Synthesis and Asymmetric Oxidation of (Caranylsulfanyl)-1*H*-imidazoles

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For the first time 2-(*cis*-caran-4-ylsulfanyl)-1*H*-imidazole, 1-methyl-2-(*cis*-caran-4-ylsulfanyl)-1*H*-imidazole, and 2-(*cis*-caran-4-ylsulfanyl)-1*H*-benzimidazole (carane = 3,7,7-trimethylbicyclo[4.1.0]heptane) were synthesized, and the asymmetric oxidation of these compounds was also carried out. It was shown that oxidation by the *Bolm* system and the modified system of *Sharpless* lead to corresponding sulfoxides with de values of 91–100%.

Introduction. – Currently, the transformation of sulfur-containing compounds for the preparation of biologically active substances are being widely studied. Imidazol and benzimidazol sulfoxides have valuable practical properties, for instance, in the asymmetric synthesis [1][2]; they are effective for the treatment of peptic ulcer disease [3][4], and they may act as antioxidants and antidepressants [5]. In addition, it has been shown that the introduction of a compact lipophilic terpene fragment in the known structure of biologically active compounds, in some cases, enhances the biological activity [6].

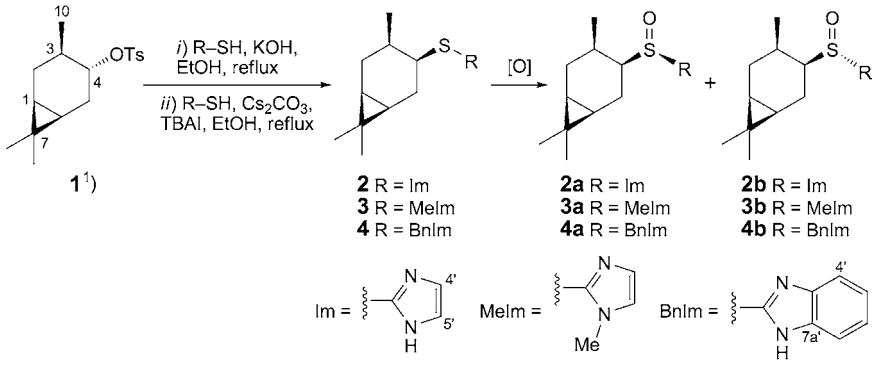
Terpenes are widely used in organic synthesis to obtain enantiomerically pure compounds [7][8] and as chiral auxiliaries or asymmetric ligands employed in enantiomerically selective transformations [9–11]. Recently, we have synthesized new chiral (neomenthylsulfanyl)-1*H*-imidazoles, and asymmetric oxidation of these sulfides (de up to 90%) was carried out [12][13].

Results and Discussion. – In the present work, the asymmetric oxidation of the newly synthesized optically active (caranyl)-1*H*-imidazoles (caran = 3,7,7-trimethylbicyclo[4.1.0]heptane) was carried out.

Initial caranyl-containing heterocyclic sulfides were obtained by two methods. By the first method, the isocaran-4-yl *p*-toluenesulfonate (**1**) reacted with an equimolar amount of the 2-sulfanyl-1*H*-imidazole or 1-methyl-2-sulfanyl-1*H*-imidazole in an alkaline alcohol solution [14] (*Scheme*, *i*). Thus, 2-{[(1*R*,3*S*,4*R*,6*S*)-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}-1*H*-imidazole (**2**) and 1-methyl-2-{[(1*R*,3*S*,4*R*,6*S*)-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}-1*H*-imidazole (**3**) were obtained in 58 and 75% yields, respectively. This method proved to be ineffective for the synthesis of 2-{[(1*R*,3*S*,4*R*,6*S*)-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}-1*H*-benzimidazole (**4**), since the yield of the desired product was low (7%). Therefore, sulfide **4** was prepared according to the second method, *i.e.*, by the reaction of **1** with the 2-sulfanyl-1*H*-

benzimidazole in the presence of the catalytic system Cs_2CO_3/Bu_4NI (TBAI; *Scheme*, *ii*, yield 68%) [15]. Application of the second method for the syntheses **2** and **3** did not increase the yields of sulfides, so the first method was used with easily accessible reagents.

Scheme. *Synthesis and Asymmetrical Oxidation of (Caranylsulfanyl)-1*H*-imidazoles*



The structures of the compounds were established by NMR spectroscopy and elemental analysis, and for sulfide **4** the X-ray crystal structure was determined (*Fig. 1*). The signals of the heterocyclic and carane fragments were observed in the ^{1}H- and ^{13}C-NMR spectra. Thus, in the ^{1}H-NMR spectrum of **2**, a signal of two imidazole H-atoms appeared at the 7.11 ppm, and a broadened *singlet* of the NH H-atom appeared at 10.05 ppm. In the ^{13}C-NMR spectrum, a signal of two imidazole C-atoms at 123.69 ppm (C(4′) and C(5′)) and a signal of a quaternary C-atom at 140.87 ppm (C(2′)) were detected. The ^{1}H-NMR spectrum of the *N*-substituted sulfanyl-1*H*-imidazole **3** was similar to that of the sulfide with unsubstituted imidazole moiety, with the difference that there is a signal of the Me group at 3.58 ppm and no signal of a NH H-atom. In the ^{1}H-NMR spectrum of the sulfanylbenzimidazole **4**, the signals of the aromatic H-atoms appear at 7.15 – 7.21 ppm (H–C(5′), H–C(6′)) and 7.50 – 7.56 ppm (H–C(4′), H–C(7′)), and a broadened *singlet* of the NH H-atom appears at 10.25 ppm.

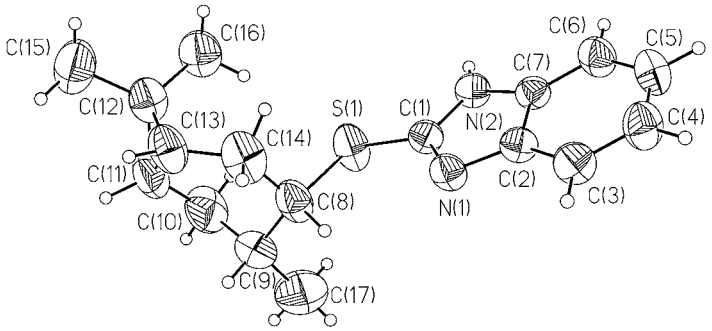


Fig. 1. *Structure of one of the two independent molecules of compound* **4** *by X-ray diffraction*

[0]) Atom numbering according to carane staleton.

In the ^{1}H-NMR spectra of all (caranylsulfanyl)-1*H*-imidazoles **2**–**4**, two typical *singlet*s of Me groups appeared at 0.92–0.96 (Me(8^1)) and 0.97–1.02 ppm (Me(9)), and one *doublet* at 0.95–0.96 ppm ($J = 6.9$ Hz) for Me(10) and the signals of H–C(4) at 3.75–4.21 ppm were detected. The ^{13}C-NMR spectra of the **2**–**4** exhibited the signals of C(4) at 47.8–49.8 ppm, which is characteristic of a cyclic monoterpenic C-atoms linked to a sulfanyl moiety.

The formation of the (caranylsulfanyl)-1*H*-imidazoles occurs *via* a bimolecular nucleophilic substitution with complete inversion of the configuration at C(4). The inversion of the configuration is established by an X-ray crystal-structure analysis of **4**. The HPLC indicated showed no diastereoisomeric isocaran-4-yl sulfides.

Two independent molecules of compound **4** crystallized in a chiral space group of the orthorhombic system (*Table 1*). The general structure of the first molecule is shown in *Fig. 1*, the second molecule has an analogous structure. The numbers of the atoms in the second molecules have an additional designation 'A'. For both molecules, bond lengths and angles were standard, and selected bond lengths and angles are compiled in *Table 2*. The cyclohexyl moiety has a pseudo-envelope conformation in which five

Table 1. *Crystallographic Data for Compounds* **4**, **2a**, *and* **3a**

	4	**2a**	**3a**
Crystal size [mm]	0.24 × 0.18 × 0.13	0.25 × 0.20 × 0.15	0.25 × 0.20 × 0.15
Crystal color	Colorless	Colorless	Yellow
Empirical formula	$C_{17}H_{22}N_2S$	$C_{13}H_{20}N_2OS$	$C_{14}H_{22}N_2OS$
Formula weight	286.43	252.37	266.40
Crystal system	Orthorhombic	Tetragonal	Monoclinic
Space group	$P2_12_12_1$	$P4_32_12$	$P2_1$
Unit cell dimensions			
a [Å]	10.2139(2)	10.7516(6)	12.8549(11)
b [Å]	14.7443(3)	10.7516(6)	7.9406(5)
c [Å]	21.1653(5)	23.8603(15)	14.3449(16)
α [°]	90	90	90
β [°]	90	90	100.142(8)
γ [°]	90	90	90
V [Å^3], Z	3187.43(12), 8	2758.2(3), 8	1441.4(2), 4
D_{calc} [g/cm^3]	1.194	1.215	1.228
μ [mm^{-1}]	0.196	0.222	0.216
θ Range for data collection	$2.61 < \theta < 33.60$	$2.68 < \theta < 28.30$	$2.94 < \theta < 26.37$
Reflections collected	25100	11757	5854
Independent reflections (R_{int})	11281 (0.0234)	3393 (0.0409)	4983 (0.0223)
Reflections with $I > 2\sigma(I)$	5093	1503	2922
Completeness (to θ, °)	99.6% (30.00)	99.7% (28.30)	97.4% (26.37)
S on F^2	1.007	1.004	1.004
R_1 [$I > 2\sigma(I)$]	0.0356	0.0326	0.0371
wR_2 [$I > 2\sigma(I)$]	0.0744	0.0516	0.0614
R_1 (all data)	0.0810	0.0932	0.0691
wR_2 (all data)	0.0765	0.0542	0.0637
Absolute structure parameter	−0.05(4)	−0.04(6)	−0.07(6)
Extinction coefficient	–	0.0076(4)	–
Largest diff. peak and hole [e A^{-1}]	0.336/−0.244	0.138/−0.164	0.189/−0.196

Table 2. *Selected Bond Lengths* [Å] *and Angles* [°] *for Compounds* **4**, **2a**, *and* **3a**

Bond lengths[a])	[Å]	Bond angles[a])	[°]
4			
S(1)–C(1)	1.7367(14)	C(12)–C(11)–C(13)	60.35(11)
S(1)–C(8)	1.8468(15)	C(11)–C(12)–C(13)	59.96(11)
N(1)–C(1)	1.3164(15)	C(11)–C(13)–C(12)	59.69(11)
C(1)–N(2)	1.3550(16)	C(1A)–S(1A)–C(8A)	101.52(6)
C(11)–C(12)	1.488(2)	C(12A)–C(11A)–C(13A)	60.28(10)
C(11)–C(13)	1.492(2)	C(11A)–C(12A)–C(13A)	59.98(11)
C(12)–C(13)	1.498(2)	C(11A)–C(13A)–C(12A)	59.73(11)
		C(1)–S(1)–C(8)	102.46(6)
S(1A)–C(1A)	1.7483(14)		
S(1A)–C(8A)	1.8374(14)		
N(1A)–C(1A)	1.3142(15)		
C(1A)–N(2A)	1.3568(17)		
C(11A)–C(12A)	1.494(2)		
C(11A)–C(13A)	1.498(2)		
C(12A)–C(13A)	1.502(2)		
2a			
S(1)–O(1)	1.4916(12)	O(1)–S(1)–C(2)	105.35(9)
S(1)–C(2)	1.7604(19)	O(1)–S(1)–C(6)	108.36(8)
S(1)–C(6)	1.8186(17)	C(2)–S(1)–C(6)	97.76(8)
C(9)–C(10)	1.499(3)	C(10)–C(9)–C(11)	59.79(14)
C(9)–C(11)	1.503(3)	C(11)–C(10)–C(9)	60.24(13)
C(10)–C(11)	1.496(3)	C(10)–C(11)–C(9)	59.97(13)
N(1)–C(2)	1.344(2)	N(3)–C(2)–N(1)	112.76(18)
C(2)–N(3)	1.303(2)		
3a			
S(1)–O(1)	1.492(2)	O(1)–S(1)–C(2)	106.58(14)
S(1)–C(2)	1.776(3)	O(1)–S(1)–C(6)	106.26(13)
S(1)–C(6)	1.822(3)	C(2)–S(1)–C(6)	97.83(15)
N(1)–C(2)	1.351(4)	C(9)–C(8)–C(10)	60.8(2)
C(2)–N(3)	1.302(4)	C(10)–C(9)–C(8)	60.5(2)
C(8)–C(9)	1.483(5)	C(9)–C(10)–C(8)	58.8(2)
C(8)–C(10)	1.509(4)	O(1A)–S(1A)–C(2A)	107.12(13)
C(9)–C(10)	1.514(5)	O(1A)–S(1A)–C(6A)	105.79(14)
S(1A)–O(1A)	1.494(2)	C(2A)–S(1A)–C(6A)	98.73(15)
S(1A)–C(2A)	1.768(3)	C(9A)–C(8A)–C(10A)	59.6(2)
S(1A)–C(6A)	1.812(3)	C(10A)–C(9A)–C(8A)	59.78(18)
N(1A)–C(2A)	1.350(4)	C(9A)–C(10A)–C(8A)	60.6(2)
C(2A)–N(3A)	1.321(3)		
C(8A)–C(9A)	1.523(4)		
C(8A)–C(10A)	1.511(4)		
C(9A)–C(10A)	1.508(4)		

[a]) Atom numbering adopted for the XRD experiment; see *Figs. 1–3*.

atoms, C(8), C(10), C(11), C(13), and C(14) (numbering adopted for the XRD experiment), are placed in a plane with a maximum deviations of < 0.04 Å, and the Me and heteroarylsulfanyl groups occupy a synclinal position. The molecular packing is

Table 3. *H-Bonds with* $H\cdots A < r(A) + 2.000$ *Å and* $< (DHA) > 110°$

D–H[a])	d(D–H) [Å]	d(H···A) [Å]	< (DHA) [°]	d(D···A) [Å]	A[a])
4					
N(2A)–H(2A)	0.914(14)	2.02(2)	157.0(9)	2.887(3)	N(1)[$x+1$, y, z]
N(2)–H(2)	0.827(15)	2.12(2)	162.5(9)	2.919(3)	N(1A)
2a					
N(1)–H(1)	0.912(18)	1.886(19)	162.8(16)	2.771(2)	O(1)[y, x, $-z$]

[a]) Atom numbering adopted for the XRD experiment; see *Figs. 1–3*.

formed by H-bonded polymer chains in which the planes of the heterocyclic fragments form a dihedral angle of 66.5°. The parameters of H-bonds are collected in *Table 3*.

For the oxidation of **2**–**4**, well-known oxidants for sulfides were used. The achiral oxidants (*meta*-chloroperoxybenzoic acid (*m*-CPBA), cumene hydroperoxide (CHP) in the presence of $[VO(acac)_2]$ (= vanadyl acetylacetonate = oxobis(pentane-2,4-dionato)vanadium(IV)), *tert*-butyl hydroperoxide (^{t}BuOOH) in the presence of $[VO(acac)_2]$], and chiral systems (*Bolm* with *Jacobsen* ligand, and a modified *Sharpless* system) were used. The results of the asymmetric oxidation are compiled in *Table 4*.

Table 4. *The Results of the Asymmetric Oxidation*

Sulfide		*m*-CPBA	TBHP/ $[VO(acac)_2]$	CHP/ $[VO(acac)_2]$	*Bolm* system[b])	*Sharpless* system[c])
2	Yield[a]) [%]	69	73	76	83	80
	de	48	51	56	100	100
3	Yield[a]) [%]	86	71	67	82	89
	de	42	48	43	91	94
4	Yield[a]) [%]	99	83	79	86	76
	de	40	50	52	91	100

[a]) The overall preparative yield of the diastereoisomers. [b]) Sulfide/$[VO(acac)_2]$/L*/H_2O_2 50 : 1 : 1.5 : 50; L* = (+)-(*S,S*)-*N,N'*-bis[3,5-di(*tert*-butyl)salicylidene]cyclohexane-1,2-diamine. [c]) Sulfide/(+)-DET/^{t}BuOOH/(^{i}PrO)$_4$Ti/H_2O/EtN(^{i}Pr)$_2$ 1 : 2 : 1 : 1 : 1 : 1; DET = diethyltartrate; solvent CH_2Cl_2.

The oxidation of sulfides **2**–**4** by *m*-CPBA, TBHP, or CHP led to sulfoxides with high average yields (67–83%) and a moderate diastereoselectivity (43–56%). The use of the chiral catalyst systems allowed us to obtain the corresponding sulfoxides with high yields (up to 89%) and very high de values (91–100%).

All the individual diastereoisomers were isolated and characterized by NMR and IR spectroscopy, crystals were grown for compounds **2a** and **3a**, and the X-ray diffraction analyses were carried out. In the IR spectra of the obtained sulfoxides **2a**, **2b**, **3a**, **3b**, **4a**, and **4b**, absorption bands characteristic of the sulfinyl moiety in the range of 1018–1042 cm^{-1} were observed. Signals of the heterocyclic and carane fragments are observed in the ^{1}H- and ^{13}C-NMR spectra. In the ^{13}C-NMR spectra of the

caranylsulfinylimidazoles, in contrast to the corresponding sulfides, the signal of C(4) shifted downfield to 62.5 – 65.3 ppm.

The oxidation of sulfide **2** by chiral catalytic systems led to the formation of one diastereoisomer **2a**. The structure and absolute configuration of **2a** were determined by means of the X-Ray diffraction data (*Fig. 2*). This predominant diastereoisomer was also formed by using other oxidants. According to the X-ray data, **2a** crystallized in a chiral space group of the tetragonal system. Selected bond lengths and angles are collected in *Table 2*. The cyclohexyl moiety has a 'boat' conformation with the heteroarylsulfanyl and Me substituents are in an eclipsed conformation. The molecular packing is formed by S–O ··· H–N bonded dimers, placed on a twofold axis. The parameters of the H-bonds are compiled in *Table 3*.

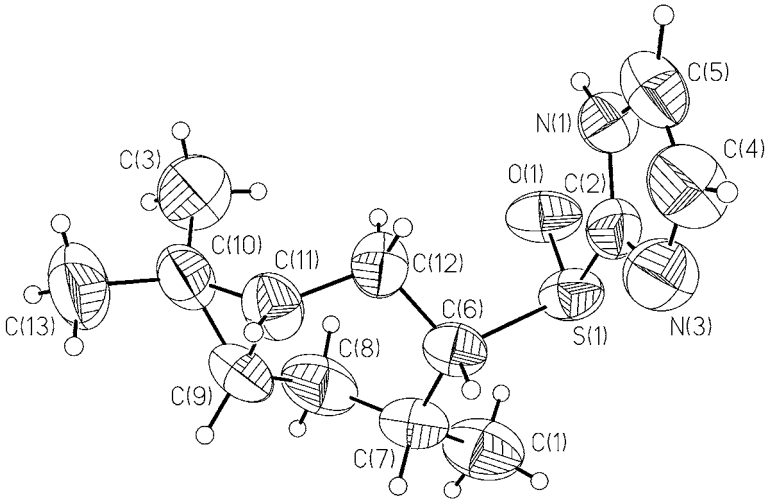


Fig. 2. *Structure of one of the two independent molecules of compound* **2a** *by X-ray diffraction*

Similarly, the oxidation of compound **4** with the modified *Sharpless* reagent led to one diastereoisomer **4a** in 76% yield. The predominant diastereoisomer in the oxidation of sulfide **3** was sulfoxide **3a**. The structure and absolute configuration of compound **3a** were determined by the X-Ray crystallography (*Fig. 3*). According to the X-ray data, compound **3a** crystallized in a chiral space group of the monoclinic system. The molecular geometry, bond lengths and angles in particular, is in agreement with the molecular structure of compound **3a**. Selected bond lengths and angles are collected in *Table 2*. In compound **2a**, the cyclohexyl moiety has a 'boat' conformation with heteroarylsulfanyl and Me substituents in an eclipsed conformation. The molecular packing has no significant short contacts.

The diastereoisomers **2a** and **3a** have the (*R*)-configuration at the S-atom. In this case, the O-atom of the sulfinyl moiety at C(4)[1]) is oriented in the direction opposite to that of the Me group at C(3). Accordingly, the formation of the sterically less obstructed (*R*)-diastereoisomer is more advantageous.

The absolute configurations of compounds **2b** and **3b** were determined by comparing them with those of sulfoxides **2a** and **3a**. No suitable crystals were grown

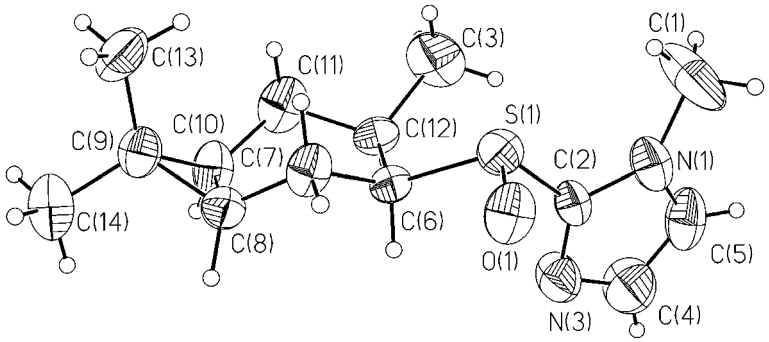


Fig. 3. *Structure of one of the two independent molecules of compound* **3a** *by X-ray diffraction*

in the case of **4a** and **4b**. The ^{1}H-NMR spectra of the (*R*)-diastereoisomers **2a** and **3a** displayed a significant similarity to that of diastereoisomer **4a** with respect to the chemical shifts and coupling constants. The spectra of compounds **2b**, **3b** and **4b** were also similar. So in the spectrum of compound **2a**, the H_α–C(5)[1]) and H_β–C(5) signals had similar chemical shifts at 1.47 – 1.62 ppm. Similarly, the H_α–C(5) and H_β–C(5) signals of diastereoisomer **4a** appeared at 1.43 – 1.76 ppm. In the spectrum of **2b**, the H_α–C(5) signal appeared at 0.83 – 0.97 and the H_β–C(5) signal at 1.48 – 1.57 ppm. In the spectrum of **4b**, the H_α–C(5) signal was detected at 0.95 – 1.13 and the H_β–C(5) signal at 1.82 – 1.87 ppm. The chemical shifts of the H-atoms at C(1) and C(6) in the (*R*)- and (*S*)-diastereoisomers were significantly different (*Fig. 4*).

Based on these observations, optical rotations, and also the yields of the diastereoisomers (**2a**: 51 – 80%, **3a**: 48 – 86%, **4a**: 40 – 82%; **2b**: up to 17%, **3b**: 3 – 25%, **4b**: up to 30%), it can be concluded that compound **4a** has an (*R*)-configuration, and **4b** has an (*S*)-configuration at the S-atom.

Conclusion. – New caranyl heteroaryl sulfides were synthesized, and the conditions for their asymmetric oxidation were established. The efficiency achieved with the *Bolm* and modified *Sharpless* chiral systems for the syntheses of diastereoisomerically pure and diastereoisomerically enriched sulfoxides is reported.

Experimental Part

General. The starting materials were obtained from commercial suppliers and used without further purification. Column chromatography (CC): *AlfaAesar Silica gel 60* (0.06 – 0.2 mm). TLC: *Sorbfil* plates. HPLC: *Thermo Finnigan Surveyor* system, *BDS Hypersil C18*, *Hypersil Gold*, *Hypercarb* columns. Optical rotations: *Kruss P3002RS* digital polarimeter. M.p.: *Gallencamp-Sanyo* apparatus; uncorrected. IR Spectra: *Shimadzu IR Prestige* spectrophotometer. NMR Spectra: *Bruker Avance-300* instrument, at 300.17 (^{1}H) and 75.48 MHz (^{13}C); $CDCl_3$ solns.; δ in ppm rel. to $CDCl_3$ as internal standard; *J* in Hz. 2D Homonuclear ^{1}H,^{1}H-COSY, NOESY spectra and heteronuclear ^{1}H,^{13}C-HMBC, HSQC spectra were used to assign the H- and C-signals. Elemental analyses: EA 1110 CHNS-O analyzer. X-Ray diffraction analyses of single crystals: X-ray diffractometer *Xcalibur S* equipped with a CCD detector (MoK_α graphite-monochromated radiation, $\lambda = 0.71073$ Å, $\tilde{\omega}$-scanning technique, the scanning step, 1°) at 295(2) K. Absorption correction was not applied. The structures were solved by the direct methods and refined applying the full matrix least-squares against F^2_{hkl} with anisotropic displacement parameters for all non-

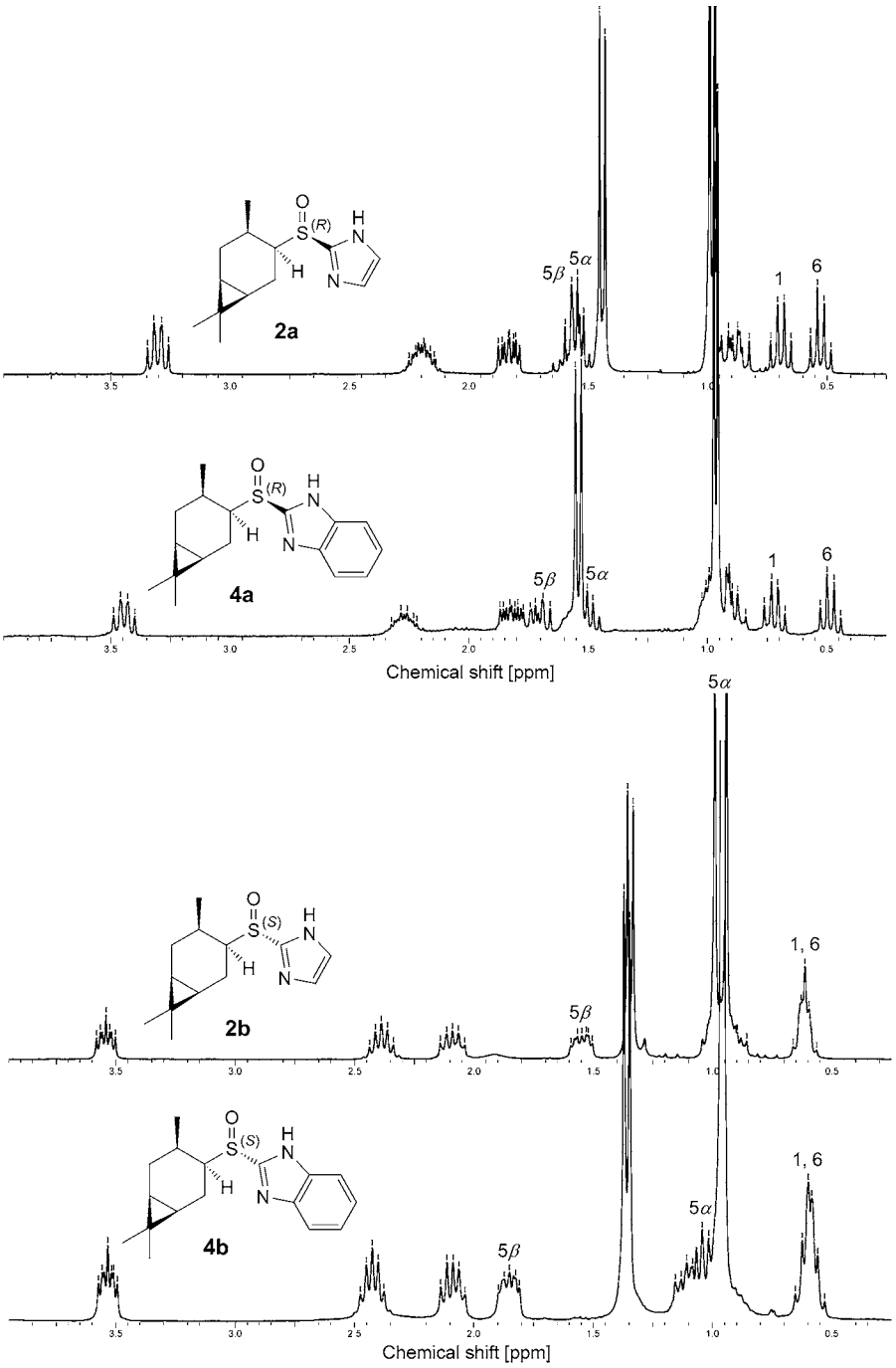


Fig. 4. *Sections of* ^{1}*H-NMR spectra of compounds* **2a** *and* **4a**, *and* **2b** *and* **4b**[1])

H-atoms using the SHELX97 program package [16]. All the H-atoms were located in different electron density maps and refined using a riding model with fixed thermal parameters. The general crystallographic data and results of refinements are compiled in *Table 1*. CCDC-851807-851809 contain the supplementary crystallographic data for this article (compounds **4**, **2a**, and **3a**). These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

(−)-Isocaran-4-ol (=*(1*R,*3*R,*4*R,*6*S*)-4,7,7-Trimethylbicyclo[4.1.0]heptan-3-ol*). Prepared from (+)-car-3-ene ($[\alpha]_D^{20} = +18$, neat) according to [17], in 98% yield.

(−)-Isocaran-4-yl 4-Methylbenzenenesulfonate (=*(1*R,*3*R,*4*R,*6*S*)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl 4-Methylbenzenesulfonate*; **1**) prepared according to [18], in quant. yield.

*2-{[(1*R,*3*S,*4*R,*6*S*)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}-1*H*-imidazole* (**2**) *and 1-Methyl-2-{[(1*R,*3*S,*4*R,*6*S*)-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}-1*H*-imidazole* (**3**). KOH (0.07 g, 1.2 mmol) in 3 ml of EtOH was added to the soln. of the corresponding thiol (1 mmol) in 5 ml of EtOH. The mixture was stirred for 10 min. Then, the temp. was raised to 78°, and EtOH soln. of **1** (0.37 g, 1 mmol) was added. The mixture was refluxed for 24 h, evaporated, extracted with $CHCl_3$, and dried (Na_2SO_4). The solvent was removed, and the products **2** and **3** were purified by CC ($CHCl_3$).

Data of **2**. Yield: 58%. Yellow crystals. M.p. 109–110°. $[\alpha]_D^{20} = +49.75$ ($c = 0.16$, EtOH). ^{1}H-NMR (300 MHz)[1]): 0.53 (*td*, *J* = 8.9, 5.6, H–C(6)); 0.67 (*td*, *J* = 8.9, 7.0, H–C(1)); 0.85 (*ddd*, *J* = 14.5, 10.0, 7.0, H_α–C(2)); 0.96 (*d*, *J* = 6.9, Me(10)); 0.96 (*s*, Me(8)); 1.00 (*s*, Me(9)); 1.38 (*ddd*, *J* = 15.3, 7.6, 5.5, H_α–C(5)); 1.81 (*ddd*, *J* = 14.5, 8.9, 5.6, H_β–C(2)); 1.87–2.02 (*m*, H–C(3)); 2.18 (*ddd*, *J* = 15.4, 8.9, 7.0, H_β–C(5)); 3.75 (*q*, *J* = 7.0, H–C(4)); 7.11 (br. *s*, H–C(4′), H–C(5′)); 10.05 (br. *s*, NH). ^{13}C-NMR (75.48 MHz)[1]): 15.8 (C(9)); 17.8 (C(7)); 18.8 (C(10)); 20.5 (C(6)); 21.4 (C(1)); 25.3 (C(2)); 25.6 (C(5)); 28.5 (C(8)); 30.8 (C(3)); 49.8 (C(4)); 123.7 (C(4′), C(5′)); 140.9 (C(2′)). Anal. calc. for $C_{13}H_{20}N_2S$ (236.38): C 66.06, H 8.53, N 11.85, S 13.57; found: C 66.89, H 8.24, N 11.25, S 13.62.

Data of **3**. Yield: 75%. Yellow oil. $[\alpha]_D^{20} = +62.88$ ($c = 0.59$, EtOH). ^{1}H-NMR (300 MHz)[1]): 0.58 (*td*, *J* = 8.9, 5.5, H–C(6)); 0.72 (*td*, *J* = 8.9, 7.0, H–C(1)); 0.88 (*ddd*, *J* = 14.5, 10.0, 7.0, H_α–C(2)); 0.95 (*d*, *J* = 6.9, Me(10)); 0.96 (*s*, Me(8)), 1.02 (*s*, Me(9)); 1.43 (*ddd*, *J* = 15.3, 7.2, 5.5, H_α–C(5)); 1.83 (*ddd*, *J* = 14.5, 8.9, 5.6, H_β–C(2)); 1.89–2.03 (*m*, H–C(3)); 2.24 (*ddd*, *J* = 15.3, 8.9, 7.2, H_β–C(5)); 3.58 (*s*, Me–N(1′)); 3.84 (*q*, *J* = 7.0, H–C(4)), 6.87 (*d*, *J* = 1.0, H–C(5′)); 7.03 (*d*, *J* = 1.0, H–C(4′)). ^{13}C-NMR (75.48 MHz)[1]): 15.8 (C(9)); 17.7 (C(7)); 18.8 (C(10)); 20.4 (C(6)); 21.5 (C(1)); 25.3 (C(5)); 25.7 (C(2)); 28.5 (C(8)); 30.7 (C(3)); 33.2 (Me–N(1′)); 49.6 (C(4)); 121.7 (C(5′)); 129.2 (C(4′)); 142.5 (C(2′)). Anal. calc. for $C_{14}H_{22}N_2S$ (250.41): C 67.15, H 8.86, N 11.19, S 12.81; found: C 67.24, H 9.01, N 11.21, S 12.54.

*2-{[(1*R,*3*S,*4*R,*6*S*)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}-1*H*-benzimidazole* (**4**). The soln. of 2-sulfanyl-1*H*-benzimidazole (0.15 g, 1 mmol), Cs_2CO_3 (0.33 g, 1 mmol), and Bu_4NI (TBAI; 0.37 g, 1 mmol) in 5 ml of EtOH was stirred for 1 h at 20°. Then, **1** (0.34 g, 1 mmol) was added. The mixture was refluxed for 24 h. The reaction was monitored by TLC (Et_2O/heptane 2:1). The mixture was evaporated, extracted with Et_2O (3 × 30 ml), and dried (Na_2SO_4). The solvent was removed, and the product **4** was purified by CC ($CHCl_3$). Yield: 68%. Colorless crystals. M.p. 184–185°. $[\alpha]_D^{20} = +55.30$ ($c = 0.27$, EtOH). ^{1}H-NMR (300 MHz)[1]): 0.49 (*td*, *J* = 9.0, 5.5, H–C(6)); 0.64 (*td*, *J* = 9.0, 7.0, H–C(1)); 0.81 (*ddd*, *J* = 14.7, 10.3, 7.0, H_α–C(2)), 0.92 (*s*, Me(8)); 0.95 (*d*, *J* = 6.9, Me(10)); 0.97 (*s*, Me(9)); 1.46 (*ddd*, *J* = 15.4, 7.2, 5.5, H_α–C(5)); 1.78 (*ddd*, *J* = 14.7, 8.9, 5.5, H_β–C(2)); 1.91–2.05 (*m*, H–C(3)); 2.37 (*ddd*, *J* = 15.3, 8.9, 7.2, H_β–C(5)); 4.21 (*q*, *J* = 7.0, H–C(4)); 7.15–7.21 (*m*, H–C(5′), H–C(6′)); 7.50–7.56 (*m*, H–C(4′), H–C(7′)); 10.25 (br. *s*, NH). ^{13}C-NMR (75.48 MHz)[1]): 15.7 (C(9)); 17.7 (C(7)); 18.9 (C(10)); 20.1 (C(6)); 21.6 (C(1)); 25.2 (C(2)); 26.0 (C(5)); 28.4 (C(8)); 30.8 (C(3)); 47.8 (C(4)); 113.8 (C(5′), C(6′)); 121.9 (C(4′), C(7′)); 139.1 (C(3a′), C(7a′)); 151.3 (C(2′)). Anal. calc. for $C_{17}H_{22}N_2S$ (286.44): C 71.28, H 7.74, N 9.78, S 11.19; found: C 71.13, H 8.03, N 10.00, S 10.84.

Oxidation of **2**–**4** *with* m-*Chloroperoxybenzoic Acid* (*m*-CPBA). *General Procedure.* The soln. of *m*-CPBA (0.246 g, 1 mmol) in $CHCl_3$ at 0° was added to 1 mmol of a sulfide **2**–**4** dissolved in 5 ml of $CHCl_3$. The mixture was stirred for 5 h and purged with dry NH_3 gas. The resulting ammonium salt as a gummy precipitate was filtered. The solvent was removed, and the products were purified by CC ($CHCl_3$/Et_2O 50:1).

Oxidation of **2**–**4** *with TBHP(or CHP)–[VO(acac)$_2$] Systems. General Procedure.* The soln. of 1 mmol of ^{t}BuOOH (TBHP) or cumene hydroperoxide (CHP) in $CHCl_3$ was added to the mixture of 1 mmol of **2**–**4** and 0.01 mmol of [VO(acac)$_2$] in 5 ml of $CHCl_3$. After 1 h of stirring at r.t., an aq. soln. of $FeSO_4 \cdot 7\,H_2O$ and citric acid was added to the mixture, and the products were extracted with Et_2O (3 × 15 ml). The extract was washed with sat. soln. of $NaHCO_3$ and NaCl, and dried (Na_2SO_4). The solvent was removed, and the products were purified by CC ($CHCl_3$/Et_2O 50:1).

Asymmetric Oxidation of **2**–**4** *with a Modified* Sharpless *System*. This reaction was conducted according to [19]. The products were purified by CC ($CHCl_3$/Et_2O 50:1).

Asymmetric Oxidation of **2**–**4** *with the* Bolm *System*. This reaction was carried out according to [20] with the *Jacobsen* ligand (+)-(*S,S*)-*N,N′*-bis[3,5-di(*tert*-butyl)salicylidene]cyclohexane-1,2-diamine [21]. The products were purified by CC ($CHCl_3$/Et_2O 50:1).

*2-[(*R*)-[(1*R,*3*S,*4*R,*6*S)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl]sulfinyl}-1*H*-imidazole* (**2a**). Yield: 51–80%. Colorless crystals. M.p. 148–149°. $[\alpha]_D^{20} = +239.89$ ($c = 0.27$; EtOH). IR (KBr): 1034 (S=O). ^{1}H-NMR (300 MHz)[1]): 0.50 (*q*, *J* = 8.5, H–C(6)); 0.67 (*q*, *J* = 8.5, H–C(1)); 0.86 (*ddd*, *J* = 14.2, 11.7, 8.5, H_α–C(2)); 0.94 (*s*, Me(9)); 0.96 (*s*, Me(8)); 1.41 (*d*, *J* = 7.1, Me(10)); 1.47–1.62 (*m*, H_α–C(5), H_β–C(5)); 1.81 (*ddd*, *J* = 14.2, 7.8, 4.6, H_β–C(2)); 2.08–2.26 (*m*, H–C(3)); 3.28 (*dt*, *J* = 9.7, 8.5, H–C(4)); 7.21 (br. *s*, H–C(4′), H–C(5′)); 12.08 (br. *s*, NH). ^{13}C-NMR (75.48 MHz)[1]): 13.7 (C(5)); 14.9 (C(9)); 18.2 (C(6)); 18.7 (C(7)); 19.0 (C(10)); 22.4 (C(1)); 26.9 (C(2)); 28.3 (C(8)); 30.3 (C(3)); 62.6 (C(4)); 119.2 (C(5′)); 131.2 (C(4′)); 145.0 (C(2′)). Anal. calc. for $C_{13}H_{20}N_2SO$ (252.38): C 61.87, H 7.99, N 11.10, S 12.71; found: C 61.50, H 8.13, N 11.04, S 12.99.

*2-[(*S*)-[(1*R,*3*S,*4*R,*6*S)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl]sulfinyl}-1*H*-imidazole* (**2b**). Yield: up to 17%. White crystal powder. M.p. 102–103°. $[\alpha]_D^{20} = -47.69$ ($c = 0.26$, $CHCl_3$). IR (KBr): 1024 (S=O). ^{1}H-NMR (300 MHz)[1]): 0.54–0.63 (*m*, H–C(6), H–C(1)); 0.83–1.01 (*m*, H_α–C(2), H_α–C(5)); 0.91 (*s*, Me(9)); 0.96 (*s*, Me(8)); 1.31 (*d*, *J* = 7.1, Me(10)); 1.48–1.57 (*m*, H_β–C(5)); 2.01–2.11 (*m*, H_β–C(2)); 2.29–2.43 (*m*, H–C(3)); 3.51 (*ddd*, *J* = 11.8, 7.2, 4.9, H–C(4)); 7.20 (br. *s*, H–C(4′), H–C(5′)); 12.70 (br. *s*, NH). ^{13}C-NMR (75.48 MHz)[1]): 15.1 (C(9)); 16.8 (C(5)); 17.7 (C(10)); 18.3 (C(7)); 20.0 (C(6)); 21.1 (C(1)); 26.4 (C(2)); 27.5 (C(3)); 28.2 (C(8)); 65.1 (C(4)); 120.7 (C(5′)); 129.2 (C(4′)); 144.4 (C(2′)). Anal. calc. for $C_{13}H_{20}N_2SO$ (252.38): C 61.87, H 7.99, N 11.10, S 12.71; found: C 61.92, H 8.07, N 11.11, S 12.60.

*1-Methyl-2-[(*R*)-[(1*R,*3*S,*4*R,*6*S)-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfinyl}-1*H*-imidazole* (**3a**). Yield: 48–86%. Yellow crystals. M.p. 95–96°. $[\alpha]_D^{20} = +87.94$ ($c = 0.34$, EtOH). IR (KBr): 1036 (S=O). ^{1}H-NMR (300 MHz)[1]): 0.60–0.71 (*m*, H–C(6), H–C(1)); 0.79–0.92 (*m*, H_α–C(2)); 1.00 (*s*, Me(8)); 1.04 (*s*, Me(9)), 1.09 (*d*, *J* = 7.0, Me(10)); 1.54–1.67 (*m*, H_α–C(5)); 1.83 (*ddd*, *J* = 14.2, 8.2, 5.67, H_β–C(2)); 1.89–2.03 (*m*, H–C(3), H_β–C(5)); 3.62–3.72 (*m*, H–C(4)); 3.94 (*s*, Me–N(1′)); 6.95 (*d*, *J* = 0.9, H–C(5′)); 7.13 (*d*, *J* = 0.9, H–C(4′)). ^{13}C-NMR (75.48 MHz)[1]): 14.9 (C(5)); 15.1 (C(9)); 18.3 (C(10)); 18.5 (C(7)); 19.6 (C(6)); 21.5 (C(1)); 26.8 (C(2)); 28.3 (C(8)); 29.2 (C(3)); 33.8 (Me–N(1′); 61.0 (C(4)); 124.7 (C(5′)); 129.4 (C(4′)); 144.2 (C(2′)). Anal. calc. for $C_{14}H_{22}N_2SO$ (266.40): C 63.12, H 8.32, N 10.52, S 12.04; found: C 64.02, H 8.01, N 11.03, S 11.93.

*1-Methyl-2-[(*S*)-[(1*R,*3*S,*4*R,*6*S)-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfinyl}-1*H*-imidazole* (**3b**). Yield: 3–25%. Yellow crystal powder. M.p. 124–125°. $[\alpha]_D^{20} = -15.13$ ($c = 0.52$, EtOH). IR (KBr): 1042 (S=O). ^{1}H-NMR (300 MHz)[1]): 0.58–0.68 (*m*, H–C(6), H–C(1)); 0.72–0.83 (*m*, H_α–C(2)); 0.92 (*s*, Me(9)); 0.95 (*s*, Me(8)); 0.93–1.06 (*m*, H_α–C(5)); 1.25 (*d*, *J* = 7.0, Me(10)); 1.28–1.39 (*m*, H_β–C(2)); 2.11–2.21 (*m*, H_β–C(5)); 2.44 (*dq*, *J* = 14.5, 7.3, H–C(3)); 3.75 (*ddd*, *J* = 11.2, 6.7, 4.7, H–C(4)); 3.93 (*s*, Me–N(1′)); 7.01 (*d*, *J* = 0.9, H–C(5′)); 7.18 (*d*, *J* = 0.9, H–C(4′)). ^{13}C-NMR (75.48 MHz)[1]): 15.3 (C(9)); 16.8 (C(5)); 17.5 (C(10)); 18.1 (C(7)); 19.9 (C(6)); 21.2 (C(1)); 26.1 (C(2)); 26.6 (C(3)); 28.2 (C(8)); 33.6 (Me–N(1′); 62.5 (C(4)); 124.6 (C(5′)); 130.1 (C(4′)); 144.9 (C(2′)). Anal. calc. for $C_{14}H_{22}N_2SO$ (266.40): C 63.12, H 8.32, N 10.52, S 12.04; found: C 63.86, H 8.30, N 10.12, S 11.81.

*2-[(*R*)-[(1*R,*3*S,*4*R,*6*S)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl]sulfinyl}-1*H*-benzimidazole* (**4a**). Yield: 40–82%. Yellow crystal powder. M.p. 98–99°. $[\alpha]_D^{20} = +43.50$ ($c = 0.77$, EtOH). IR (KBr): 1040 (S=O). ^{1}H-NMR (300 MHz)[1]): 0.47 (*q*, *J* = 8.5, H–C(6)); 0.70 (*q*, *J* = 8.5, H–C(1)); 0.84–1.02 (*m*, H_α–C(2)); 0.85 (*s*, Me(8)); 0.92 (*s*, Me(9)); 1.43–1.57 (*m*, H_α–C(5)); 1.59 (*d*, *J* = 7.0, Me(10)); 1.68–1.76 (*m*, H_β–C(5)); 1.84 (*ddd*, *J* = 14.3, 8.0, 4.1, H_β–C(2)); 2.21–2.38 (*m*, H–C(3)); 3.48 (*q*, *J* = 9.0, H–C(4)); 7.30–7.36 (*m*, H–C(5′), H–C(6′)); 7.59–7.76 (*m*, H–C(4′), H–C(7′)); 12.04 (br. *s*, NH). ^{13}C-NMR (75.48 MHz)[1]): 13.8 (C(5)); 14.7 (C(9)); 17.6 (C(6)); 18.8 (C(7)); 19.3 (C(10)); 22.9 (C(1)); 26.9 (C(2));

28.2 (C(8)); 30.9 (C(3)); 63.0 (C(4)); 123.4 (C(4′) C(5′), C(6′), C(7′)); 143.9 (C(3a′), C(7a′)); 152.88 (C(2′)). Anal. calc. for $C_{17}H_{22}N_2SO$ (302.43): C 67.51, H 7.33, N 9.26, S 10.60; found: C 67.60, H 7.27, N 9.53, S 10.31.

*2-[(*S*)-[(1*R,*3*S,*4*R,*6*S)-4,7,7-Trimethylbicyclo[4.1.0]hept-3-yl]sulfinyl]-1*H*-benzimidazole* (**4b**). Yield: up to 30%. White crystal powder. M.p. 113–114°. $[\alpha]_D^{20} = -7.76$ ($c = 0.57$, EtOH). IR (KBr): 1018 (S=O). ^{1}H-NMR (300 MHz)[1]): 0.50–0.62 (*m*, H–C(6), H–C(1)); 0.92 (*s*, Me(9)); 0.93 (*s*, Me(8)); 0.92–1.13 (*m*, H_α–C(2), H_α–C(5)); 1.33 (*d*, $J = 7.0$, Me(10)); 1.82–1.87 (*m*, H_β–C(5)); 2.06 (*dt*, $J = 14.2$, 7.9, H_β–C(2)); 2.40 (*dq*, $J = 14.8$, 7.3, H–C(3)); 3.50 (*ddd*, $J = 11.0$, 7.1, 4.5, H–C(4)); 7.29–7.35 (*m*, H–C(5′), H–C(6′)); 7.60–7.77 (*m*, H–C(4′), H–C(7′)); 12.78 (br. *s*, NH). ^{13}C-NMR (75.48 MHz)[1]): 15.1 (C(9)); 17.0 (C(5)); 17.6 (C(10)); 18.3 (C(7)); 19.7 (C(6)); 21.4 (C(1)); 26.5 (C(2)); 27.4 (C(3)); 28.1 (C(8)); 65.3 (C(4)); 123.6 (C(4′), C(5′), C(6′), C(7′)); 143.86 (C(3a′), C(7a′)); 151.80 (C(2′)). Anal. calc. for $C_{17}H_{22}N_2SO$ (302.44): C 67.51, H 7.33, N 9.26, S 10.60; found: C 67.56, H 7.38, N 9.17, S 10.62.

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