Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2009, **19**, 284–286
Mendeleev Communications

Unexpected epoxidation product in oxidation of *N*-tosyl-7-methoxy-1,3a,4,8b-tetrahydrocyclopenta[*b*]indole with potassium permanganate

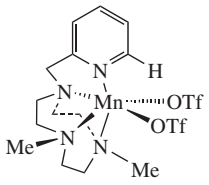
Rail R. Gataullin*[a] and Kyrill Yu. Suponitsky*[b]

[a] *Institute of Organic Chemistry, Ufa Scientific Centre of the Russian Academy of Sciences, 450054 Ufa, Russian Federation. Fax: +7 347 235 6066; e-mail: gataullin@anrb.ru*
[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 499 135 5085; e-mail: kirshik@yahoo.com*

DOI: 10.1016/j.mencom.2009.09.019

An unexpected product of *N*-tosyl-7-methoxy-1,3a,4,8b-tetrahydrocyclopenta[*b*]indole oxidation with potassium permanganate under alkaline conditions was isolated. Along with (2*R*,3*S*,3a*R*,8b*S*)-*N*-tosyl-7-methoxy-2,3-dihydroxy-1,2,3,3a,4,8b-hexahydrocyclopenta[*b*]indole, (3*SR*,3a*RS*,8b*SR*)-*N*-tosyl-7-methoxy-3-hydroxy-1,2-epoxy-1,2,3,3a,4,8b-hexahydrocyclopenta[*b*]indole was formed.

The oxidation of alkenes with potassium permanganate is frequently used for the synthesis of *cis*-diols and oxygen-containing organic compounds.[1] An extensive study on the oxidative transformation with this reagent revealed almost all possible reaction products.[2] Generally, a vicinal *cis*-diol is the final product of olefin oxidation by $KMnO_4$ under alkaline conditions. The conditions for carboxylic acid formation upon treatment of an olefin with this oxidant are also well known.[1–3] Only few examples of olefin epoxidation with potassium permanganate can be found in the literature.[4,5] Epoxide formation in the reaction of $KMnO_4$ with tetrafluoroethylene in anhydrous HF at –78 °C was described. This reaction results in a mixture of tetrafluoroethylene oxide and its isomerisation product – trifluoroacetic acid fluoroanhydride.[4] The allylic oxidation of olefins with peracetic acid catalyzed by di(trifluoromethanesulfono)[1,4-dimethyl-7-(pyridin-2-ylmethyl)-1,4,7-triazonan]-manganese [$Mn(CF_3SO_3)_2$(^{H,Me}PyTACN)] is also known (though the yeild is lower than 1%). However, in this case, manganese does not exist in the form of the permanganate ion.[5] The oxidation of cycloalkenones with $KMnO_4$ in the presence of carboxylic acids, which results in α-carboxyl alkyl substituted cycloalkenone formation with the retention of double bonds, should also be mentioned.[6–8]



$Mn(CF_3SO_3)_2$(^{H,Me}PyTACN)

In order to synthesize 2,3-dihydroxy-substituted 1,2,3,3a,4,8b-hexahydrocyclopenta[*b*]indole, we have carried out the oxidation of 1,3a,4,8b-tetrahydrocyclopenta[*b*]indole by $KMnO_4$. However, this reaction resulted in the formation of an unusual product, namely, (1a*R*,2*S*,2a*R*,7b*S*,7c*R*)-6-methoxy-3-(4-methylphenylsulfonyl)-1a,2,2a,3,7b,7c-hexahydrooxireno[2′,3′:3,4]cyclopenta[*b*]indol-2-ol.

The reaction of compound **2** with TsCl gives tosylate **3**, which reacts with I_2 in methylene chloride leading to indoline **4**. The boiling of **4** in an excess of pyperidine results in tetrahydrocyclopenta[*b*]indole **5** formation in a good yield. The structure of the product is confirmed by elemental analysis and by comparison of the spectral data† with those obtained earlier for similar compounds.[9]

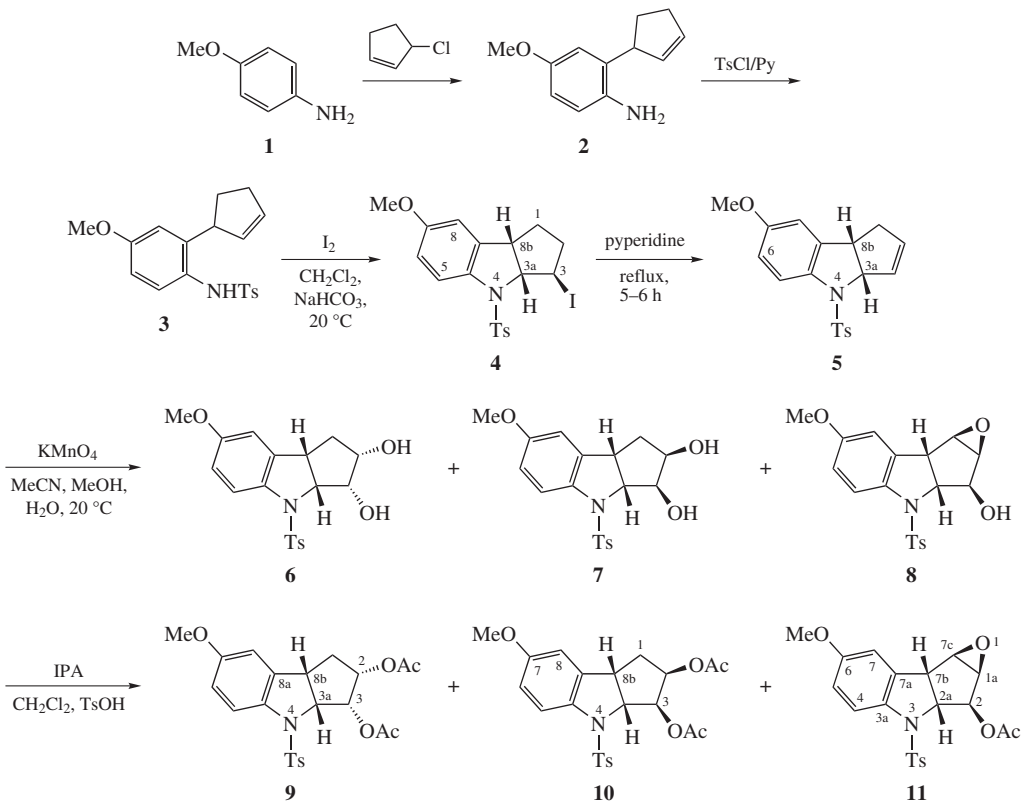
The reaction of **5** with $KMnO_4$ in MeCN/MeOH/H_2O results in a complex mixture of products. We suppose that it consists of diols **6**, **7** and epihydrine **8**. Our attempts to separate this mixture chromatographically were unsuccessful. The mixture thus obtained displays an ^{1}H NMR spectrum similar to that of the initial reaction mixture with unresolved signals of protons.

The reaction of compounds **6**–**8** with isopropenyl acetate in CH_2Cl_2 in the presence of the catalytic amounts of TsOH resulted in their O-acetates **9**–**11**, which were isolated by chromatography on silica gel.‡

† The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-300 spectrometer (300.13 and 75.47 MHz in $CDCl_3$). The internal standard was TMS. The elemental analysis was carried out using an M-185B Analyzer. Column chromatography was carried out on silica gel (Lankaster LS 40/100 μm). For qualitative analysis, we used TLC plates Sorbfil (Sorbpolimer, Russia) with the detection of substances with I_2.

4: A mixture of tosylate **3** (5 g, 14.6 mmol), I_2 (6.71 g, 26.4 mmol), $NaHCO_3$ (20.3 g) in CH_2Cl_2 (150 ml) was stirred for 24 h at 20 °C. CH_2Cl_2 (100 ml) was then added to the reaction mixture, treated with 10% $Na_2S_2O_3$ solution (3×100 ml), water (100 ml) and dried with Na_2SO_4. The solvent was evaporated *in vacuo*. The crystallization of the residue from EtOH led to the precipitation of a dark thick crystalline mass. By this reason, the residue was chromatographed on silica gel (70 g), R_f 0.4. The yield was 2.4 g (35.6%), mp 147–149 °C (dark crystals from EtOH). ^{1}H NMR, δ: 1.70–2.60 (m, 4H, $2CH_2$), 2.35 (s, 3H, Me), 3.65 (t, 1H, H^{8b}, $J_{H^{8b},H^{1A}}$ 8.4 Hz, $J_{H^{8b},H^{3a}}$ 8.4 Hz), 3.75 (s, 3H, OMe), 4.73 (d, 1H, H^{3a}, *J* 8.4 Hz), 4.87 (d, 1H, H^3, *J* 3.9 Hz), 6.60 (d, 1H, H^8, *J* 1.5 Hz), 6.73 (dd, 1H, H^6, J_1 1.5 Hz, J_2 8.9 Hz), 7.22 (m, 2H, *J* 8.3 Hz), 7.53 (d, 1H, H^5, *J* 8.9 Hz), 7.61 (d, 2H, H_{Ar}, *J* 8.3 Hz). Found (%): C, 48.41, H, 4.12, I, 26.81, N, 2.75, S, 6.65. Calc. for $C_{19}H_{20}INO_3S$ (%): C, 48.62, H, 4.30, I, 27.04, N, 2.98, S, 6.83.

5: Derivative **4** (2.4 g, 5.1 mmol) was dissolved in pyperidine (20 ml) and heated under pyperidine boiling for 6 h. The solvent excess was evaporated *in vacuo*, dissolved in CH_2Cl_2 (250 ml), washed with 5% HCl solution and then twice with water. The organic phase was dried with $MgSO_4$, the solvent was evaporated *in vacuo*, the residue was crystallized from EtOH. The yield was 1.57 g (90%), mp 124 °C. ^{1}H NMR, δ: 2.38 (s, 3H, Me), 2.45 (d, 1H, H^{1A}, J_{gem} 17.0 Hz), 2.79 (ddq, 1H, H^{1B}, J_{gem} 17.0 Hz, J_2 8.3 Hz, J_3 1.9 Hz), 3.46 (dd, 1H, H^{8b}, J_1 8.0 Hz, J_2 8.3 Hz), 3.80 (s, 3H, OMe), 5.22 (dd, 1H, H^{3a}, J_1 1.9 Hz, J_2 8.0 Hz), 5.82–5.90 (m, 2H, H^2, H^3), 6.60 (d, 1H, H^8, *J* 2.5 Hz), 6.77 (dd, 1H, H^6, J_1 2.5 Hz, J_2 8.8 Hz), 7.15 (d, 2H, *J* 8.0 Hz), 7.50–7.59 (m, 3H). Found (%): C, 66.67; H, 5.45; N, 3.93; S, 9.19. Calc. for $C_{19}H_{19}NSO_3$ (%): C, 66.84; H, 5.61; N, 4.10; S, 9.39.



‡ *Oxidation method.* To a solution of **5** (1.4 g, 4.1 mmol) in 30 ml of MeCN and 7 ml of MeOH, 3.55 g $KMnO_4$ (as solution in 5 ml of water) was added. This led to intense warming-up of the reaction mixture. After that, reaction mixture was stirred at room temperature for 3 h. The residue was filtered off, washed with CH_2Cl_2, and the organic solvents were evaporated. The residue was diluted with 25 ml of H_2O, the water layer was saturated with NaCl, extracted with CH_2Cl_2, dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. The compound mixture was purified with silica gel; the eluent was CH_2Cl_2. This attempt was unsuccessful. Therefore, the mixture (1.1 g) was dissolved in 10 ml of CH_2Cl_2, and then isopropenyl acetate (4 ml) and *para*-toluenesulfonic acid (40 mg) were added; the mixture was stirred, the reaction was controlled using TLC (eluent, benzene–EtOAc, 4:1). After the reaction was completed, 10 ml of H_2O were added and the mixture was extracted with CH_2Cl_2 (70 ml). The organic layer was washed with H_2O and dried with Na_2SO_4. The solvent was evaporated *in vacuo*. In order to isolate compounds **9**–**11**, the residue was chromatographed on silica gel (30 g), eluted with benzene. After compound **9** was passed from the column, 5% ethyl acetate was added to the eluent. Epoxide **11**, and after that compound **10** were isolated.

9: Yield 0.05 g (3%), amorphous solid. ^{1}H NMR, δ: 1.35, 1.50, 2.40 (s, 3H, 3Me), 1.75 (ddd, 1H, H^{1A}, J_1 2.2 Hz, J_2 8.7 Hz, J_{gem} 13.6 Hz), 2.30–2.45 (m, 1H, H^{1B}), 3.70 (q, 1H, H^{8b}, J 8.7 Hz), 3.75 (s, 3H, OMe), 4.20 (d, 1H, H^{3a}, J 8.7 Hz), 4.71 (dt, 1H, H^2, J_1 2.2 Hz, J_2 5.5 Hz), 5.13 (d, 1H, H^3, J 5.5 Hz), 6.55 (d, 1H, H^8, J 2.5 Hz), 6.75 (dd, 1H, H^6, J_1 2.5 Hz, J_2 8.8 Hz), 7.22 (d, 2H, H_{Ar}, J 8.1 Hz), 7.60 (d, 1H, H^5, J 8.8 Hz), 7.69 (d, 2H, H_{Ar}, J 8.1 Hz). Found (%): C, 59.97; H, 5.37; N, 2.94; S, 6.81. Calc. for $C_{23}H_{25}NO_7S$ (%): C, 60.12; H, 5.48; N, 3.05; S, 6.98.

10: Yield 0.3 g (16%). ^{1}H NMR ($CDCl_3$) δ: 1.98 (dt, 1H, H^{1A}, J_1 4.6 Hz, J_{gem} 13.7 Hz), 2.05, 2.13, 2.38 (s, 3H, 3Me), 2.30 (ddd, 1H, H^{1B}, J_1 4.6 Hz, J_2 9.6 Hz, J_{gem} 13.7 Hz), 3.53 (dt, 1H, H^{8b}, J_1 4.6 Hz, J_2 9.6 Hz), 3.75 (s, 3H, Me), 4.53 (dd, 1H, H^{3a}, J_1 4.6 Hz, J_2 9.6 Hz), 5.19 (q, 1H, H^2, J 4.6 Hz), 5.34 (t, 1H, H^3, J 4.6 Hz), 6.55 (d, 1H, H^8, J 2.4 Hz), 6.78 (dd, 1H, H^6, J_1 2.4 Hz, J_2 8.9 Hz), 7.19 (d, 2H, H_{Ar}, J 8.0 Hz), 7.54 (m, 3H, H_{Ar}). ^{13}C NMR, δ: 20.6, 20.7, 21.4 (3Me), 35.0 (C^1), 40.4 (C^{8b}), 55.5 (Me), 68.8, 72.3, 77.8 (C^{3a}, C^3, C^2), 109.9, 113.5, 117.9 (C^5, C^6, C^8), 127.2, 129.5 ($C^{2'}$, $C^{6'}$, $C^{3'}$, $C^{5'}$), 133.9, 134.1, 136.8, 144.0 (C^{4a}, C^7, $C^{1'}$, $C^{4'}$), 157.6 (C^7), 169.6, 169.7 (2C=O). Found (%): C, 59.98; H, 5.30; N, 2.88; S, 6.82. Calc. for $C_{23}H_{25}NO_7S$ (%): C, 60.12; H, 5.48; N, 3.05; S, 6.98.

The structures of compounds **10** and **11** were determined by single crystal X-ray crystallography. All our attempts to grow single crystals of isomer **9** suitable for an X-ray study were unsuccessful. Its structure was determined by the elemental analysis and spectral methods.

The ORTEP views of **10** and **11** are shown in Figure 1.§ An asymmetric unit cell of both compounds contains one molecule. Some differences in the molecular geometries of **10** and **11** are observed. The central dihydropyrrole ring is planarized in both molecules: it is planar in **10** [mean deviation is 0.008(3) Å] while in **11**, it adopts planarized envelope geometry with the C(3A) atom slightly moved out [by 0.204(3) Å] of the plane of four remaining atoms. The orientations of the *p*-tolylsulfonyl group are somewhat different by the inclination of the S(1)–N(4) bond relative to the dihydropyrrole ring. More pronounced differences are found for the remaining part of the molecules. In **10**, the cyclopentane fragment adopts an envelope conformation, while it is in a planarized twist form in **11**, which is due to the influence of the rigid epoxy group. In both molecules, the substituents of the cyclopentane fragment are *trans* oriented to the dihydropyrrole ring. The crystal structures of both compounds are stabilized by ordinary van der Waals and weak C–H···O interactions.

*(1a*R*,2*S*,2a*R*,7b*S*,7c*R*)-6-Methoxy-3-(4-methylphenylsulfonyl)-1a,2,2a,3,7b,7c-hexahydrooxireno[2',3':3,4]cyclopenta[*b*]indol-2-yl acetate* **11**: yield 0.15 g (8.8%), mp 165 °C (EtOH). ^{1}H NMR, δ: 2.20 (s, 3H, Me), 2.35 (s, 3H, Me), 3.51 (d, 1H, H^{7b}, J 7.7 Hz), 3.63 (d, 1H, H^{7c}, J 2.8 Hz), 3.69 (dd, 1H, H^{1a}, J_1 1.7 Hz, J_2 2.8 Hz), 3.78 (s, 3H, OMe), 4.28 (dd, 1H, H^{2a}, J_1 4.6 Hz, J_2 7.7 Hz), 5.26 (dd, 1H, H^2, J_1 1.7 Hz, J_2 4.6 Hz), 6.64 (dd, 1H, H^7, J_1 0.9 Hz, J_2 2.6 Hz), 6.85 (ddd, 1H, H^5, J_1 0.6 Hz, J_2 2.6 Hz, J_3 8.9 Hz), 7.17 (d, 2H, H_{Ar}, J 8.0 Hz), 7.43 (d, 2H, H_{Ar}, J 8.0 Hz), 7.61 (d, 1H, H^4, J 8.9 Hz). ^{13}C NMR, δ: 20.8, 21.4, 55.6 (3Me), 46.5 (C^{7b}), 56.4, 57.8 (C^{7c}, C^{1a}), 67.5 (C^{2a}), 80.7 (C^2), 110.1, 114.2 (C^4, C^5), 120.4 (C^7), 127.2, 129.5 ($C^{2'}$, $C^{6'}$, $C^{3'}$, $C^{5'}$), 132.1, 133.9, 135.1 (C^{3a}, C^{7a}, $C^{4'}$), 144.1 ($C^{1'}$), 157.9 (C^6), 170.7 (C=O). Found (%): C, 60.53; H, 4.92; N, 3.14; S, 7.55. Calc. for $C_{21}H_{21}NO_6S$ (%): C, 60.71; H, 5.09; N, 3.37; S, 7.72.

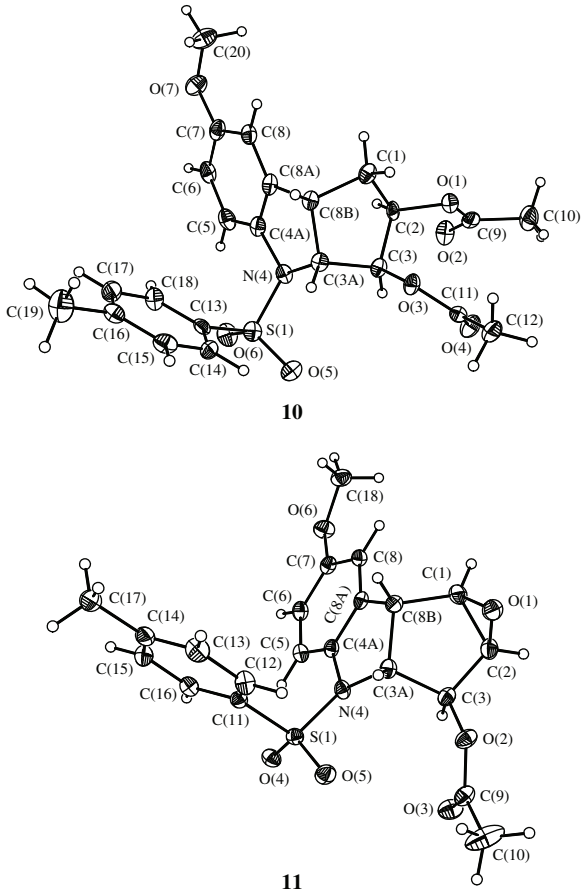
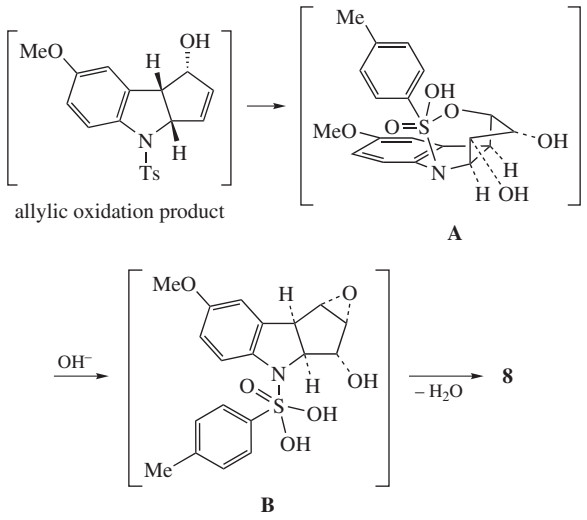


Figure 1 ORTEP view of compounds **10** and **11**. Thermal displacement ellipsoids are drawn at the 50% probability level.

It is well known that the heating of cyclohexene with MnO_2 in acetic acid at 110 °C for 2 h leads to the allylic oxidized product – cyclohex-2-enyl acetate in 66% yield. However, this reaction requires the presence of 10 mol% potassium bromide.[10]

Because the oxidation of the double bond of compound **5** proceeds with simultaneous reduction of permanganate to MnO_2, this MnO_2 should act as a reagent for an allylic oxidation. The intramolecular transformation of this product can lead to intermediate **A**, which can be transformed into epoxide **B**, and after that into compound **8** under alkaline conditions. The examples of the specific influence of sulfonyl groups in some reactions of olefins with elecrtophilic reagents with their direct participation in these transformations are known.[11]



This work was supported by the Federal Programme on the Support of Leading Scientific Schools (grant no. SSH-3019.2008.3).

References

1 A. H. Hains, *Methods for the Oxidation of Organic Compounds*, Academic Press, London, 1985.
2 S. Dash, S. Patel and B. K. Mishra, *Tetrahedron*, 2009, **65**, 707.
3 A. G. Fatiadi, *Synthesis*, 1987, 85.
4 G. G. Belen'kii, L. S. German and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1968, 554 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1968, **17**, 538).
5 A. Garcia-Bosh, A. Company, X. Fontrodona, X. Ribas and M. Costas, *Org. Lett.*, 2008, **10**, 2095.
6 A. S. Demir and H. Findik, *Tetrahedron*, 2008, **64**, 6196.
7 C. Tanyeli, A. Tosun, E. Turkut and B. Sezen, *Tetrahedron*, 2003, **59**, 1055.
8 M. G. Vinogradov, S. P. Verenchikov, T. M. Fedora and G. I. Nikishin, *Zh. Org. Khim*. 1975, **11**, 947 (in Russian).
9 R. R. Gataullin, R. R. Ishberdina, O. V. Shitikova, F. F. Minnigulov, L. V. Spirikhin and I. B. Abdrakhmanov, *Khim. Geterotsikl. Soedin*., 2006, 1184 [*Chem. Heterocycl. Compd*. (*Engl. Transl.*), 2006, **42**, 1025].
10 J. R. Gilmore and J. M. Moller, *Chem. Commun. C*, 1971, 2355.
11 J. I. G. Cadogan, D. K. Cameron, I. Gosney, R. M. Highcock and S. F. Newlands, *J. Chem. Soc., Chem. Commun*., 1986, 766.

Received: 30th March 2009; Com. 09/3309

§ The single crystals of compounds **10** and **11** suitable for the X-ray study were grown by the slow crystallization from 95% ethanol. Reflections for compounds **10** and **11** were collected on a SMART APEX2 CCD diffractometer [λ(MoKα) = 0.71073 Å, graphite monochromator, ω-scans] at 100 K. The structures were solved by the direct methods and refined by the full-matrix least-squares procedure against F^2 in anisotropic approximation. All the hydrogen atoms were placed in geometrically calculated positions and refined within a riding model.

For **10** ($C_{23}H_{25}O_7NS$): monoclinic, space group $P2_1/c$: a = 16.142(3), b = 6.9301(13) and c = 19.846(3) Å, β = 92.617(4)°, V = 2217.8(7) Å^3, Z = 4, M = 459.50, d_{calc} = 1.376 g cm^{-3}, μ = 0.191 mm^{-1}, F(000) = 968, wR_2 = 0.1197, GOF = 0.982 for 4350 independent reflections with $2\theta < 52°$, R_1 = 0.0632 for 2151 reflections with $I > 2\sigma(I)$.

For **11** ($C_{21}H_{21}O_6NS$): monoclinic, space group $C2/c$: a = 30.595(2), b = 8.3348(5) and c = 20.6251(11) Å, β = 131.8850(10)°, V = 3915.6(4) Å^3, Z = 8, M = 415.45, d_{calc} = 1.409 g cm^{-3}, μ = 0.205 mm^{-1}, F(000) = 1744, wR_2 = 0.0960, GOF = 1.041 for 4689 independent reflections with $2\theta < 56°$, R_1 = 0.0422 for 3736 reflections with $I > 2\sigma(I)$.

CCDC 742874 and 742875 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.