Formation and X-ray structural study of enantiopure fused 1,5-oxathiocane derivatives

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The reaction of (E,R_S)-3-[(1S)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene † 1 with benzaldehyde or p-nitrobenzaldehyde, when carried out in dichloromethane in the presence of trimethylsilyl trifluoromethanesulfonate, leads mainly to enantiopure condensed 2-aryl-4-ethylidene-1,5-oxathiocane S-oxides. The reaction path begins with the ionic addition of the enantiopure diene 1 onto the C=O group activated by trimethylsilyl cation attack on the carbonyl oxygen. The almost complete diastereoselection observed in the following closure of the eight-membered ring is interpreted as being a consequence of the conformational control on cyclization which leads to the thermodynamically favoured isomer. The crystal structure of the 2,4-dinitrophenylhydrazone of the α,β-unsaturated aldehyde 5, obtained by reacting diene 1 with p-nitrobenzaldeyde, supports the stereochemical results.

As part of an ongoing programme aimed towards development of the chemistry and applications of enantiopure hydroxyalkyl-sulfinyldienes in asymmetric synthesis,[1] we were interested in assessing their reactivity towards aldehydes, having an ultimate goal of the synthesis of pyranoid derivatives (carbohydrate precursors) by stereocontrolled hetero-Diels–Alder (HDA) cycloadditions. We selected, as heterodienophiles, benzaldehyde and its p-nitro- and p-methoxy-analogues, showing typical electron-withdrawing and -donating substituents; these aldehydes were reacted (Scheme 1) with (E,R_S)-3-[1S)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene 1, which had shown complete regioselectivity and very high $endo/exo$ and diastereofacial selectivities in its cycloaddition with methyl acrylate in the presence of Lewis acids such as $LiClO_4$ and $ZnCl_2$.[1b,d] However, the attempted HDA reactions were very sluggish at room temperature, with or without Lewis acids, and resulted in diene decomposition when more severe reaction conditions were adopted. Unexpected results were instead obtained when the reaction was performed in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf), whose capacity for promoting 'ionic' DA reactions is well known.[2]

This paper reports on the reaction of diene 1 with aromatic aldehydes and TMSOTf. The structure of the main product 5 of the reaction of 1 with p-nitrobenzaldehyde was assigned on the basis of an X-ray structural study of its 2,4-dinitrophenylhydrazone derivative 6, which was shown to be enantiopure. To the best of our knowledge the enantiopure compounds 3–6 are novel. There have been a few reports in the literature concerning [b,g][3] and [c,f][4] dibenzo-fused oxathiocane derivatives, along with a description of the use of 1,5-oxathiocane-2,8-dione in polypropylene resin applications.[5]

Results and discussion

Synthesis of compounds 3–6
Benzaldehyde and its p-nitro- and p-methoxy-derivatives were reacted in turn with enantiopure diene 1 in dichloromethane solution and in the presence of TMSOTf. p-
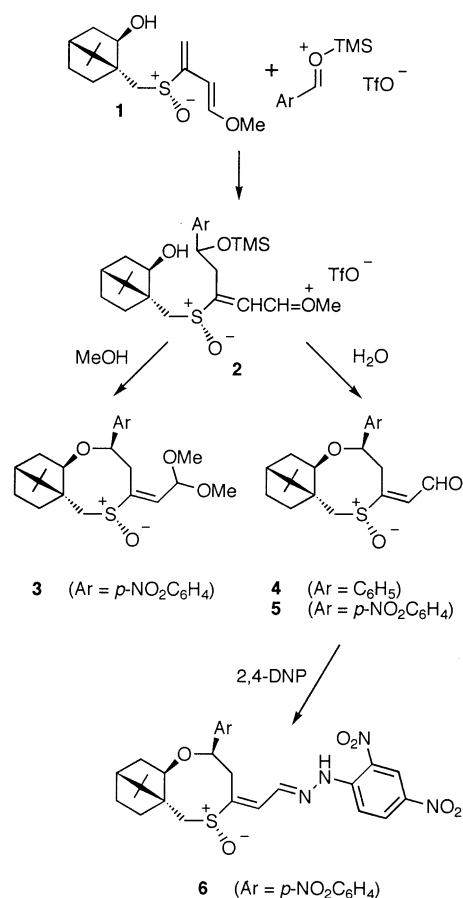
Scheme 1

Methoxybenzaldehyde was recovered unaltered, but the other two aldehydes showed analogous and reproducible chemical behaviour towards the diene. The main products of the reaction were obtained in *ca.* 50% yield after chromatographic purification, and the spectral analysis showed some unexpected features, *i.e.* there were no OMe groups detected and there was evidence of an α,β-unsaturated formyl group. Moreover, their
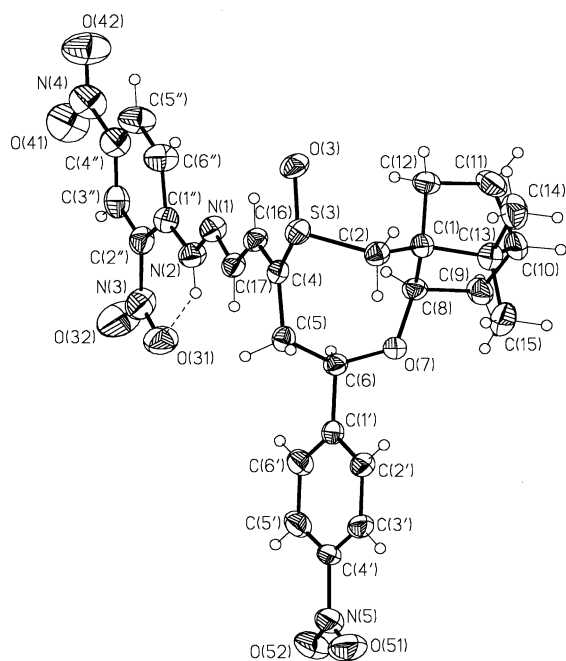
Fig. 1 Perspective picture of the molecule of compound **6** showing the numbering scheme and intramolecular hydrogen bond (dotted line). Non-H atoms are shown as 40% probability displacement ellipsoids.

Table 1 Selected bond lengths (Å) and angles (°) for **6**

C(1)–C(2)	1.514(5)	C(1)–C(8)	1.547(5)
C(1)–C(12)	1.547(5)	C(1)–C(13)	1.565(5)
C(2)–S(3)	1.804(4)	S(3)–O(3)	1.505(3)
S(3)–C(4)	1.786(4)	C(4)–C(16)	1.340(5)
C(4)–C(5)	1.508(5)	C(5)–C(6)	1.533(5)
C(6)–O(7)	1.425(4)	C(6)–C(1')	1.522(5)
O(7)–C(8)	1.450(4)	C(8)–C(9)	1.551(5)
C(9)–C(10)	1.524(6)	C(10)–C(11)	1.526(6)
C(10)–C(13)	1.536(6)	C(11)–C(12)	1.566(6)
C(13)–C(15)	1.530(6)	C(13)–C(14)	1.543(6)
C(16)–C(17)	1.441(5)	C(17)–N(1)	1.287(5)
N(1)–N(2)	1.371(4)	N(2)–C(1'')	1.355(5)
C(2)–C(1)–C(8)	116.0(3)	C(2)–C(1)–C(12)	117.2(3)
C(8)–C(1)–C(12)	104.6(3)	C(2)–C(1)–C(13)	112.8(3)
C(8)–C(1)–C(13)	102.9(3)	C(12)–C(1)–C(13)	101.6(3)
C(1)–C(2)–S(3)	121.5(3)	O(3)–S(3)–C(4)	107.9(2)
O(3)–S(3)–C(2)	109.4(2)	C(4)–S(3)–C(2)	99.9(2)
C(16)–C(4)–C(5)	126.9(3)	C(16)–C(4)–S(3)	117.3(3)
C(5)–C(4)–S(3)	115.6(3)	C(4)–C(5)–C(6)	113.9(3)
O(7)–C(6)–C(1')	106.8(3)	O(7)–C(6)–C(5)	112.7(3)
C(1')–C(6)–C(5)	109.9(3)	C(6)–O(7)–C(8)	115.0(3)
O(7)–C(8)–C(1)	113.5(3)	O(7)–C(8)–C(9)	110.3(3)
C(1)–C(8)–C(9)	103.0(3)	C(10)–C(9)–C(8)	103.5(3)
C(9)–C(10)–C(11)	107.8(4)	C(9)–C(10)–C(13)	102.3(3)
C(11)–C(10)–C(13)	102.8(4)	C(10)–C(11)–C(12)	103.2(3)
C(1)–C(12)–C(11)	102.8(3)	C(15)–C(13)–C(10)	114.1(4)
C(15)–C(13)–C(14)	106.6(4)	C(10)–C(13)–C(14)	113.7(4)
C(15)–C(13)–C(1)	114.9(4)	C(10)–C(13)–C(1)	93.4(3)
C(14)–C(13)–C(1)	114.1(4)	C(4)–C(16)–C(17)	124.6(4)
N(1)–C(17)–C(16)	117.9(3)	C(17)–N(1)–N(2)	116.0(4)
C(1'')–N(2)–N(1)	119.1(3)		

NMR data were indicative of a highly diastereoselective reaction. The definitive assignment of the structure of condensed oxathiocanes **4** and **5** was achieved by X-ray crystallographic analysis of (E,E,1S,6R,8R,10R,R_S)-13,13-dimethyl-4-[2-(2,4-dinitrophenylhydrazono)ethylidene]-6-(4-nitrophenyl)-7-oxa-3-thiatricyclo[8.2.1.0[1,8]]tridecane 3-oxide **6**, obtained by condensation of **5** with 2,4-dinitrophenylhydrazine (2,4-DNP).

The proposed reaction course is shown in Scheme 1. We suggest that the reaction begins with the formation of **2**, which arises from the nucleophilic addition of diene **1** onto the carbon atom of the aldehyde function activated by trimethylsilyl cation attack to the carbonyl oxygen. The acid catalysed closure of the oxathiocane ring to give **4** and **5** occurs by way of the isoborneol hydroxy group and the carbocation which is easily formed from **2** due to the aryl group, which has an increased activating effect when the *p*-nitro group is present. Moreover, the hydrolytic loss of the methoxy moiety takes place during the aqueous work-up of the crude reaction mixture, giving the α,β-unsaturated formyl group in **4** and **5**. The recovery of only one C–Ar epimer of the fused oxathiocane *S*-oxides **4** and **5** is a consequence of conformational control during the eight-membered ring closure, which leads to the formation of the thermodynamically favoured isomer.

In order to establish the intermediacy of **2** further, the alkaline work-up of the crude reaction mixture was performed in methanol instead of water. Isolation of the α,β-unsaturated dimethyl acetal **3** adds substantial support to the hypothesis that **2** is the reactive intermediate in the path from **1** and *p*-nitrobenzaldehyde, towards enantiopure sulfoxide **5**.

Further work will be performed in order to estimate the general scope of this synthetic approach to the 1,5-oxathiocane system.

Description of the structure of compound 6

An X-ray crystal structure was determined for the 2,4-dinitrophenylhydrazone derivative **6**, as single crystals of oxathiocanes **4** or **5** could not be obtained. Fig. 1 shows the molecular structure and atomic numbering scheme of (E,E,1S,6R,8R,10R,R_S)-13,13-dimethyl-4-[2-(2,4-dinitrophenylhydrazono)ethylidene]-6-(4-nitrophenyl)-7-oxa-3-thiatricyclo-[8.2.1.0[1,8]]tridecane 3-oxide **6**, as determined by X-ray single-

crystal diffraction. Selected bond distances and angles are given in Table 1. To the best of our knowledge, this is the first structural characterization of a 1,5-oxathiocane derivative (Cambridge Crystallographic Database, release April 1996, v. 5.11).[6]

A boat–chair (BC) conformation, which represents the energy minimum for a cyclooctane system,[7] is exhibited by the heterocycle in **6**, as pointed out by the following considerations. Two weighted least-squares mean planes can be identified in the eight-membered ring (off-planar distances are reported in brackets): *n* 1 for C(1) [−0.081(4) Å], S(3) [0.006(1) Å], C(4) [−0.059(4) Å], C(8) [0.083(4) Å] and *n* 2 for C(4) [0.048(4) Å], C(5) [−0.062(4) Å], O(7) [0.030(3) Å], C(8) [−0.060(4) Å]. Two further planes *n* 3 [C(5), C(6), O(7)] and *n* 4 [C(1), C(2), S(3)] have been computed. Respective dihedral angles [1–2 = 66.0(1)°; 1–3 = 3.9(3)°; 1–4 = 54.9(3)°; 2–3 = 63.3(2)°; 2–4 = 120.5(3)°] provide evidence for a BC conformation of the heterocycle.

The C–C bond lengths of the oxathiocane ring in **6** range from 1.508(5) Å for C(4)–C(5) [typical length of C(sp²)–C(sp³) bond] up to 1.547(5) Å for C(1)–C(8). The bond distances C(2)–S(3) = 1.804(4), S(3)–O(3) = 1.505(3) and S(3)–C(4) = 1.786(4) Å agree very well with the corresponding values reported for analogous sulfoxides.[1d,8] Relevant steric interactions between the fused isoborneol moiety and C(2) [C(2)···C(8) = 2.595(6), C(2)···C(12) = 2.612(6), C(2)···C(13) = 2.564(6) Å] are responsible for the unusually large angle C(1)–C(2)–S(3) [121.5(3)°].[8] Perhaps analogous steric requirements affect the geometrical parameters of O(7) [C(6)–O(7) = 1.425(4), O(7)–C(8) = 1.450(4) Å, C(6)–O(7)–C(8) = 115.0(3)°]. The cyclohexane ring C(1)–C(8)–C(9)–C(10)–C(11)–C(12) is constrained in a boat conformation while both the cyclopentane rings C(1)–C(8)–C(9)–C(10)–C(13) and C(1)–C(12)–C(11)–C(10)–C(13) show envelope conformations, slightly distorted by steric requirements of the geminal methyl groups.[9]

The 4-[2-(2,4-dinitrophenylhydrazono)ethylidene] substituent shows a double (E) configuration, and the corresponding bond distances [C(4)–C(16) = 1.340(5), C(16)–C(17) = 1.441(5), C(17)–N(1) = 1.287(5), N(1)–N(2) = 1.371(4) and N(2)–C(1'') = 1.355(5) Å] and angles are in good agreement with literature values [10] for phenylhydrazone moieties. The expected π con-
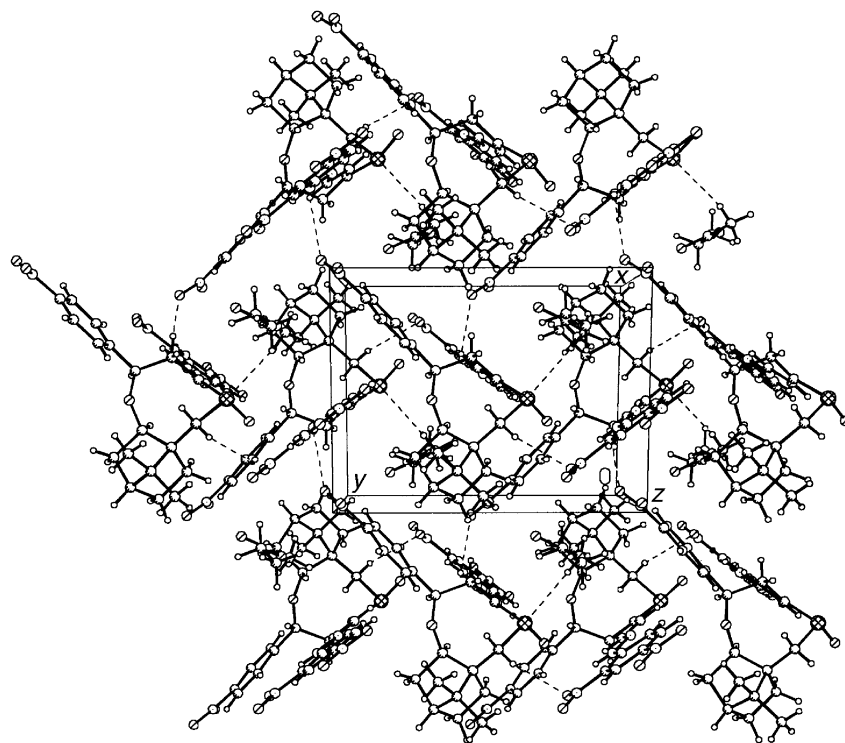
Fig. 2 Perspective view of the crystal packing for **6** along the *c*-axis. The intermolecular hydrogen bonds are represented by dotted lines and the sulfur atoms by cross-hatched circles.

jugation involves the 2″,4″-dinitro substituents in the compound under study: all the atoms of the fragment 2,4-$(NO_2)_2C_6H_3$–NH–N=CH–CH= lie on its mean plane, as evidenced by the torsion angles C(4)–C(16)–C(17)–N(1) = −180.0(4)°, C(16)–C(17)–N(1)–N(2) = −179.7(3)°, C(17)–N(1)–N(2)–C(1″) = 175.6(4)°, C(5″)–C(4″)–N(4)–O(42) = 1.4(7)° and C(1″)–C(2″)–N(3)–O(31) = 1.2(6)°. A strong intramolecular hydrogen bond is observed between the N(2) hydrogen atom and O(31) [O(31)···H(2) = 2.029(4), O(31)···N(2) = 2.631(5) Å, O(31)···H(2)–N(2) = 126.3(4)°]. A small but significant torsion [14.2(3)°] is observed between 4′-NO_2 and C_6H_4 mean plane.

Compound **6** shows five chiral centres. It is enantiomerically pure in the crystal packing (Fig. 2), owing to the polar space group $P2_1$. The assignment of the absolute configuration is supported by the value [−0.1(1)] which the Flack parameter[11] has converged to. Compound **6** co-crystallizes equimolecularly with the solvent ethyl acetate.‡ Besides the normal van der Waals interactions, the crystal packing is mainly stabilized by intermolecular hydrogen bonding. Inside the asymmetric unit, S(3) interacts with an hydrogen atom of ethyl acetate: S(3)···H–C(20) = 130.8(6)°; S(3)···H(20) = 2.857(6) Å. We suggest that the sulfur atom is involved in this interaction rather than sulfinyl oxygen, owing to reduced sterical availability of this latter atom. Further hydrogen bonds are observed among different asymmetric units: O(31)^*i*···H(2A)–C(2) = 146.9(4)°, O(31)^*i*···H(2A) = 2.528(5) Å, O(52)^*ii*···H(17)–C(17) = 121.0(5)°; O(52)^*ii*···H(17) = 2.530(6) Å, with *i* = −*x* + 1, *y* + 1/2, −*z* + 1 and *ii* = −*x* + 2, *y* + 1/2, −*z* + 1.

Experimental

TLC was carried out on commercially available precoated plates (Aldrich silica gel 60 F 254) and the products were visualized with iodine. Silica gel used for column chromatography was Aldrich 60. Petrol refers to light petroleum, bp 60–80 °C. Mps were measured on a microscopic apparatus and are uncorrected. Specific rotations $[a]_D^{20}$ were measured in $CHCl_3$ solu-

‡ Atomic numbering scheme for ethyl acetate: C(20)H_3–C(18)[O(19)]–O(21)–C(22)H_2–C(23)H_3.

tions with a JASCO DIP-360 digital polarimeter and are given in 10^{-1} deg cm² g^{-1}. Elemental analyses were performed by REDOX, Milano (Italy). IR spectra were taken with a Perkin-Elmer 1600 FT spectrometer in $CDCl_3$ solutions. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer at 300 and 75 MHz respectively in $CDCl_3$ solutions with $SiMe_4$ as internal standard; abbreviations used, s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet, br = broad; *J* values are given in Hz; the assignments are supported by attached proton test (APT) and heteronuclear shift-correlated experiments. FAB mass spectra (*m*-nitrobenzyl alcohol as matrix) were determined with a Finnigan MAT 90 instrument.

(*E*,1*S*,6*R*,8*R*,10*R*,*R*$_S$)-13,13-Dimethyl-4-(formylmethylidene)-6-phenyl-7-oxa-3-thiatricyclo[8.2.1.0^{1,8}]tridecane 3-oxide 4

To a solution of benzaldehyde (0.22 cm³, 2.16 mmol) in anhydrous dichloromethane (2 cm³), TMSOTf (0.07 cm³, 0.35 mmol) was added at 0 °C under a N_2 atmosphere. The mixture was stirred for 0.5 h and then diene **1** (100 mg, 0.35 mmol) in dry dichloromethane (2 cm³) was added, maintaining the temperature of the ice bath. The mixture was allowed to warm spontaneously to ambient temperature, monitoring the reaction by TLC [dichloromethane–ethyl acetate (8:2) as the eluent] until the total disappearance of diene was observed. After 3.5 h the reaction was quenched by neutralizing with aq. NaOH (0.2 M) under stirring. The product was extracted with dichloromethane, the organic extracts were washed with saturated aq. NaCl solution, dried over Na_2SO_4, concentrated and the residue purified by column chromatography eluting with dichloromethane. This gave compound **4** as a pale yellow oil (64 mg, 0.18 mmol, 50%) (Found: C, 70.4; H, 7.4. Calc. for $C_{21}H_{26}O_3S$: C, 70.36; H, 7.31%); δ_H 0.91 (3 H, s, H_3-14), 1.0–2.0 (7 H, m, H_2-9, 11, 12, H-10), 1.14 (3 H, s, H_3-15), 2.39 (1 H, dd, $J_{5A,5B}$ 14.5, $J_{5B,6}$ 9.8, H_B-5), 3.11 (1 H, d AB, $J_{2A,2B}$ 14.9, H_B-2), 3.50 (1 H, d AB, H_A-2), 3.52 (1 H, dt, $J_{5A,6} = J_{5A,16}$ 1.9, H_A-5), 3.66 (1 H, dd, $J_{8,9ax}$ 8.1, $J_{8,9eq}$ 3.9, H-8), 4.90 (1 H, dd, H-6), 7.05 (1 H, dd, $J_{16,17}$ 3.7, H-16), 7.3–7.5 (5 H, m, Ph) and 10.01 (1 H, d, H-17); δ_C 20.15 (C-14), 20.23 (C-15), 27.54 and 29.44 (C-11, 12), 38.43 (C-5), 40.43 (C-9), 43.67 (C-10), 47.16 (C-13), 49.87 (C-1),

53.98 (C-2), 83.89 (C-6), 85.93 (C-8), 125.29 (C-3′, 5′), 126.61 (C-16), 127.68 (C-4′), 128.45 (C-2′, 6′), 142.13 (C-1′), 165.66 (C-4) and 187.61 (C-17); m/z (%) 359 (M + 1, 35), 149 (100), 137 (50), 135 (78), 121 (50), 107 (65), 105 (50), 93 (48), 91 (76), 81 (49), 79 (51), 77 (61), 69 (51), 67 (54), 57 (45), 55 (76), 43 (49) and 41 (63).

(*E*,1*S*,6*R*,8*R*,10*R*,*R*$_S$)-13,13-Dimethyl-4-(formylmethylidene)-6-(4-nitrophenyl)-7-oxa-3-thiatricyclo[8.2.1.0^{1,8}]tridecane 3-oxide 5

Counpound **5** was obtained as a pale yellow oil (214 mg, 0.53 mmol, 50%) from *p*-nitrobenzaldehyde (960 mg, 6.35 mmol), TMSOTf (0.2 cm^3, 1 mmol) and diene **1** (300 mg, 1.05 mmol), following the procedure described above. The purification of compound **5** by column chromatography was performed eluting with dichloromethane to which small increasing amounts of ethyl acetate were added up to 5% (Found: C, 62.6; H, 6.3; N, 3.4. Calc. for C$_{21}$H$_{25}$NO$_5$S: C, 62.51; H, 6.25; N, 3.47%); ν_{max}/cm^{-1} 2958, 2927, 1587, 1522 and 1350 (NO$_2$) and 1082 (SO); δ_H 0.92 (3 H, s, H$_3$-14), 1.0–2.0 (7 H, m, H$_2$-9, 11, 12, H-10), 1.14 (3 H, s, H$_3$-15), 2.28 (1 H, dd, $J_{5A,5B}$ 14.1, $J_{5B,6}$ 9.9, H$_B$-5), 3.11 (1 H, d AB, $J_{2A,2B}$ 15.1, H$_B$-2), 3.49 (1 H, d AB, H$_A$-2), 3.51 (1 H, br d, H$_A$-5), 3.65 (1 H, dd, $J_{8,9ax}$ 7.9, $J_{8,9eq}$ 4.0, H-8), 5.03 (1 H, br d, $J_{5A,6}$ < 1, H-6), 7.16 (1 H, br d, $J_{16,17}$ 2.0, H-16), 7.70 (2 H, d, J_o 8.6, H-2′, 6′), 8.24 (2 H, d, H-3′, 5′) and 9.97 (1 H, d, H-17); δ_C 20.04 (C-14), 20.10 (C-15), 27.45 and 29.62 (C-11, 12), 38.62 (C-5), 40.37 (C-9), 43.50 (C-10), 46.73 (C-13), 49.91 (C-1), 53.89 (C-2), 82.51 (C-6), 86.31 (C-8), 123.61 (C-3′, 5′), 126.00 (C-16), 126.27 (C-2′, 6′), 147.27 (C-4′), 149.18 (C-1′), 164.39 (C-4) and 187.91 (C-17); m/z (%) 404 (M + 1, 3) and 149 (100).

(*E*,1*S*,6*R*,8*R*,10*R*,*R*$_S$)-4-(2,2-Dimethoxyethylidene)-13,13-dimethyl-6-(4-nitrophenyl)-7-oxa-3-thiatricyclo[8.2.1.0^{1,8}]-tridecane 3-oxide 3

To a solution of *p*-nitrobenzaldeyde (227 mg, 1.5 mmol) in anhydrous dichloromethane (3 cm^3), TMSOTf (0.05 cm^3, 0.25 mmol) was added at 0 °C under a N$_2$ atmosphere. The mixture was stirred for 0.5 h and then diene **1** (72 mg, 0.25 mmol) in dry dichloromethane (1 cm^3) was added, maintaining the temperature of the ice bath. The mixture was allowed to warm spontaneously to ambient temperature and the reaction was quenched by neutralizing with a NaHCO$_3$ suspension in methanol under stirring. The solid was removed by filtration and washed with dry dichloromethane. The combined organic layers were concentrated and the residue purified by column chromatography eluting firstly with petrol–dichloromethane (1:1) and then with dichloromethane to which small increasing amounts of ethyl acetate were added up to 5%. This gave compound **3** as a yellow oil (62 mg, 0.14 mmol, 55%) (Found: C, 62.1; H, 6.9; N, 3.1. Calc. for C$_{23}$H$_{31}$NO$_6$S: C, 61.45; H, 6.95; N, 3.12%); δ_H 0.91 (3 H, s, H$_3$-14), 1.0–2.0 (7 H, m, H$_2$-9, 11, 12, H-10), 1.14 (3 H, s, H$_3$-15), 2.15 (1 H, dd, $J_{5A,5B}$ 14.9, $J_{5B,6}$ 9.8, H$_B$-5), 3.01 (1 H, d AB, $J_{2A,2B}$ 15.0, H$_B$-2), 3.13 (1 H, dt, $J_{5A,6}$ 1.8, $J_{5A,16}$ 1.7, H$_A$-5), 3.31 (1 H, d AB, H$_A$-2), 3.38 (3 H, s, OMe), 3.42 (3 H, s, OMe), 3.86 (1 H, dd, $J_{8,9ax}$ 7.7, $J_{8,9eq}$ 4.6, H-8), 4.97 (1 H, dd, H-6), 5.27 (1 H, d, $J_{16,17}$ 4.8, H-17), 6.47 (1 H, dd, H-16), 7.51 (2 H, d, J_o 8.6, H-2′, 6′) and 8.21 (2 H, d, H-3′, 5′); δ_C 20.20 (C-14), 20.38 (C-15), 27.55 and 29.40 (C-11, 12), 36.74 (C-5), 40.60 (C-9), 43.63 (C-10), 47.24 (C-13), 49.61 (C-1), 52.42 (OMe), 52.89 (OMe), 53.22 (C-2), 81.90 (C-6), 85.65 (C-8), 100.23 (C-17), 123.66 (C-3′, 5′), 126.29 (C-2′, 6′), 129.72 (C-16), 145.48 (C-4′), 149.74 (C-1′) and 164.00 (C-4); m/z (%) 450 (M + 1, 34), 155 (41), 138 (52), 137 (100), 107 (64), 91 (41), 90 (36), 89 (59), 79 (35), 78 (37), 77 (71), 41 (36) and 39 (40).

(*E*,*E*,1*S*,6*R*,8*R*,10*R*,*R*$_S$)-13,13-Dimethyl-4-[2-(2,4-dinitrophenylhydrazono)ethylidene]-6-(4-nitrophenyl)-7-oxa-3-thiatricyclo[8.2.1.0^{1,8}]tridecane 3-oxide 6

The 2,4-DNP reagent was prepared by dissolving 800 mg of 70% 2,4-DNP (2.83 mmol) in 4 cm^3 of concentrated sulfuric acid and adding 6 cm^3 of water dropwise while stirring the mixture to ensure complete solution; 20 cm^3 of 95% ethanol were added to this warm solution. This 2,4-DNP reagent (2 cm^3) was added to a solution of 1,5-oxathiocane **5** (70 mg, 0.17 mmol) in 95% ethanol (2 cm^3). Formation of the orange insoluble 2,4-dinitrophenylhydrazone **6** was immediately observed. The product was purified by column chromatography with petrol–ethyl acetate (8:2) as the eluent and crystallization from ethyl acetate. This gave compound **6** (almost quantitative yield) as orange crystals; mp 176 °C; $[\alpha]_D^{20}$ −325.5 (*c* 0.002 12) (Found: C, 55.5; H, 5.4; N, 11.9. Calc. for C$_{27}$H$_{29}$N$_5$O$_8$S: C, 55.57; H, 5.01; N, 12.00%); ν_{max}/cm^{-1} 3295 (NH), 2956, 2927, 1617, 1522 and 1340 (NO$_2$) and 1092 (SO); δ_H 0.95 (3 H, s, H$_3$-14), 1.0–2.0 (7 H, m, H$_2$-9, 11, 12, H-10), 1.17 (3 H, s, H$_3$-15), 2.55 (1 H, dd, $J_{5A,5B}$ 15.0, $J_{5B,6}$ 9.1, H$_B$-5), 3.19 (1 H, d AB, $J_{2A,2B}$ 14.8, H$_B$-2), 3.34 (1 H, br d, H$_A$-5), 3.34 (1 H, d AB, H$_A$-2), 3.82 (1 H, dd, $J_{8,9ax}$ 7.8, $J_{8,9eq}$ 3.8, H-8), 4.89 (1 H, dd, $J_{5A,6}$ 2.5, H-6), 7.21 (1 H, d, J_o 9.8, H-6″), 7.59 (2 H, d, J_o 8.8, H-2′, 6′), 7.98 and 8.01 (2 H, 2 s, H-16, 17), 8.26 (2 H, d, H-3′, 5′), 8.37 (1 H, dd, J_m 2.3, H-5″), 9.14 (1 H, d, H-3″) and 11.32 (1 H, s, NH); δ_C 20.15 (C-14), 20.56 (C-15), 27.44 and 30.04 (C-11, 12), 35.82 (C-5), 40.37 (C-9), 43.84 (C-10), 49.33 and 49.67 (C-1, 13), 53.64 (C-2), 81.80 (C-6), 86.10 (C-8), 117.04 (C-16), 123.22 (C-3″), 123.88 (C-3′, 5′), 126.58 (C-2′, 6′), 126.90 (C-6″), 130.12 (C-2″), 130.24 (C-5″), 139.17 (C-4″), 141.17 (C-17), 144.11 (C-1″), 147.58 (C-4′), 148.44 (C-1′) and 150.65 (C-4); m/z (%) 584 (M + 1, 43), 155 (44), 149 (82), 138 (56), 137 (100), 135 (47) and 108 (53).

Crystal data for compound 6

C$_{31}$H$_{37}$N$_5$O$_{10}$S, M_r = 671.72 g mol^{-1}, monoclinic, space group $P2_1$, a = 9.724(2), b = 11.862(3), c = 15.253(2) Å, β = 106.31(1)°, V = 1688.6(6) Å^3, Z = 2, D_c = 1.321 g cm^{-3}, λ(Mo-Kα) = 0.710 73 Å, μ = 0.158 mol^{-1}, $F(000)$ = 708, T = 296 K, R = 0.0461 for 3152 independent reflections. Crystals suitable for X-ray analysis were obtained by recrystallization from ethyl acetate solution.§

Data collection and processing for compound 6

A crystal of dimensions 0.25 × 0.12 × 0.12 mm was used for intensity data collection with a Siemens R3m/V four-circle diffractometer using graphite monochromated Mo-Kα radiation. Accurate unit-cell dimensions and crystal orientation matrices were obtained from least-squares refinement of 2θ, ω, χ and φ values of 20 strong reflections in the range 13 < 2θ < 30°. Crystal stability was confirmed by the constancy of three check reflections monitored every 197 reflections. Of 3152 independent reflections measured by the ω–2θ scan technique, in the range 3 < 2θ < 50 (0 < h < 12, 0 < k < 15, −19 < l < 19), 2376 having net intensity I > 1$\sigma(I)$ were used for the solution of the structure. Refinement was carried on all reflections except one (1 1 0, flagged for systematic errors). Corrections for Lorentz, polarization and absorption effects were made.

Structural analysis and refinement for compound 6

The structure was solved by direct methods with SIR-92 program;[12] subsequent calculations were mainly carried out by the SHELXTL-Plus[13] and SHELXL93[14] programs; the final geometrical calculations were carried out with PARST program.[15] All the H atoms were added at calculated positions and included in the structure factor calculation with a common thermal parameter (U = 0.07 Å^2). The structure was aniso-

tropically refined by the full-matrix least-squares on F^2 method. The final residuals were $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o| = 0.0461$, $R_w = [\Sigma_w(F_o^2 - F_c^2)^2/\Sigma_w(F_o^2)^2]^{1/2} = 0.0732$ and GOF = 0.906. The weighting scheme used in the last refinement cycle was $w = [\sigma^2(F_o^2) + (0.0361\ P)^2]^{-1}$, where $P = (F_o^2 + 2\ F_c^2)/3$. Final difference map peaks were in the range 0.133, -0.137 e $Å^{-3}$; max $\Delta/\sigma = 0.001$. Extinction correction was performed: extinction coefficient = 0.0084(9). Flack's absolute structure parameter was $-0.1(1)$. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography.[16]

Acknowledgements

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