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Synthesis and crystal structure of a novel camphor based thioacetal

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The synthesis of the very first example of a thioacetal containing two camphor skeleta is described. The acetal was prepared by treating 10-mercapto-*iso*-borneol with camphorquinone and its stereochemistry confirmed by NMR spectroscopy and X-ray crystallography.

Keywords: camphor, thioacetal

Chiral auxiliaries consisting of functionalised camphor skeleta have proven to be highly versatile in asymmetric reactions.[1,2] They are suitable for the design of conformationally rigid derivatives and are readily available. However, chiral auxiliaries containing more than one camphor skeleton are rare.[12]

We wish to report the synthesis and structure of a novel thioacetal **4** comprising of two camphor skeleta. 10-Mercapto-*iso*-borneol **2**[13] was synthesised by reducing camphor-10-sulphonyl chloride **1**[14] with LAH. The required *exo* alcohol, 10-mercapto-*iso*-borneol **2**, was separated from the *endo* isomer **3** by column chromatography and characterised by NMR spectroscopy. The acetal **4** was prepared by treating compound **2** with camphorquinone followed by subsequent purification of the compound by column chromatography. The structure was elucidated by NMR spectroscopy and confirmed by X-ray crystallography (Fig. 3).

It has been observed[15] that treatment of camphorquinone with diols, results in formation of acetals at both C-3 and C-2 positions. In this case, the C-2 position is more hindered and the thioacetalisation occurred exclusively at the C-3 position. The regioselectivity of the reaction was determined from the NMR experiments. X-ray diffraction analysis of compound **4** was undertaken so that the stereochemistry of the product could be established.

The molecular structure and absolute configuration of compound **4** is shown in Fig. 3. The structure reveals that the sulfur atom is located at the *exo* position and the oxygen atom at the *endo* position of the thioacetal moiety. The two bornane skeleta

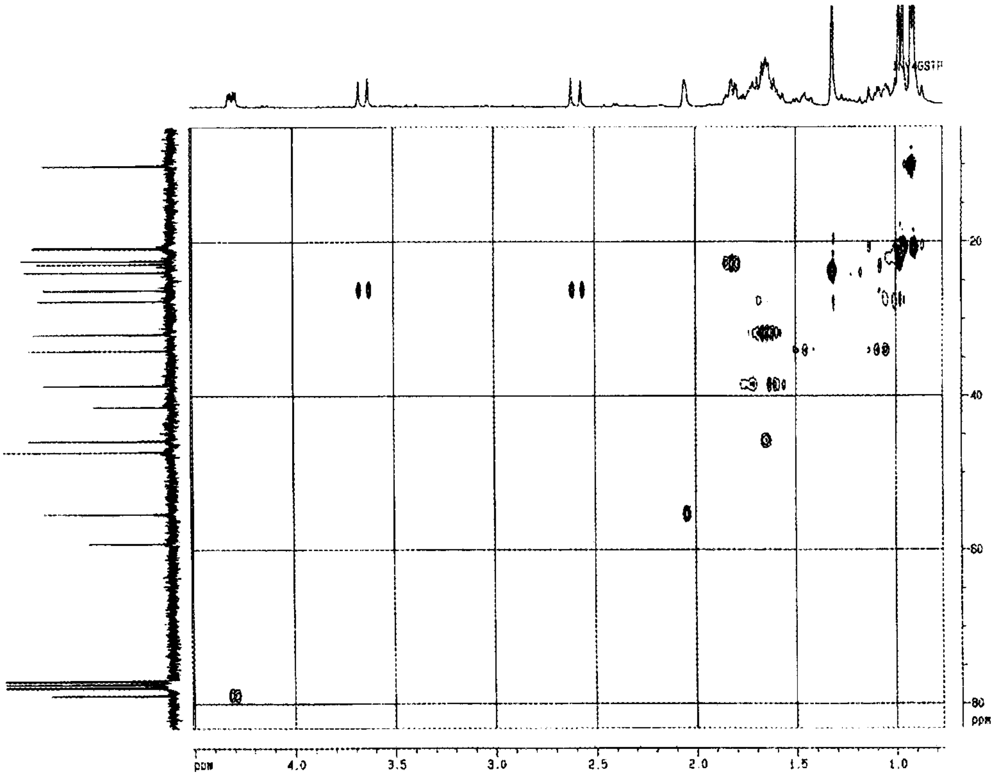

Fig. 1 HETCOR NMR spectrum of thioacetal **4**

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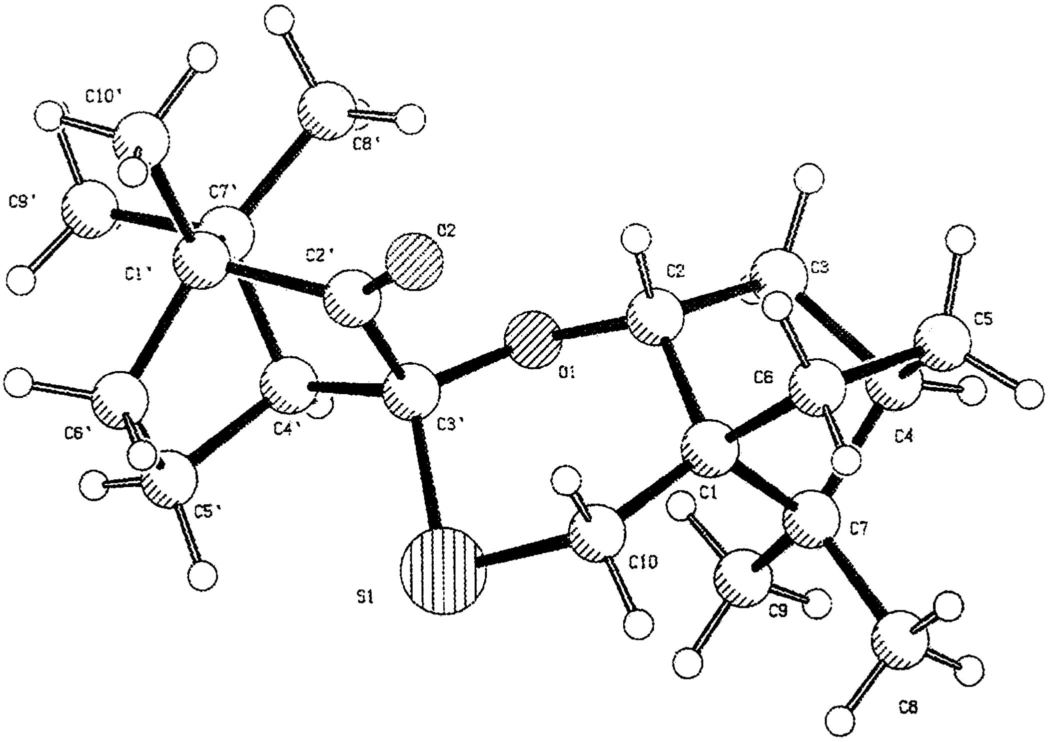


Fig. 3 An ORTEP view of the molecular structure of acetal **4**. Thermal ellipsoids are drawn at a 50% probability level.

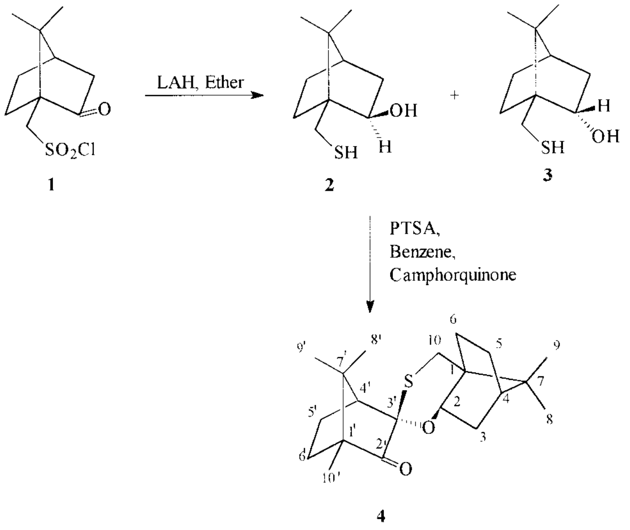
Table 1 Crystal data and structure refinement for compound **4**

Empirical formula	$C_{20}H_{30}O_2S$	
Formula weight	334.50	
Crystal system	Orthorhombic	
Space group	$P\ 2_12_12_1$	
Unit cell dimensions	a = 6.769(1)Å	α = 90°.
	b = 12.548(1) Å	β = 103.875(2)°
	c = 11.028(1)Å	
Volume	909.36(17) Å^3	γ = 90°.
Z	2	
Density (calculated)	1.222 Mg/m^3	
Absorption coefficient	0.186 mm^{-1}	
F(000)	364	
Crystal size	0.25 × 0.17 × 0.12 mm^3	
Reflections collected	4145	
Completeness to theta =	25.70° 98.2%	
Goodness-of-fit on F^2	1.011	
Final R indices [I>2sigma(I)]	R1 = 0.0434, wR2 = 0.0829	
R indices (all data)	R1 = 0.0717, wR2 = 0.0917	

have similar geometries and show no unusual features. The two six membered rings are in a boat conformation due to bridging by atoms C7 and C7′. The planes defined by the atoms Cl, C7 and C4 and the atoms Cl, C2, C3 and C4 intersect at an angle of 126.2(2)°. The planes defined by the atoms Cl′,C7′ and C4′ and the atoms Cl′, C2′, C3′ and C4′ intersect at an angle of 122.6(2)°. The bond angles involving the atoms C7 and C7′ deviate from the tetrahedral values and the bridgehead angles Cl–C7–C4 and C1′–C7′–C4′ are 93.2(2) and 93.7(2)° respectively. The two S-C bond distances [1.815(3) and 1.835(3) Å] differ but are comparable with typical S–C bond distances.[16] The remaining bond distances and angles appear to be normal.

Experimental

Infrared spectra were recorded on a Perkin Elmer 1600 Series Fourier Transform infrared spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Brüker Avance 300 MHz spectrometer. Optical rotations were determined with a Perkin Elmer 241 Polarimeter using $CHCl_3$, and the specific rotation is given in units of 10^{-1} deg/cm^2/g^1. Mass spectra were obtained using a MASPEC II VG70SEQ high resolution mass spectrometer. The melting points were recorded using a Du Pont 910 Standard DSC module connected to a Du Pont Thermal analyser and are uncorrected. X-ray diffraction data for compound **4** were collected at 173K using a Nonius Kappa CCD with 1.5 kW graphite monochromated Mo radiation. The strategy for the data collection was evaluated using COLLECT.[17] Two sets of data were collected: a 182 deg phi scan and one omega scan to collect cusp data. These were scaled and reduced using DENZO-SMN.[18] Unit cell dimensions were refined on all data. The chiral space group $P2_1$ was chosen on the basis of systematic absences present in the diffraction pattern. The structure was solved and refined using SHELX97.[19] Hydrogen atoms were placed in calculated positions and refined as riding atoms. The chirality of the molecule could be established unambiguously from diffraction data. Molecular graphics used were obtained with PLATON.[20]



Scheme 1 Preparation of a novel camphor-derived thioacetal **4**.

Preparation of thioacetal **4***:* A solution of camphorquinone (2.0 g, 0.012 mol) in benzene (50 ml), 10-mercapto-iso-borneol **2** (2.2 g, 0.012 mol) and a catalytic amount of *p*-toluenesulfonic acid were refluxed for 2 hours, while water was removed azeotropically in a Dean-Stark apparatus. The mixture was then washed with dilute NaOH, followed by water, and the aqueous phase extracted with ethyl acetate (4 × 25 ml). The combined organic extracts were dried using anhydrous $MgSO_4$ and concentrated *in vacuo.* This crude mixture, when subjected to column chromatography using hexane–ethyl acetate (98:2) as eluent, yielded the thioacetal **4** (2.1 g, 52%), m.p. 149°C; ν_{max}/cm^{-1} (liquid film) 1740 (CO); δ_H(300 MHz, $CDCl_3$) 0.88, 0.90, 0.94, 0.96 and 1.29 (15H, 5xs, 8′-, 9′-, 10′-, 8-and 9-CH_3), 0.99–1.00 (1H, m, 6′-H_{exo}), 1.39–1.47 (1H, m, 6′–H_{endo}), 1.55–1.77 (7H, m, 4-H, 3-, 5- and 6-CH_2), 1.77–1.82 (2H, m, 5′-CH_2), 2.02 (1H, t, 4′-H), 2.56 and 3.62 (2H, 2xd, 10-CH_2) and 4.27 (1H, dd, 2-H); δ_c (75 MHz, $CDCl_3$) 9.74, 20.32, 20.39 and 21.96 (C-8, C-9, C-8′ and C-9′), 23.49 (C-10′), 22.43 (C-5′), 25.81 (C-10), 27.22 and 31.56 (C-5 and C-6), 33.69 (C-6′), 38.23 (C-3), 45.45 (C-4), 41.00, 46.85 and 46.87 (C-1, C-7 and C-7′), 54.98 (C-4′), 58.76 (C-1′), 78.90 (C-2), 84.30 (C-3′) and 213.26 (C-2′); $[\alpha]_D$ 35.7° (c 0.65, $CHCl_3$); *m/z* 334 (M^+, 12.35%) (Found M^+: 334.18651. $C_{20}H_{30}O_2S$ requires: M, 334.416).

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Techniques used: ^1H ^{13}C DEPT, HETCOR and COSY NMR spectroscopy, IR, HRMS, chromatography, X-ray crystallography and optical rotation.

References: 20

Figure 1: HETCOR NMR spectrum of thioacetal **4**

Figure 2: COSY NMR spectrum of compound **4**

Appendix: Crystal structure data for compound **4** (CCDC deposit number 161418)

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