Pergamon

Tetrahedron, Vol. 53, No. 21, pp. 7341-7346, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00417-1

C-C Bond Fission *via* Sulphones: A New Ring Cleavage of Cyclic β-Keto Phenylsulphones

Roberto Ballini,* Giovanna Bosica, and Tiziana Mecozzi

Dipartimento di Scienze Chimiche dell'Università, Via S. Agostino, 1, I-62032 Camerino, Italy

Abstract: Reaction of β-keto sulphones with 2N NaOH, at 70 °C, in aqueous media and in presence of cetyltrimethylammonium chloride (CTACl), produces the C-C bond fission between the carbonyl group and the carbon bearing the sulphone. © 1997 Elsevier Science Ltd.

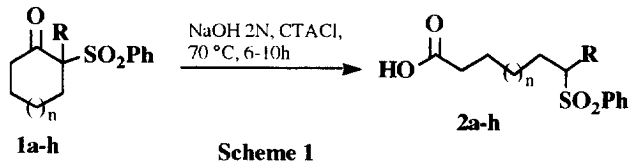
From the point of view of strategic potential, the overwhelming majority of organic reactions can be divided into three very important classes: *(i)* namely carbon-carbon bond-forming processes (including chainlengthening reactions, cyclizations, and annulations), *(ii)* functional groups interconversion, and *(iii)* C-C bond fission.[1-3]

It is impossible to devise any synthetic sequence to arrive at a particular product without using such kinds of reactions as strategic tool to achieve the goal.

Sulphones have proved to be valuable as intermediates in single and double bond carbon-carbon formation,[4-7] and as precursors of carbonyl derivatives,[4] while less common is their employment in the C-C bond fission in which, the few examples reported regard the cleavage in the cyclic mode to give macrocyclic systems ("Zip Reaction"),[8,9] or the preparation of α-halo sulphones.[10] Thus, the elaboration of new procedures for the C-C bond cleavage through sulphones would be of considerable interest.

Ring cleavage often represents a particularly effective route to α,ω-difunctionalized frameworks, and, in this context, we found (Scheme 1) that cyclic β-keto phenylsulphones **1**[11] can be efficiently cleaved, after 6-10h at 70 °C, by employing an aqueous solution of 2N sodium hydroxide and in the presence of catalytic amount of cetyltrimethylammonium chloride (CTACl) as cationic surfactant, leading to the corresponding carboxylic acids **2**.

Moreover, by this C-C bond fission between the carbonyl group and the carbon bearing the sulphone (retro Claisen condensation) a variety of cyclic keto-sulphones are cleaved in respectable yield regardless the ring size (Table 1).



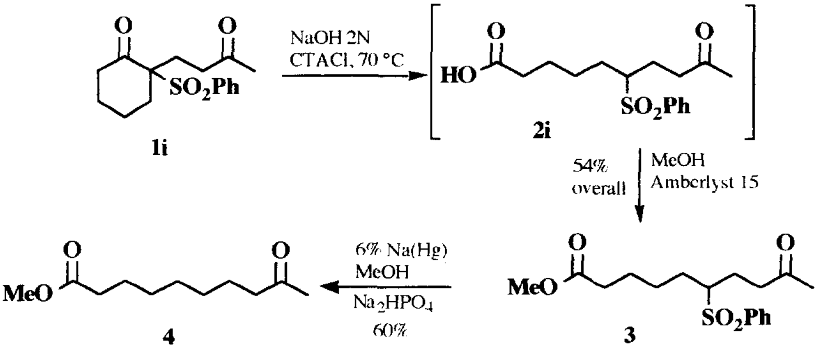
Scheme 1

Table 1

Entry	n	R	Yield (%) 2
a	0	H	98
b	1	H	97
c	2	H	80
d	7	H	78
e	0	$PhCH_2$	72
f	1	$PhCH_2$	71
g	1	$CH_2{=}CHCH_2$	64
h	1	CH_3	72

The compounds **2**, due to the high versatility of both carboxylic and sulphone functionalities, added to the possibility to obtain the sulfur-free compounds,[12] represent important building blocks in organic synthesis. On the other hand, it is important to point out that these procedures are performed in an aqueous medium so that, they enable to make this reaction in an inexpensive medium, with evident economical advantages, expecially for widespread industrial use. Moreover, this methodology can enlarge the use of sulphones as precursors for the C-C bond fission.

As an application of our method, we report here the synthesis of methyl 9-oxodecanoate **4** (Scheme 2), a key prostaglandin intermediate,[13] and a good staring material for the synthesis of 9-oxo-(*E*)-2-decenoic acid (queen substance),[14] from the β-keto phenylsulphone **1i**, *via* its ring cleavage by 2N NaOH-CTACl, at 70°C, to the free acid **2i**. This acid can be directly converted into its methyl ester **3** with the use of methanol in the presence of Amberlyst 15 ion exchange resin[15] (54% overall yield from **1i**). Treatment of the sulfone **3** with excess 6% Na(Hg) in methanol in the presence of 4 eq of disodium hydrogen phosphate[16] at 0 °C, led 60% of desulfonylation product **4**.



Scheme 2

In conclusion, this procedure represents an important utilization of cyclic β-keto sulfones as source of valuable polyfunctionalized molecules.

Experimental

General. All ^{1}H NMR were recorded in CDCl$_3$ at 200 MHz on a Varian Gemini instrument; *J* values are given in Hz. IR spectra were recorded with a Perkin Elmer 257 spectrometer. Mass spectra were performed with EI technique. Reaction progress was monitored by TLC. Elementary analyses were performed using a C, H, S Analyzer Model 185 from Hewlett-Packard. All the products were purified by flash chromatography[17] on Merck silica gel (0.040-0.063 mm). The β-keto sulfones **1a-i** were prepared by standard methods.[4,11]

General Procedure for the Ring Cleavage of Cyclic β-Keto Phenylsulfones 1a-h. To a mixture of β-keto phenylsulphone **1** (2 mmol), in NaOH 2N (2.5 ml), was added, at room temperature, cetyltrimethylammonium chloride (CTACl, 0.6 ml, 0.47 mmol). The mixture was stirred at 70 °C for 6-10 h (TLC), then cooled, acidified with 2N HCl, and extracted with dichloromethane (3 x 20 ml). The organic phase was dried over magnesium sulphate, concentrated, and the crude product was purified by flash chromatography (hexane/EtOAc, 1:1) affording the pure compound **2a-h**.

2a: ν_{max}/cm^{-1} 2900 (OH), 1700, 1370; ^{1}H NMR (200 MHz) δ 1.62-1.9 (m, 4H), 2.35 (t, 2H, J = 6.9 Hz), 3.12 (m, 2H), 7.5-7.73 (m, 3H), 7.85-7.95 (m, 2H). MS (EI) m/e 242 (M^+), 141, 125, 94, 87, 77, 73, 65, 60 (100%), 51, 45. Anal. Calcd. for $C_{11}H_{14}O_4S$: C, 54.53; H, 5.82; S, 5.82. Found: C, 54.65; H, 5.97; S, 5.68.

2b: ν_{max}/cm^{-1} 2900 (OH), 1705, 1380; ^{1}H NMR (200 MHz) δ 1.22-1.8 (m, 6H), 2.3 (t, 2H, J = 6.9 Hz), 3.08 (m, 2H), 7.5-7.7 (m, 3H), 7.82-7.94 (m, 2H). MS (EI) m/e 256 (M^+), 141, 125, 94, 87, 77, 73, 60 (100%), 51, 45, 41. Anal. Calcd. for $C_{12}H_{16}O_4S$: C, 56.23; H, 6.29; S, 12.50. Found: C, 56.08; H, 6.43; S, 12.37.

2c: ν_{max}/cm^{-1} 2940 (OH), 1690, 1370; ^{1}H NMR (200 MHz) δ 1.15-1.85 (m, 8H), 2.35 (t, 2H, J = 7.3 Hz); 3.1 (t, 2H, J = 7.9 Hz), 7.5-7.7 (m, 3H), 7.8-8.0 (m, 2H). MS (EI) m/e 270 (M^+), 141, 129, 125, 101, 94, 87, 77, 73, 60 (100%), 51, 45. Anal. Calcd. for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71; S, 11.86. Found: C, 57.97; H, 6.88; S, 11.68.

2d: ν_{max}/cm^{-1} 2950 (OH), 1680, 1370; ^{1}H NMR (200 MHz) δ 1.11 (m, 18H), 2.35 (t, 2H, J = 7.4 Hz), 3.08 (m, 2H), 7.5-7.7 (m, 3H), 7.88-7.95 (m, 2H). MS (EI) m/e 340 (M^+), 199, 171, 157, 141, 129, 125, 94, 85, 77, 73 (100%), 71, 65, 61, 51. Anal. Calcd. for $C_{18}H_{28}O_4S$: C, 63.50; H, 8.29; S, 9.42. Found: C, 63.77; H, 8.44; S, 9.28.

2e: ν_{max}/cm^{-1} 2930 (OH), 1695, 1370; ^{1}H NMR (200 MHz) δ 1.3-2.0 (m, 4H), 2.15 (t, 2H, J = 6.9 Hz), 2.6-2.8 (m, 1H), 3.15-3.35 (m, 2H), 7.0-7.95 (m, 10H). MS (EI) m/e 332 (M^+), 241, 191, 141, 94, 91 (100%), 87, 77, 73, 60 (100%), 51, 45. Anal. Calcd. for $C_{18}H_{20}O_4S$: C, 65.04; H, 6.06; S, 9.64. Found: C, 65.20; H, 5.94; S, 9.41.

2f: ν_{max}/cm^{-1} 2900 (OH), 1690, 1365; ^{1}H NMR (200 MHz) δ 1.2-1.95 (m, 6H), 2.15 (t, 2H, J = 6.9 Hz), 2.6-2.8 (m, 1H), 3.15-3.35 (m, 2H), 7.0-7.95 (m, 10H). MS (EI) m/e 346 (M^+), 255, 205, 141, 125, 94, 91, 87, 77, 65, 60 (100%), 51, 45, 41. Anal. Calcd. for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40; S, 9.25. Found: C, 66.00; H, 6.58; S, 9.08.

2g: ν_{max}/cm^{-1} 2900 (OH), 1695, 1370; ^{1}H NMR (200 MHz) δ 1.35-1.75 (m, 6H), 2.3 (t, 2H, J = 6.9 Hz), 2.52-2.68 (m, 4H), 2.92-3.07 (m, 1H), 5.0-5.12 (m, 2H), 5.6-5.83 (m, 1H), 7.5-7.72 (m, 3H), 7.82-7.92 (m, 2H). MS (EI) m/e 296 (M^+), 245, 195, 141, 125, 101, 94, 87, 73, 60 (100%), 51, 45. Anal. Calcd. for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80; S, 10.82. Found: C, 60.98; H, 6.97; S, 10.70.

2h: ν_{max}/cm^{-1} 2900 (OH), 1690, 1370; ^{1}H NMR (200 MHz) δ 1.25 (d, 3H, J = 7.0 Hz), 1.15-1.75 (m, 6H), 2.38 (t, 2H, J = 6.9 Hz), 2.98-3.1 (m, 1H), 7.5-7.72 (m, 3H), 7.85-7.95 (m, 2H). MS (EI) m/e 270 (M^+), 169, 142, 141, 129, 125, 101, 94, 87, 77, 73, 60 (100%), 51, 45. Anal. Calcd. for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71; S, 11.86. Found: C, 57.95; H, 6.59; S, 11.95.

Preparation of Methyl 6-Phenylsulfone-9-oxodecanoate (3). To a mixture of β-keto phenylsulphone **1i** (0.92 g, 3 mmol), in NaOH 2N (20 ml), was added, at room temperature, cetyltrimethylammonium chloride (CTACl, 0.4 ml, 0.32 mmol). The mixture was stirred at 70 °C for 10 h (TLC), then cooled, acidified with 2N HCl, and extracted with dichloromethane (3 x 20 ml). The organic phase was dried over magnesium sulphate. Removal of the solvent afforded the crude acid **2i** that was dissolved in methanol (10 ml) and stirred 15 h in the presence of Amberlyst 15 ion exchange resin (0.4 g). The resin was removed by filtration, and after evaporation of the solvent, the crude ester was purified by flash chromatography (hexane/EtOAc, 8:2), affording 0.55 g (54%) of the compound **3** as an oil: ν_{max}/cm^{-1} 1735, 1710 (CO), 1370; ^1H NMR (200 MHz) δ 1.16-1.95 (m, 8H), 2.15 (s, 3H), 2.15-2.7 (m, 4H), 3.0-3.13 (m, 1H), 3.68 (s, 3H), 7.5-7.7 (m, 3H), 7.82-7.95 (m, 2H). Anal. Calcd. for $C_{17}H_{24}O_5S$: C, 59.97; H, 7.10; S, 9.4. Found: C, 60.10; H, 7.00; S, 9.28.

Desulfonylation of (3) to Methyl 9-Oxodecanoate (4). To a solution of 0.51 g (1.5 mmol) of **3** and 6 mmol of anhydrous disodium hydrogen phosphate in 15 ml of dry methanol, cooled at 0 °C, was added 2.25 g of pulverized 6% sodium amalgam. The solution was stirred for 30 min at 0 °C, then for 30 min at room temperature. The mixture was poured into water (50 ml) and extracted with Et_2O (3 x 20 ml). The organic phase was dried ($MgSO_4$), evaporated and the crude product purified by flash chromatography (hexane/EtOAc, 8:2), yielding 0.18 g (60 %) of the pure product **4**. Bp 70 °C/0.4 torr; ν_{max}/cm^{-1} 1735, 1710 (CO); ^1H NMR (200 MHz) δ 1.15-1.90 (m, 10H), 2.13 (s, 3H), 2.10-2.65 (m, 4H), 3.65 (s, 3H). MS (EI) m/e 158 (M^+ -42), 127, 116, 101, 84, 74, 57 (100%), 42. Anal. Calcd. for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07; Found: C, 66.03; H, 9.99.

Acknowledgement: The authors thank MURST of Italy, University of Camerino, and C.N.R.-Italy for the financial assistance.

References

1 Corey , E. J.; Cheng, X-M. *The Logic of Chemical Synthesis*, John Wiley and Sons: New York, 1989.

2 Lindberg, T. *Strategies and Tactics in Organic Synthesis*, Academic Press, Inc.; San Diego, 1994, vol. 1.

3 Ho, T. L. *Tactics of Organic Synthesis*, John Wiley and Sons: New York, 1994.

4 Simpkins, N. S. *Sulphones in Organic Synthesis*, Pergamon Press: Oxford, 1994.

5 Julia , M.; Paris, J.-M. *Tetrahedron Lett.* **1973**, 4833.

6 Trost, B. M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107.

7 Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019.

8 Stach, H.; Hesse, M. *Tetrahedron* **1988**, *44*, 1573.

9 Bhat , V.; Cookson, R. C. *J. Chem. Soc., Chem. Commun.* **1981**, 1123.

10 Scholz, D. *Liebigs Ann. Chem.* **1984**, 264.

11 The β-keto sulphones **1a-i** were prepared by standard methods: Ballini, R.; Bosica, G.; Marcantoni, E. *Tetrahedron* **1996**, *52*, 10705 and references cited therein.

12 (a) Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453; (b) Block, E. *Reactions of Organosulfur Compounds*, Academic Press: New York, 1978; (c) Field, L. *Synthesis* **1978**, 713.

13 Roberts, S. M.; Scheinmann, F. *New Synthetic Routes to Prostaglandines and Tromboxanes*, Academic Press: London, 1982

14 Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887 and references cited therein.

15 Petrini, M.; Ballini, R.; Rosini, G. *Synthetic Commun.* **1988**, *18*, 847

16 Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, *39*, 3477.

17 Still, W. C.; Kahan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(*Received in UK* 24 *February* 1997; *accepted* 10 *April* 1997)