Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 1709–1717

TETRAHEDRON: *ASYMMETRY*

Enantiospecific synthesis of substituted 1-norbornanesulfonic acids and 1-norbornanesulfenic and sulfonic acid derivatives†

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Received 23 November 1999; revised 22 March 2000; accepted 24 March 2000

Abstract

New homochiral 1-norbornanesulfenic and sulfonic acid derivatives **2**–**7**, as well as the sulfonic acids **8**, are easily synthesised starting from 2-methylene-1-norbornylthiotriflates **1**. This new class of homochiral bridgehead thiosulfonates was prepared by us from naturally occurring (+)-camphor and (–)-fenchone. Nucleophilic substitution at the sulfenyl sulfur atom is the key step for this synthetic strategy.

1. Introduction

Homochiral camphor-based derivatives have been extensively used in asymmetric synthesis either as chiral auxiliaries (e.g. Oppolzer's sultam) or ligands in enantioselective catalysis.[1–6] Among the chiral catalysts, DAIB[2] and related compounds have played a central role for enantioselective addition of diethylzinc to aldehydes.

In recent years, many difunctional sulfur derivatives have gained interest as ligands in asymmetric catalysis.[7–15] Moreover, β-aminothiols have shown a remarkable enhancement of reaction rate, enantioselectivity and asymmetric amplification over the corresponding β-aminoalcohols with the same structure.[10] Some new difunctional camphor sulfur derivatives have recently proved to be effective chiral catalysts in asymmetric epoxidation[11,12] or aziridination,[13] enantioselective addition of dialkylzinc to aldehydes[14] and ketones,[15] and chiral controllers for stereoselective Pauson–Khand reactions.[16] In addition, primary 2-hydroxy-3-camphorsulfenamides have recently been used as chiral auxiliaries in the enantioselective synthesis of primary amines with high *ee*.[17] Most

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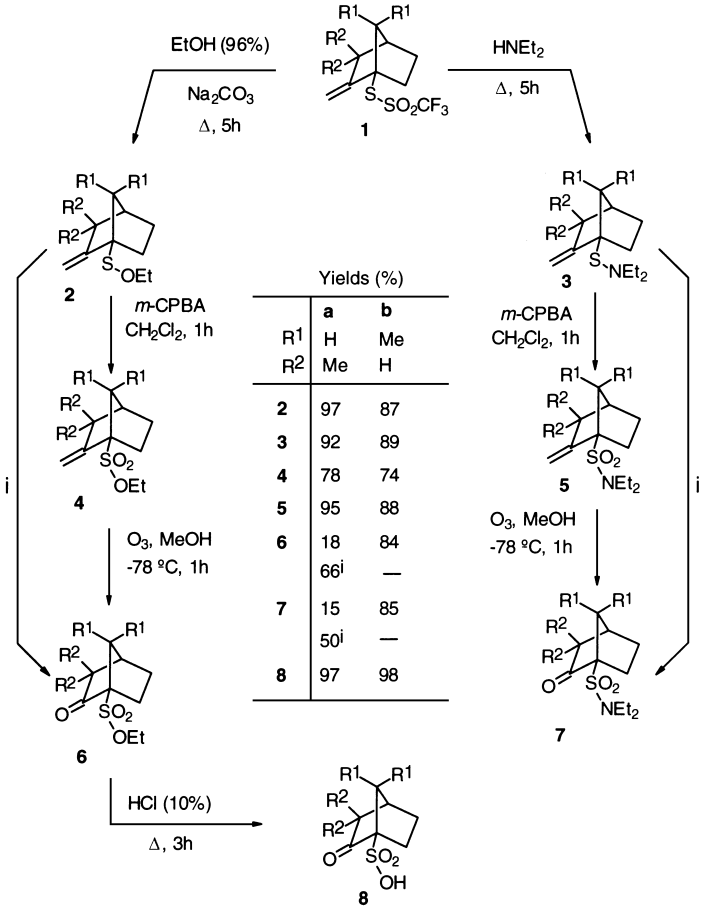
† Dedicated to Professor José Luis Soto on the occasion of his 70th birthday.

0957-4166/00/$ - see front matter
PII: S0957-4166(00)00122-1

of this type of compound reported to date have been synthesised from 10-camphorsulfonic acid (CSA) as the chiral starting material. This is obviously due to the availability of this important acid and to the lack of straightforward synthetic routes to other similar sulfur compounds. Thus, only a few chiral sulfonic acids or their derivatives have been reported in the literature,[18] CSA being the only one widely employed.[19] Therefore, the synthesis and design of new chiral camphor- or norbornane-derived compounds with a sulfur functionality are of particular interest.

2. Results and discussion

As a continuation of our studies on the chemistry and preparation of bridgehead homochiral norbornylic compounds,[20–23] we wish to report here on the enantiospecific synthesis of different substituted 2-methylene- and 2-oxo-1-norbornanesulfonic and sulfenic acid derivatives **2**–**7**, as well as sulfonic acids **8**. These compounds offer interesting possibilities for the preparation and application of chiral norbornylic compounds with a sulfur functionality in position 1. The results are summarised in Scheme 1.



Yields (%)		
	a	**b**
R^1	H	Me
R^2	Me	H
2	97	87
3	92	89
4	78	74
5	95	88
6	18	84
	66[i]	—
7	15	85
	50[i]	—
8	97	98

Scheme 1. (i) $RuCl_3$ (cat.)/$NaIO_4$, $H_2O/CH_3CN/CCl_4$

We have previously reported a simple procedure for the preparation of substituted 1-norbornyl-thiotriflates **1** and thiols[24] from commercially available (+)-camphor and (–)-fenchone. The key step for the introduction of a sulfur atom at the bridgehead position of the norbornane framework is the reaction of 1-methyl-2-norbornanethiones with trifluoromethanesulfonic anhydride.

Unlike analogous bridgehead triflates, which solvolyse via S_N1 in similar conditions,[25] the solvolysis of thiotriflates **1** in 96% EtOH takes place more mildly, under S–S bond fission, by nucleophilic attack over the sulfenyl sulfur atom, giving the bridgehead sulfenates **2**. Analogously, the solvolysis of **1** in diethylamine yields the sulfenamides **3**. This procedure constitutes a good strategy for the preparation of different functionalised 1-norbornylic sulfur derivatives.

It is noteworthy that the presence of the methylene group at C-2 in combination with all the possible different degrees of oxidation of the bridgehead-attached sulfur atom constitutes an interesting source of functionality at both C-1 and C-2 positions of the norbornane framework, which allows us to synthesise new valuable homochiral 1,2-norbornane derivatives. Thus, oxidation of **2** and **3** with MCPBA in CH_2Cl_2 gave the corresponding sulfonates **4** and sulfonamides **5**, respectively, in good yields. Homochiral 2-oxo-1-norbornanesulfonate **6b** and sulfonamide **7b** were obtained by ozonolysis of **4b** and **5b**, respectively, in excellent yields. However, the ozonisation of **4a** and **5a** under the same reaction conditions was unsuccessful, giving the corresponding epoxides as main products. Formation of epoxides has been reported in the literature in the ozonisation of hindered olefins.[26]

Preparation of **6a** and **8a** was also achieved in a single step by oxidation of **2a** and **3a**, respectively, with $RuCl_3{\cdot}H_2O/NaIO_4$ (Sharpless method).[27] However, in the case of **5a** the yield of **7a** is only moderate (50%) due to the formation of other unidentified compounds. Although one more step is required for preparation of **6b** and **7b**, ozonolysis is very clean and easy to perform. On the other hand, 2-methylene-1-norbornanesulfonates **4** and sulfonamides **5** are also of interest because the methylene group constitutes a source of both prochirality and functionality at the C-2 position.

Sulfonic acids **8** were obtained in quantitative yields by hydrolysis of sulfonates **6** in refluxing 10% hydrochloric acid. This procedure is very convenient due to its experimental simplicity since, once the reaction is finalised, evaporation of both aqueous hydrochloric acid and ethanol formed by hydrolysis gives the sulfonic acid **8** as a white solid. Recrystallisation of **8a** and **8b** from acetonitrile/carbon tetrachloride gave the pure compounds.

In summary, we have presented a facile and convenient procedure for the preparation of valuable 2-methylene- and 2-oxo-1-norbornanesulfonic (and sulfenic) acid derivatives which are promising precursors of a wide variety of chiral ligands. The major proximity of the sulfonyl group at the C-1 stereogenic center, with respect to the 10-camphorsulfonic acid and its derivatives, may be advantageous in some applications. Moreover, the intermediate sulfenamides **5** and sulfenates **4** also constitute an important class of bridgehead sulfur compounds whose properties and applications are an interesting matter of study. Further works in this area are in progress.

3. Experimental

3.1. General

NMR spectra were recorded on a Bruker-AM 300 (300 MHz for ^1H and 75 MHz for ^{13}C) spectrometer and a Bruker-AC 200 (200 MHz for ^1H and 50 MHz for ^{13}C) with TMS as internal

standard; J values are given in hertz. IR spectra were recorded on a Perkin–Elmer 781 spectrometer and a Shimadzu FTIR spectrometer. Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. Reaction solvents were distilled from an appropriate drying agent before use. Mass spectra were recorded on a GC–MS Shimadzu QP5000 (60 eV) mass spectrometer. HRMS data were obtained using a VG AutoSpec instrument. For gas chromatography, a Perkin–Elmer Sigma 300 chromatograph equipped with capillary OV 101 column was used. Molecular rotation data were recorded on a Perkin–Elmer 241 polarimeter. Concentrations are given as g/100 mL of solvent.

3.2. Typical procedure for the synthesis of sulfenates **2**

A stirred solution of thiotriflate **1** (0.94 g, 3.1 mmol) and Na_2CO_3 in suspension (1.37 g, 12.9 mmol) in 25 mL of absolute ethanol was refluxed for 24 h. After completion of the reaction, CH_2Cl_2 (50 mL) was added. The mixture was washed with H_2O (3×25 mL) and dried ($MgSO_4$). After evaporation of the solvent, the crude oil was purified by column chromatography (silica gel/pentane).

3.2.1. (1R)-Ethyl 3,3-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfenate **2a**

Yield 97%: $[\alpha]_D^{20} = -62.7$ ($c = 0.57$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.98 (s, 1H); 4,74 (s, 1H); 3.84 (q, $J = 7.0$ Hz, 2H); 2.06 (ddd, $J = 9.5$ Hz, 4.2, 2.1, 1H); 1.96 (m, 2H); 1.87–1.74 (m, 2H); 1.68–1.53 (m, 2H); 1.36–1.21 (m, 1H); 1.19 (t, $J = 7.0$ Hz, 3H); 1.10 (s, 3H); 1.05 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 101.2, 75.9, 65.9, 46.4, 43.9, 43.1, 31.8, 29.3, 26.0, 24.9, 16.2 ppm. IR (CCl_4) ν 3080, 1660, 1460, 1390, 1290, 1110, 1030, 900 cm^{-1}. MS m/z 212 (33), 183 (5), 169 (82), 167 (48), 141 (9), 125 (22), 111 (13), 105 (26), 93 (45), 91 (52), 79 (34), 77 (30), 69 (28), 65 (20), 59 (28), 41 (100). HRMS (EI): calculated for $C_{12}H_{20}OS$ 212.1235 (M^+), found 212.1234.

3.2.2. (1S)-Ethyl 7,7-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfenate **2b**

Yield 87%: $[\alpha]_D^{20} = -99.7$ ($c = 0.10$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (t, $J = 2.3$ Hz, 1H); 4.84 (t, $J = 1.9$ Hz, 1H); 3.78 (q, $J = 7.0$ Hz, 2H); 2.47 (dm, $J = 16.0$ Hz, 1H); 2.15–1.75 (m, 5H); 1.52–1.25 (m, 1H); 1.15 (t, $J = 7.0$ Hz, 3H); 1.06 (s, 3H); 0.89 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.2, 105.4, 75.9, 69.6, 50.0, 43.9, 37.2, 31.8, 27.8, 20.3, 19.7, 16.1 ppm. IR (CCl_4) ν 3100, 1660, 1470, 1450, 1390, 1020, 900 cm^{-1}. MS m/z 212 (35), 167 (48), 157 (22), 141 (5), 133 (18), 125 (19), 111 (20), 107 (20), 105 (21), 93 (29), 91 (49), 77 (29), 69 (56), 55 (19), 41 (100). HRMS (EI): calculated for $C_{12}H_{20}OS$ 212.1235 (M^+), found 212.1232.

3.3. Typical procedure for the synthesis of sulfenamides **3**

A solution of the corresponding thiotriflate **1** (0.90 g, 3.0 mmol) in diethylamine (20 mL) was heated for 5 h (55°C). After completion of the reaction and evaporation of the diethylamine, pentane (20 mL) was added. The mixture was washed with H_2O (3×25 mL) and dried (Na_2CO_3). After evaporation of the solvent the crude oil was purified by column chromatography (silica gel/pentane).

3.3.1. (1R)-N,N-Diethyl-3,3-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfenamide **3a**

Yield 92%: $[\alpha]_D^{20} = -45.8$ ($c = 0.73$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.84 (s, 1H); 4.67 (s, 1H); 2.93 (q, $J = 7.0$ Hz, 4H); 2.00–1.73 (m, 5H); 1.68–1.49 (m, 2H); 1.10 (t, $J = 7$ Hz, 6H); 1.06 (s,

3H); 1.04 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 100.6, 63.9, 52.7, 46.2, 44.3, 43.6, 32.8, 29.3, 26.1, 25.3, 13.5 ppm. IR (CCl_4) ν 3100, 1660, 1470, 1390, 1300, 1110, 1030, 900 cm^{-1}. MS m/z 239 (46), 224 (12), 206 (9), 170 (22), 151 (11), 133 (14), 125 (30), 113 (15), 105 (28), 93 (30), 91 (44), 77 (28), 72 (99), 69 (20), 58 (100), 43 (26), 41 (95). HRMS (EI): calculated for $C_{14}H_{25}NS$ 239.1708 (M^+), found 239.1701.

3.3.2. (1S)-N,N-Diethyl-7,7-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfenamide ***3b***

Yield 89%: $[\alpha]_D^{20} = -45.5$ ($c = 0.54$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 (s, 1H); 4.79 (s, 1H); 2.96 (q, $J = 7.1$ Hz, 4H); 2.44 (dm, $J = 16.0$ Hz, 1H); 2.31 (td, $J = 12.0$, 4.0 Hz, 1H); 1.98 (d, $J = 16.0$ Hz, 1H); 1.88 (m, 1H); 1.75 (m, 1H); 1.46–1.23 (m, 2H); 1.08 (t, $J = 7.1$ Hz, 6H); 1.05 (s, 3H); 0.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 105.1, 67.7, 52.6, 49.2, 47.6, 43.8, 37.2, 32.4, 27.9, 20.1, 20.0, 13.1 ppm. IR (CCl_4) ν 3100, 1660, 1460, 1390, 1310, 1290, 1180, 900 cm^{-1}. MS m/z 239 (27), 224 (6), 206 (8), 167 (6), 125 (17), 105 (15), 91 (30), 77 (18), 72 (100), 69 (32), 58 (41), 43 (25), 41 (71). HRMS (EI): calculated for $C_{14}H_{25}NS$ 239.1708 (M^+), found 239.1708.

3.4. Typical procedure for the synthesis of sulfonates ***4*** *and sulfonamides* ***5***

A solution of **2** or **3** (3.8 mmol) and *m*-CPBA (60%) (2.18 g, 7.6 mmol) in 20 mL of CH_2Cl_2 was stirred for 2 h. After completion of the reaction, the mixture was washed with 5% aqueous $Na_2S_2O_3$ (2×15 mL), aqueous saturated solution of $NaHCO_3$ (2×20 mL) and dried over $MgSO_4$. After evaporation of the solvent the crude oil was purified by column chromatography.

3.4.1. (1R)-Ethyl 3,3-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfonate ***4a***

Purified by column chromatography (silica gel/CH_2Cl_2). Yield 78%: $[\alpha]_D^{20} = +103.3$ ($c = 0.49$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.39 (s, 1H); 4.88 (s, 1H); 4.33 (m, 2H); 2.38 (m, 2H); 2.03 (m, 1H); 1.95–1.55 (m, 4H); 1.38 (t, $J = 7.1$ Hz, 3H); 1.10 (s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.5, 104.5, 73.0, 66.0, 46.4, 44.0, 40.6, 314, 29.3, 25.9, 24.6, 15.4 ppm. IR (CCl_4) ν 3090, 1660, 1460, 1340, 1190, 1140, 1020, 910 cm^{-1}. MS m/z 20 ($M^{+\cdot}$–44, 2), 173 (5), 134 (56), 119 (88), 106 (100), 105 (36), 93 (30), 91 (63), 79 (25), 77 (23), 67 (16), 55. (17), 41 (52). HRMS (FAB): calculated for $C_{12}H_{21}O_3S$ 245.1211 $(M+H)^+$, found 245.1209.

3.4.2. (1S)-Ethyl 7,7-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfonate ***4b***

Purified by column chromatography (silica gel/CH_2Cl_2). Yield 74%: $[\alpha]_D^{20} = +9.1$ ($c = 1.70$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 (s, 1H); 5.01 (s, 1H); 4.37 (m, 2H); 2.66–2.46 (m, 2H); 2.07–1.77 (m, 4H); 1.39–1.29 (m, 1H); 1.37 (t, $J = 7.0$ Hz, 3H); 1.23 (s, 3H); 1.17 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.5, 108.6, 75.3, 64.9, 51.1, 46.1, 37.1, 32.1, 27.0, 21.1, 20.6, 15.4 ppm. IR (CCl_4) ν 3090, 1660, 1460, 1390, 1190, 1010, 910 cm^{-1}. MS m/z 244 (3), 216 (3), 201 (5), 173 (38), 135 (68), 134 (55), 119 (75), 105 (37), 91 (100), 79 (45), 77 (38), 69 (19), 55 (22), 43 (44), 41 (82). HRMS (EI): calculated for $C_{12}H_{20}O_3S$ 244.1133 (M^+), found 244.1141.

3.4.3. (1R)-N,N-Diethyl-3,3-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfonamide ***5a***

Purified by column chromatography (silica gel/50% CH_2Cl_2–pentane). Yield 95%: $[\alpha]_D^{20} = -18.0$ ($c = 0.25$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52 (s, 1H); 4.89 (s, 1H); 3.37 (m, 4H); 2.28–2.07 (m, 2H); 1.96 (m, 1H); 1.91–1.79 (m, 1H); 1.76–1.60 (m, 3H); 1.17 (t, $J = 7.2$ Hz, 6H); 1.11 (s, 3H); 1.10 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4, 104.7, 75.8, 46.1, 44.3, 41.1, 40.2, 31.9, 29.1, 26.0, 24.8, 14.1 ppm. IR (CCl_4) ν 3090, 1660, 1460, 1330, 1210, 1160, 1020, 930 cm^{-1}.

MS m/z 243 (M^+–28, 12), 228 (4), 192 (11), 136 (2), 121 (22), 107 (15), 93 (32), 91 (21), 72 (100), 58 (28), 41 (27). HRMS (FAB): calculated for $C_{14}H_{26}NO_2S$ 272.1684 $(M+H)^+$, found 272.1687.

*3.4.4. (1S)-*N,N*-Diethyl-7,7-dimethyl-2-methylene-1-bicyclo[2.2.1]heptanesulfonamide* ***5b***

Purified by column chromatography (silica gel/CH_2Cl_2). Yield 88%: $[\alpha]_D^{20} = -1.4$ ($c = 0.77$, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 5.42 (t, $J = 2.8$ Hz, 1H); 4.95 (t, $J = 2.5$ Hz, 1H); 3.35 (m, 4H); 2.65–2.38 (m, 2H); 2.00–1.60 (m, 5H); 1.15 (t, $J = 8.5$ Hz, 6H); 1.15 (s, 3H); 1.11 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.7, 108.3, 78.1, 50.8, 46.0, 40.8, 37.5, 32.3, 27.3, 21.4, 20.7, 13.6 ppm. IR (CCl_4) ν 3090, 1660, 1460, 1330, 1210, 1160, 1020, 930 cm^{-1}. MS m/z 271 (12), 256 (6), 228 (14), 202 (46), 192 (10), 135 (10), 119 (28), 107 (29), 93 (58), 91 (52), 72 (100), 58 (92), 41 (75). HRMS (EI): calculated for $C_{14}H_{25}NO_2S$ 271.1606 (M^+), found 271.1599.

3.5. Synthesis of (1R)-ethyl 3,3-dimethyl-2-oxo-1-bicyclo[2.2.1]heptanesulfonate ***6a***

To a solution of sulfenate **2a** (0.54 g, 2.5 mmol) in a mixture of CCl_4 (20 mL), MeCN (20 mL) and H_2O (30 mL) were added $NaIO_4$ (0.55 g, 25.4 mmol) and $RuCl_3 \cdot H_2O$ (0.2 g, 0.09 mmol). After it was heated for 24 h at 40°C, the reaction mixture was diluted with H_2O (30 mL) and extracted with CH_2Cl_2 (3×20 mL). The organic layer was washed with H_2O (2×20 mL) and dried ($MgSO_4$). After evaporation of the solvent, the crude was purified by column chromatography (silica gel/20% CH_2Cl_2–pentane). Yield 0.40 g (66%): mp = 83.3–83.9°C. $[\alpha]_D^{20} = +22.1$ ($c = 0.52$, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 4.49 (m, 2H); 2.50–2.31 (m, 3H); 2.09 (dd, $J = 10.6$, 1.8 Hz, 1H); 1.98–1.81 (m, 3H); 1.38 (t, $J = 7.2$, 3H); 1.15 (s, 3H); 1.09 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 75.5, 68.1, 49.0, 44.6, 38.2, 27.4, 24.3, 23.4, 21.5, 15.4 ppm. FTIR (CCl_4) ν 1762, 1464, 1356, 1184, 1003, 922 cm^{-1}. MS m/z 202 (M^+–44, 2), 176 (6), 148 (14), 108 (20), 93 (10), 69 (100), 41 (36). HRMS (EI): calculated for $C_{11}H_{18}O_4S$ 246.0926 (M^+), found 246.0932.

3.6. Synthesis of (1S)-ethyl 7,7-dimethyl-2-oxo-1-bicyclo[2.2.1]heptanesulfonate ***6b***

A solution of corresponding sulfonate **4b** (0.62 g, 2.5 mmol) in 30 mL of methanol cooled to –78°C was ozonised for 1 h. After this time, dimethyl sulfide (0.4 mL, 5.4 mmol) was added. The reaction mixture was diluted with H_2O (40 mL) and extracted with CH_2Cl_2 (4×25 mL). The organic layer was washed with H_2O (2×20 mL) and dried ($MgSO_4$). After evaporation of the solvent, the crude was purified by crystallisation from hexane. Yield 0.52 g (84%): mp = 52.9–53.8°C. $[\alpha]_D^{20} = -30.3$ ($c = 0.52$, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 4.51 (m, 2H); 2.67–2.52 (m, 2H); 2.25–2.11 (m, 2H); 2.05–1.92 (m, 1H); 2.00 (d, $J = 19.0$ Hz, 1H); 1.56–1.45 (m, 1H); 1.38 (t, $J = 7.0$ Hz, 3H); 1.29 (s, 3H); 1.23 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 206.1, 79.3, 67.8, 50.1, 44.2, 43.3, 26.9, 26.6, 21.1, 20.7, 15.4 ppm. FTIR (CCl_4) ν 1761, 1352, 1180, 997, 920 cm^{-1}. MS m/z 203 (M^+–43, 5), 202 (7), 138 (26), 137 (20), 136 (22), 121 (15), 109 (30), 93 (50), 79 (29), 69 (49), 67 (89), 41 (100). HRMS (FAB): calculated for $C_{11}H_{19}O_4S$ 247.1004 $(M+H)^+$, found 247.1007.

*3.7. Synthesis of (1R)-*N,N*-diethyl-3,3-dimethyl-2-oxo-1-bicyclo[2.2.1]heptanesulfonamide* ***7a***

To a solution of corresponding sulfenamide **3a** (0.56 g, 2.6 mmol) in a mixture of CCl_4 (20 mL), MeCN (20 mL) and H_2O (30 mL) were added $NaIO_4$ (0.56 g, 26.4 mmol) and $RuCl_3 \cdot H_2O$

(0.02 g, 0.09 mmol). After it was stirred for 5 h, the reaction mixture was diluted with H_2O (40 mL) and extracted with CH_2Cl_2 (3×20 mL). The organic layer was washed with H_2O (2×20 mL) and dried ($MgSO_4$). After evaporation of the solvent, the crude was purified by column chromatography (silica gel/40% CH_2Cl_2–pentane). Yield 0.35 g (50%): $[\alpha]_D^{20} = 7.9$ ($c = 1.07$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.55–3.35 (m, 4H); 2.48–2.32 (m, 2H); 2.29 (m, 1H); 2.07 (d, $J = 10.7$ Hz, 1H); 1.99–1.70 (m, 3H); 1.18 (t, $J = 7.0$ Hz, 6H); 1.13 (s, 3H); 1.08 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) 212.1, 78.3, 49.1, 44.2, 41.3, 38.6, 27.6, 24.5, 23.3, 21.5, 14.5 ppm. FTIR (CCl_4) ν 1747, 1326, 1137 cm^{-1}. MS m/z 258 (M^+–15, 6), 123 (5), 109 (10), 93 (15), 72 (100), 67 (20), 41 (23). HRMS (FAB): calculated for $C_{13}H_{24}NO_3S$ 274.1477 $(M+H)^+$, found 274.1467.

3.8. Synthesis of (1S)-N,N-diethyl-7,7-dimethyl-2-oxo-1-bicyclo[2.2.1]heptanesulfonamide 7b

A solution of sulfonamide **5b** (0.61 g, 2.5 mmol) in 30 mL of methanol cooled to –78°C was ozonised for 1 h. After this time dimethyl sulfide (0.4 mL, 5.4 mmol) was added (0.3 mL). The reaction mixture was diluted with H_2O (40 mL) and extracted with CH_2Cl_2 (4×25 mL). The organic layer was washed (2×20 mL) and dried ($MgSO_4$). After evaporation of the solvent, the crude was purified by crystallisation from hexane. Yield 0.58 g (85%): mp = 96.8–98.7°C. $[\alpha]_D^{20} = -28.8$ ($c = 0.61$, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.46 (m, 4H); 2.63–2.49 (m, 2H); 2.23–2.06 (m, 2H); 1.93 (d, $J = 18.7$ Hz, 1H); 1.81 (ddd, $J = 13.2$ Hz, 9.6, 4.4, 1H); 1.45 (ddd, $J = 12.1$ Hz, 9.2, 4.0, 1H); 1.28 (s, 3H); 1.24 (s, 3H); 1.17 (t, $J = 7$ Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) 208.2, 81.9, 50.5, 44.0, 43.6, 41.1, 26.9, 26.7, 21.5, 21.1, 14.4 ppm. FTIR (KBr) ν 1760, 1360, 1340, 1210, 1150, 1030, 890 cm^{-1}. MS m/z 258 (M^+–15, 7), 194 (3), 137 (6), 123 (7), 109 (15), 95 (11), 72 (100), 71 (34), 67 (22), 41 (22). HRMS (EI): calculated for $C_{13}H_{23}NO_3S$ 273.1399 (M^+), found 273.1394.

3.9. Typical procedure for the synthesis of sulfonic acid 8

A stirred suspension of sulfonate **6** (0.50 g, 2.3 mmol) in 20 mL of HCl (10%) was refluxed for 2 h. After evaporation of the solvent, the crude solid was washed with CH_2Cl_2 and recrystallised from acetonitrile/carbon tetrachloride yielding the pure product.

3.9.1. (1R)-3,3-Dimethyl-2-oxo-1-bicyclo[2.2.1]heptanesulfonic acid 8a

Yield (97%): mp = 206.3–213.8°C (dec). $[\alpha]_D^{20} = +23.6$ ($c = 0.27$, CH_3CN). ^{1}H NMR (200 MHz, D_2O) δ 2.44–2.20 (m, 3H); 2.06–1.63 (m, 4H); 1.10 (s, 3H), 1.06 (s, 3H) ppm. ^{13}C NMR (75 MHz, CD_3CN) δ 213.1, 76.0, 49.8, 45.3, 38.0, 28.1, 24.0, 23.6, 21.8 ppm. FTIR (KBr) ν 3530, 3419, 1741, 1161 cm^{-1}. MS m/z 148 (M^+–70, 10), 108 (6), 83 (7), 69 (43), 41 (100). HRMS (EI): calculated for $C_9H_{14}O_4S$ 218.0613 (M^+), found 218.0605.

3.9.2. (1S)-7,7-Dimethyl-2-oxo-1-bicyclo[2.2.1]heptanesulfonic acid 8b

Yield (96%): mp = 200.1–206.4°C (dec). $[\alpha]_D^{20} = -32.5$ ($c = 0.25$, CH_3OH). ^{1}H NMR (200 MHz, D_2O) δ 2.73–2.38 (m, 2H); 2.26–2.13 (m, 1H); 2.06 (d, $J = 18.6$ Hz, 1H); 1.93–1.76 (m, 1H); 1.61–1.42 (m, 1H); 1.25 (s, 3H); 1.16 (s, 3H) ppm. ^{13}C NMR (50 MHz, D_2O) δ 215.5, 78.9, 50.0, 44.9, 44.3, 28.0, 26.8, 21.8, 21.3 ppm. FTIR (KBr) ν 3413, 1726, 1452, 1205 cm^{-1}. MS m/z 218 (5), 175 (8), 148 (11), 136 (12), 121 (10), 109 (12), 93 (22), 69 (100), 67 (95), 41 (37). HRMS (EI): calculated for $C_9H_{14}O_4S$ 218.0613 (M^+), found 218.0616.

Acknowledgements

We thank the DGCYT (Spain) for financial support of this work (Grant PB 97-0264).

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