tolyl-pent-1-yl) phenylsulfone [(R) -***5h***]*

1.70g (10 mmol) acetone-SAMP-hydrazone and 2.58g (10 mmol) *p*-methyl-benzylidene phenylsulfone afforded 1.99g (63%) of a colourless solid, m.p. 91°C. IR (KBr):ν= 3080, 3040, 3020; 2980-2900, 1715 (CO), 1525, 1450, 1430, 1410, 1370, 1330, 1310, 1300, 1280, 1270, 1170, 1140, 1120, 1090, 920, 830, 810, 780, 750, 740, 690, 620cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$):δ= 2.02 (s, 3H, CH_3CO), 2.25 (s, 3H, CH_3), 2.94 (dd, J= 17.5, 8.5, 1H, C<u>H</u>HCO), 3.13 (dd, J= 17.5, 5.2, 1H, CH<u>H</u>CO), 3.40 (dd, J= 16.4, 5.8, 1H, CH<u>H</u>SO_2), 3.52 (dd, J= 16.4, 8.0, 1H, C<u>H</u>HSO_2), 3.72 (m, 1H, CH), 6.99 (m, 4H, $H_{arom.}$), 7.48, 7.59 and 7.77 (3m, 5H, $H_{arom.}$) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$):δ= 20.95, 30.39, 35.34, 48.87, 60.78, 127.20, 127.90, 129.13, 129.39, 133.48, 136.80, 138.34, 139.53, 205.87 ppm. MS (70 eV); m/z (rel. int.): 317 (0.1, M^++1), 316 (0.15, M^+), 255 (2), 176 (3.5), 175 (27), 174 (26), 173 (3), 160 (3), 159 (22), 133 (7.5), 132 (7), 131 (3), 118 (3), 117 (6), 116 (2), 115 (4.5), 91 (6), 77 (8.5), 44 (2.5), 43 (100).

$C_{18}H_{20}O_3S$ (316.4) calc. C 68.32 H 6.37
found C 68.02 H 6.36

*(R)-(4-Oxo-2-p-methoxyphenyl-pent-1-yl) phenylsulfone [(R) -**5i**]*

1.70g (10 mmol) acetone-SAMP-hydrazone and 2.74g (10 mmol) p-methoxy-benzylidenephenylsulfone yielded after purification by column chromatography (silica gel, ethylacetate) 2.50g (75%) of a pale yellow oil, which crystallized, m.p. 73°C. IR (KBr):ν= 2950, 1710 (CO), 1610, 1515, 1300, 1250, 1150, 1090, 1030, 840, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$):δ= 2.01 (s, 3H, CH_3), 2.87 (dd, J= 17.4, 8.0, 1H, C<u>H</u>HCO), 3.09 (dd, J= 17.4, 5.4, 1H, CH<u>H</u>CO), 3.37 (dd, J= 14.1, 6.4, 1H, C<u>H</u>HSO_2), 3.53 (dd, J= 14.4, 7.5, 1H, CH<u>H</u>SO_2), 3.68 (m, 1H, CH), 3.71 (s, 3H, =CH_3), 6.73 and 6.98 (2 m, 4H, $H_{arom.}$), 7.47, 7.58 and 7.76 (3m, 5H, $H_{arom.}$) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$):δ= 30.40, 35.03, 49.02, 55.17, 60.81, 114.06, 127.84, 128.38, 129.12, 133.25, 133.49, 139.56, 158.53, 205.94 ppm. MS (70 eV); m/z (rel. int.): 332 (2,M^+), 190 (100), 175 (20), 148 (11), 134 (11), 91 (6), 77 (8), 43 (97).

$C_{18}H_{20}O_4S$ (332.4) calc. C 64.98 H 6.06
found C 64.65 H 5.88

*(R)-(4-Oxo-4-phenyl-2-p-tolyl-but-1-yl) phenylsulfone [(R) -**5j**]*

2.32 (10 mmol) acetophenone-SAMP-hydrazone and 2.58g (10 mol) p-methylbenzylidenephenylsulfone gave 2.19g (58%) of a colourless solid, m.p. 77°C. IR (KBr):ν= 3080, 3040, 1690 (CO), 1585, 1515, 1450, 1410, 1360, 1330, 1290, 1260, 1220, 1190, 1170, 1140, 1120, 1090, 980, 970, 940, 820, 760, 750, cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$):δ= 2.16 (s, 3H, CH_3), 3.20-3.50 (m, 4H, CH_2CO, CH_2SO_2), 3.72 (m, 1H, CH), 6.95, 7.42 and 7.76 (3m, 14H, $H_{arom.}$) ppm. MS (70 eV); m/z (rel. int.): 378 (0.04, M^+), 251 (2), 238 (2.5), 237 (14), 236 (2), 208 (3), 141 (1), 117 (4), 116 (2), 115 (2), 106 (7.5), 105 (100), 91 (3.5), 78 (2.5), 77 (26), 51 (4), 44 (2).

$C_{23}H_{22}O_3S$ (378.5) calc. C 72.98 H 5.85
found C 73.20 H 6.04

*(R)-5,6,6-Trimethyl-heptane-3-one [(R) -**8**]*

3.2g (10.8 mmol) of oxosulfone (R) -**5b** and 50g (0.13 mol) of sodium amalgam (6%), prepared from 4.5g sodium and 70.5g mercury, were refluxed in 100 ml ethanol for 20 h. After addition of 100 ml water and three times extraction with ether, the combined organic phases were dried over sodium sulfate and concentrated in vacuo. The crude alcohol (*R,S/R*) -**7** was dissolved in 20 ml methylene chloride and was directly oxidized by addition to a suspension of 5.0g (29 mmol) pyridinium chlorochromate in 20 ml methylene chloride at room temperature and stirring over night. After the oxidation was complete (TLC control), 50 ml ether were added three times and decanted and the remaining black tar was stirred several times with small ether portions. After filtering through silica gel and removal of the solvent in vacuo, the crude ketone was purified by distillation; 0.6 g (36%) of a colourless oil, b.p. 136°C /140 Torr; α_D^{22}= +14.4° (neat)[lit.: $^{21}\alpha_D^{22}$= -7.0° (neat) (*S*)-configuration]. IR (film): ν= 2960, 2910, 2880, 1720 (CO), 1470, 1460, 1455, 1420, 1380, 1370, 1290, 1250, 1220, 1160, 1120, 1030, 990, 930 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$):δ= 0.8 (d, J= 7, 3H, CH_3), 0.85 (s, 9H, *t*-Bu), 1.03 (t, J= 7.5, 3H, CH_3), 1.73 - 2.58 (compl.m, 5H, CH_2COCH_2CH) ppm MS (70 eV); m/z (rel. int.): 157 (0.4, M^++1), 156 (1,2,M^+), 141 (7), 127 (41), 101 (10), 100 (27), 99 (17), 85 (28), 72 (11), 71 (30.5), 57 (100), 56 (4), 55 (5.5), 43 (25.5), 42 (3), 41 (25.5).

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A list of structure amplitudes, anisotropic thermal parameters, H-atoms parameters, distances and angles involving H atoms and additional crystallographic data have been deposited in the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1 EW, U.K..