

## Preparation of [ $^{13}\text{C}_2$ ]DMSO

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### SUMMARY

An expedient two-step synthesis of [ $^{13}\text{C}_2$ ]DMSO, starting from commercially available [ $^{13}\text{C}$ ]methyl iodide, is described. The product obtained in 57% yield is of high chemical ( $\geq 99\%$ ) and isotopic purity (= 98%  $^{13}\text{C}_2$ , 2%  $^{13}\text{C}_1$ ), as judged by NMR-spectroscopy and a GC-MS-assay.

Key Words: [ $^{13}\text{C}_2$ ]dimethyl sulfide, selective oxidation of dimethyl sulfide,  $\text{AX}_3\text{A}'\text{X}'_3$ - spin system.

### INTRODUCTION

Recently, we made the discovery that a  $\gamma,\delta$ -epoxyketone undergoes a seemingly unprecedented reaction with the dimethyl anion in DMSO, yielding a product which possesses two more carbon atoms than the starting material (1) (for related previous observations see (2)). In the context of finding out about the possible reaction mechanism, we became interested whether the two extra carbon atoms originate from a single, or two separate molecules of DMSO. Since the classical method to address this kind of problem consists in a cross-over experiment (3), we needed a sample of doubly labeled [ $^{13}\text{C}_2$ ]DMSO as one of the components of the solvent (the other half consisting of commercially available [ $^{12}\text{C}_2$ ]DMSO). Somewhat surprisingly, a computer-assisted literature search<sup>1</sup> revealed that no report on the preparation of the required [ $^{13}\text{C}_2$ ]DMSO exists; therefore, the method described below was developed<sup>2</sup>.

### RESULTS AND DISCUSSION

Since [ $^{13}\text{C}$ ]methyl iodide is commercially available in highly enriched quality (99%  $^{13}\text{C}$ ), the following synthetic scheme was adopted: in the first step, [ $^{13}\text{C}$ ]methyl iodide was allowed to react with an aq. solution of  $\text{Na}_2\text{S}$  at  $0^\circ\text{C}$  to give [ $^{13}\text{C}_2$ ]dimethyl sulfide in 88% yield (5). The seemingly trivial second step, oxidation of this intermediate to [ $^{13}\text{C}_2$ ]DMSO, proved to be more difficult than anticipated in the planning stage of this synthesis: well-established procedures for the selective mono-oxidation of higher sulfides, such as tert.-butyl hypochlorite (6,7) or benzoyl nitrate (8), invariably furnished significant amounts of the over-oxidized compound [ $^{13}\text{C}_2$ ]dimethyl sulfone<sup>3</sup> and other byproducts as well. After many trials with unlabeled dimethyl sulfide it was found that treatment with

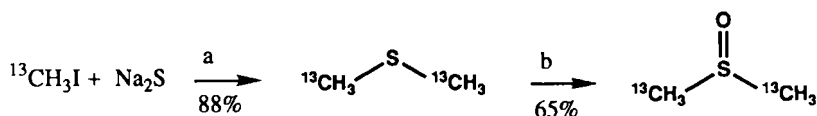
<sup>1</sup> The authors would like to thank Dr. E. Zass, ETH Zürich, for carrying out a CAS online-search for [ $^{13}\text{C}$ ] and [ $^{13}\text{C}_2$ ]DMSO which, on 15 November 1990, disclosed but a single reference ((4)).

<sup>2</sup> An altogether different route to (*R*)-enriched [ $^{13}\text{C}$ ]DMSO has been described by Pirkle and Pavlin (4).

<sup>3</sup> For our purposes [ $^{13}\text{C}_2$ ]DMSO served not only as a reagent, but as solvent as well. Therefore, the chemical purity of our preparation had to exceed 99.5%.

less than one equivalent<sup>4</sup> of 96% *m*-chloroperbenzoic acid (9) gives a product (65% yield) which is contaminated with at most 0.5% of [<sup>13</sup>C<sub>2</sub>]dimethyl sulfone (<sup>1</sup>H-NMR-evidence).

### SCHEME



Reagents: a) H<sub>2</sub>O, 0°, 4h r.t., b) 96% *m*-chloroperbenzoic acid, CH<sub>2</sub>Cl<sub>2</sub>, -78°

As expected, the product obtained gives rise to rather complex <sup>1</sup>H- and (<sup>1</sup>H-uncoupled) <sup>13</sup>C-NMR spectra (see Fig. 1 and 2), due to its AX<sub>3</sub>A'X'<sub>3</sub>-spin system (see *e.g.* (10) and references therein).

### EXPERIMENTAL

To a soln. of 6.4 g (26.4 mmol) of Na<sub>2</sub>S (*Merck, p.a.*) in 6.4 ml of H<sub>2</sub>O, contained in a 25 ml-glass tube (9 x 2 cm) were added 5.0 g (35 mmol) of [<sup>13</sup>C]methyl iodide (*Aldrich-Sigma*, isotopic purity 99%) during 30 min. at 0°C. After vigorous stirring for 4 h, 1 ml of an aq. 2.5 N NaOH soln. and 1 ml of an aq. 0.1 M Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> soln. were added. The vial was connected with a receiving flask of the same dimensions *via* an U-shaped glass tube (standard NS 14.5 joints) to give a closed system. While the receiving flask was cooled with liquid N<sub>2</sub>, the reaction vial was allowed to reach room temperature. After 70 min., the condensed material, consisting of essentially pure [<sup>13</sup>C<sub>2</sub>]dimethyl sulfide (88% yield), was warmed to -78°C and treated with 35 ml of an ethereal soln. of 2.26 g (13 mmol) 96% *m*-chloroperbenzoic acid (11) over a period of 90 min.. The mixture was allowed to reach room temperature and after adding 44 mg (0.018 mmol) of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>·5 H<sub>2</sub>O (*Fluka*, puriss.) and 2.05 g (14.9 mmol) of K<sub>2</sub>CO<sub>3</sub> (*Fluka*, puriss.) stirring was continued for an additional 16 h. The insoluble material was removed by filtration and was washed with 100 ml of CH<sub>2</sub>Cl<sub>2</sub>. The combined filtrates were evaporated and the oily residue was distilled at 100 Torr (oven temperature: ca. 170°C) in a Kugelrohr apparatus (*Büchi AG*, CH-9230 Flawil) to yield 800.7 mg (9.99 mmol, 57% over all) of more than 99% pure [<sup>13</sup>C<sub>2</sub>]DMSO as a colorless liquid.

IR: (*Perkin Elmer* 1600 FTIR, 2% in CCl<sub>4</sub>, cell length: 205μm): 2986.3 (w) [2996.4]<sup>5</sup>, 2911.4 (w) [2914.8], 1431.7 (s) [1434.4], 1411.8 (m), 1399.2 (m) [1402.1], 1303.9 (m) [1304.3], 1068.1 (vs) [1069.4], 1000.9 (s) [1010.4], 938.4 (m) [945.7], 912.1 (m) [920.3], 676.9 (m) [690.8], 646.0 (w) [660.7].

<sup>4</sup> Control experiments had shown that any excess of *m*-chloroperbenzoic acid rapidly oxidizes DMSO to dimethyl sulfone, even at -78°C.

<sup>5</sup> The values in square brackets were taken from a spectrum of a sample of unlabeled DMSO, recorded under the same conditions.

GC-MS (HP 5890 Series II GC with HP 5971A MS: EI (70 eV), column: SPT 5 (Supelco), 30 m, 0.25 mm, film thickness: 0.25 μm, flow: 0.3 m s<sup>-1</sup> He, temp. program: 37° -> 45° with 70° / min., hold at 45° for 1.5 min., then gradient with 5° / min. up to 170°): ret. time for DMSO: 5.89 min. MS: 82 (4), 81 (1), 80 (82), 66 (5), 65 (2), 64 (100), 63 (23), 48 (16), 47 (10), 46 (40), 30 (4), 16 (6). <sup>1</sup>H-NMR (Varian Gemini, 200 MHz, CDCl<sub>3</sub>): *m* centered at 2.58 ppm (see Fig. 1).

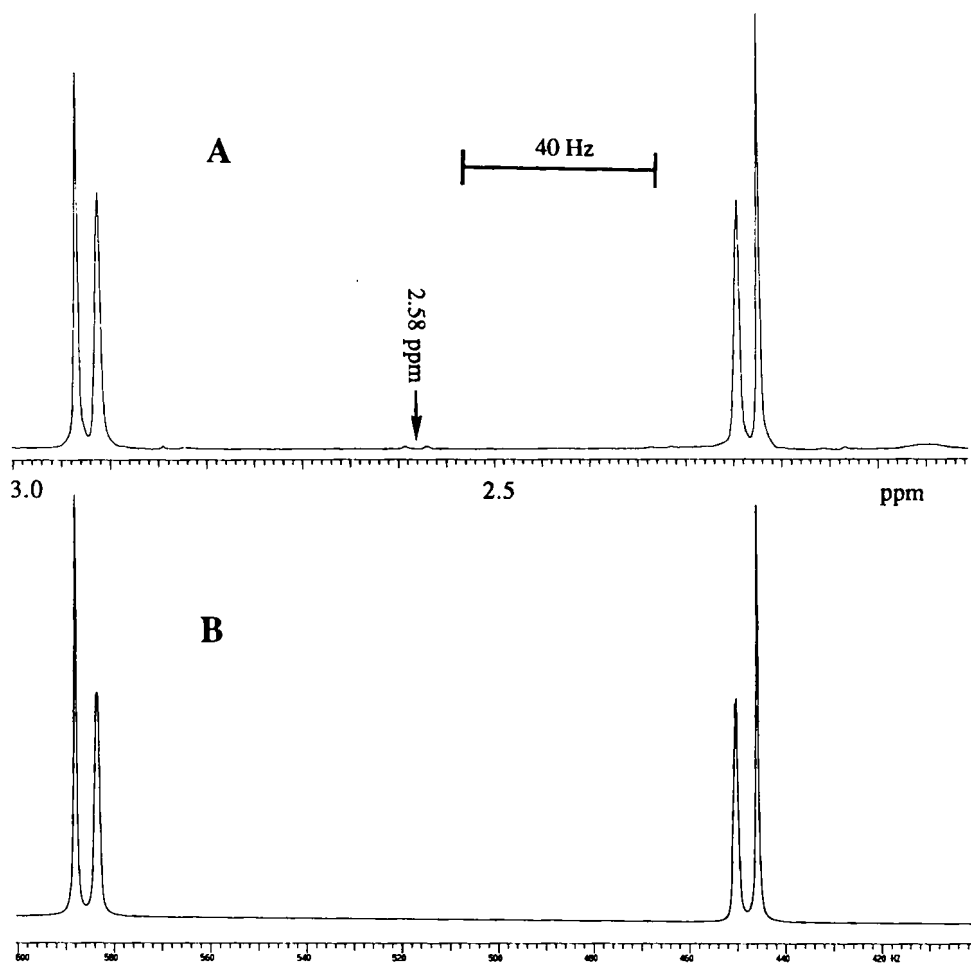


Fig. 1. A: Experimental <sup>1</sup>H-NMR spectrum of [<sup>13</sup>C<sub>2</sub>]DMSO.

B: X-Part of a spin simulation<sup>6</sup> of an AX<sub>3</sub>A'X'<sub>3</sub> spin system with J<sub>AA'</sub> = -0.1 Hz, J<sub>AX</sub> = J<sub>A'X'</sub> = 137.8 Hz, J<sub>AX'</sub> = J<sub>A'X</sub> = 4.5 Hz and J<sub>XX'</sub> = 0.4 Hz<sup>7,8</sup>.

<sup>6</sup> Carried out with the program LAOCOON, incorporated in the Varian Gemini spectrometer.

<sup>7</sup> We would like to thank PD Dr. E. Pretsch, ETH Zürich, for a helpful discussion and for a first simulation of the spectra with the aid of the program MIMER.

<sup>8</sup> Similar parameters have been found by Pirkle and Pavlin (4): J<sub>AX</sub> = 138 Hz, J<sub>AX'</sub> = 4.6 Hz, J<sub>XX'</sub> = 0.45 Hz.

$^{13}\text{C}$ -NMR (Varian Gemini, 50 MHz,  $\text{CDCl}_3$ ): broad-band  $^1\text{H}$ -decoupled: s at 40.7 ppm.  $^1\text{H}$ -undecoupled spectrum: see Fig.2.

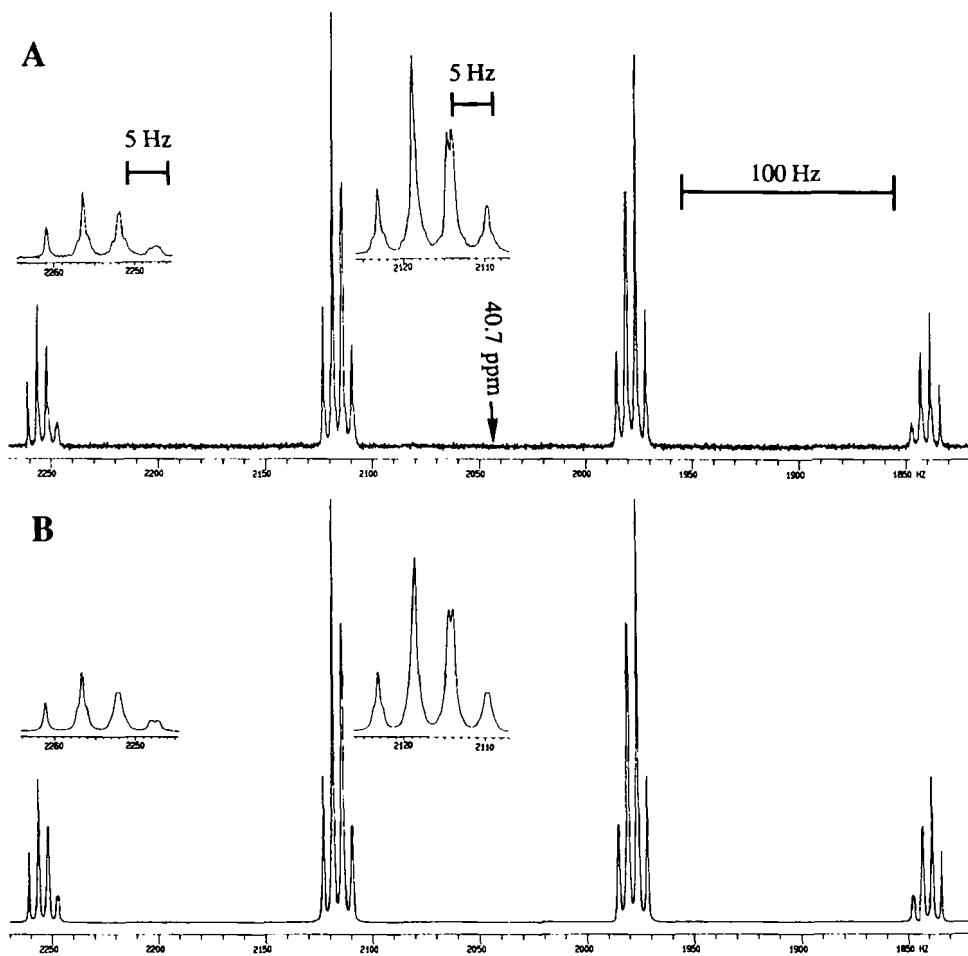


Fig. 2. A: Experimental  $^1\text{H}$ -undecoupled  $^{13}\text{C}$ -NMR spectrum of  $[\text{C}^{13}_2]\text{DMSO}$ .  
B: A-Part of the spin simulation (see Fig. 1).

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