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Spectral Assignments and Reference Data

Complete ^{1}H and ^{13}C NMR spectral assignment of *N*-aralkylsulfonamides, *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines and *N*-sulfonyl-2,3,4,5-tetrahydro-1*H*-2-benzazepines. Conformational analysis of *N*-[((3′,4′-dichlorophenyl)methyl)sulfonyl]-3-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepin

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The complete and unambiguous assignment of the ^{1}H NMR and ^{13}C NMR spectra of 26 *N*-aralkylsulfonamides, *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines and *N*-sulfonylbenz[*c*]azepines was performed on the basis of APT, DEPT, homonuclear (gs-COSY) and ^{1}H-detected heteronuclear one-bond (gs-HMQC) and long-range (gs-HMBC) correlation experiments. The methylated 2,3,4,5-tetrahydro-1*H*-2-benzazepine derivative 26 adopts a chair conformation as determined by ^{1}H-^{1}H coupling analysis and γ-gauche *effect*s. This is supported by a single-crystal X-ray structure analysis. Copyright © 2005 John Wiley & Sons, Ltd.

KEYWORDS: ^{1}H NMR; ^{13}C NMR; *N*-aralkylsulfonamides; *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines; *N*-sulfonyl-2,3,4,5-tetrahydro-1*H*-2-benzazepines; conformational analysis; x-ray diffraction

INTRODUCTION

N-Aralkylsulfonamides, *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines and *N*-sulfonyl-2,3,4,5-tetrahydro-1*H*-2-benzazepines are important synthetic intermediates, and also exist as substructures of various biologically active compounds.[1–10] *N*-Aralkylsulfonamides were obtained using several slightly modified classical methods,[11,12] *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines and *N*-sulfonyl-2,3,4,5-tetrahydro-1*H*-2-benzazepines were synthesized by intramolecular sulfonylamidomethylation of *N*-aralkylsulfonamides in acid medium.[12,13] Some ^{1}H NMR of the title compounds – recorded at low-field instruments[13,14] – were partially reported before, but here we present a full ^{1}H and ^{13}C NMR signal assignments for the first time.

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EXPERIMENTAL

The syntheses of **1**–**25** have been described earlier.[13,14] *N*-[((3′,4′-Dichlorophenyl)methyl)sulfonyl]-3-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepin (**26**) has not yet been reported in literature, but its synthesis was performed in analogy to **25**; yield of the final sulfonoamidomethylation step 71%; mp 138.5–139.0 °C; IR, solid state, 2956 (w), 2868 (w), 1471 (m), 1386 (m), 1353 (m), 1325 (s) [SO_2, ν_{as}], 1140 (s) [SO_2, ν_s], 1090 (m), 1030 (m), 1003 (s), 896 (s), 830 (s), 817 (s), 768 (s), 748 (s), 662 cm^{-1} (s); positive ESI-MS: m/z $[M+H]^+$, $C_{18}H_{20}NO_2SCl_2$ requires 384.0592, found 384.0584; $[M+H-SO_2]^+$ (base peak), $C_{18}H_{20}NCl_2$ requires 320.0973, found 320.1020; negative ESI-MS: m/z $[M-H]^-$, $C_{18}H_{18}NO_2SCl_2$ requires 382.0435, found 382.0443. For NMR data, see Tables 2 and 3.

Room temperature ^{1}H (400.1 MHz) and ^{13}C (100.6 MHz) NMR measurements were performed on a Bruker Avance DPX-400 spectrometer. The chemical shift standard was internal tetramethylsilane for ^{1}H and ^{13}C (δ 0 ppm). Digital resolutions in the 1D NMR spectra were 0.14 Hz/point for ^{1}H, 0.24 Hz/point for ^{13}C, pulse angles were *ca*. 30°, and sample concentrations were 0.095–0.230 M. Signal assignments were assisted by APT (attached-proton test), DEPT, gs-COSY, gs-HMQC, and gs-HMBC experiments using standard Bruker software.

Single-crystal X-ray diffraction measurements were performed on a Stoe IPDS image plate diffractometer. The structure was solved and refined by routine methods. All H atoms were initially determined on difference Fourier maps. However, in the final cycles of least squares refinement, the H atoms were allowed to ride on the respective C atoms with idealized bond distances and angles.

IR spectra have been recorded on a Bruker Vector 22 Attenuated Total Reflection (ATR) and electrospray mass spectra on a Micromass LCT. Semiempirical (AM1) calculations and various conformations of **26** were performed using Spartan '04 of the Wavefunction® software package.

RESULTS AND DISCUSSION

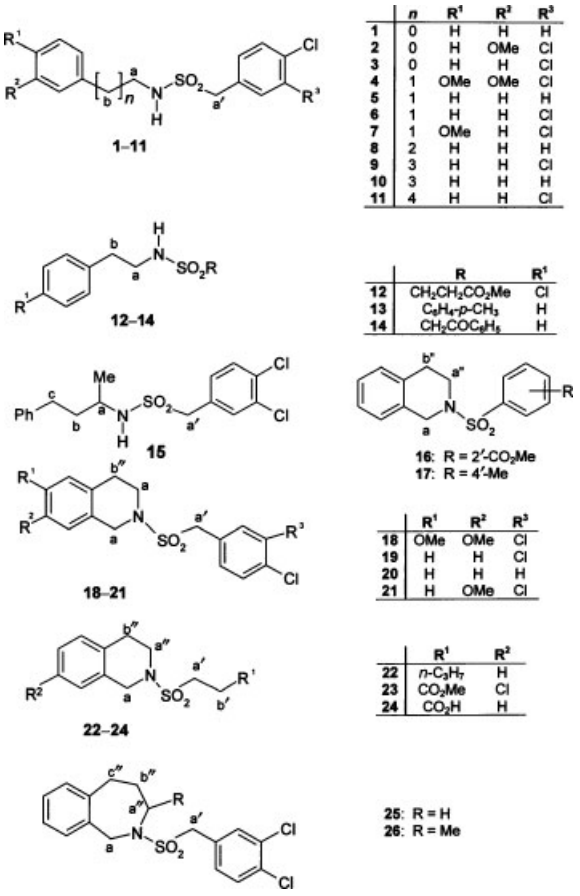
We report the assignment of the ^{1}H NMR and ^{13}C NMR spectra for **1**–**26** based on routine 1D and 2D NMR experiment (APT, DEPT, COSY, HMQC, and HMBC). The results were found to be consistent with the structures in all respect. Structures are given in Scheme 1; ^{1}H NMR and ^{13}C NMR spectral data of compounds **1**–**26** are collected in Tables 1–3. For a better comparability of the NMR data in the tables, we refrained from atom numbering according to IUPAC rules and marked the atoms by letters (a, b, c. . .).

^{1}H NMR spectra

^{1}H NMR spectra of **1**–**24** showed well-resolved multiplets for almost all aliphatic signals. However, **25** and **26** have some multiplets with more complex coupling patterns (see discussion below). The NH protons in compounds **1**–**15** have chemical shifts ranging between δ 4.23 and 4.97 ppm. These signals showed well-resolved triplets in all spectra with a linewidth between δ 2.9 and 5.3 Hz. The H-a protons showed signals in the range of δ 2.97–4.20 ppm for the nonheterocyclic compounds **1**–**15** and δ 4.24–4.49 ppm for the heterocyclic **16**–**26**. As expected, the δ-values decrease by increasing distance from the nitrogen atom, owing to decaying inductive effects. H-a′ proton signals, located in α-position relative to the sulfur atom (**1**–**12**, **14**–**15**, **18**–**26**) appear in the range δ 2.92–4.49 ppm. For a subgroup of these compounds in which H-a′ is benzylic (**1**–**11**, **15**, **18**–**21**, **25**, **26**), the range of the chemical shifts narrows to δ 3.80–4.21 ppm.

MRC

Spectral Assignments and Reference Data



	n	R¹	R²	R³
1	0	H	H	H
2	0	H	OMe	Cl
3	0	H	H	Cl
4	1	OMe	OMe	Cl
5	1	H	H	H
6	1	H	H	Cl
7	1	OMe	H	Cl
8	2	H	H	H
9	3	H	H	Cl
10	3	H	H	H
11	4	H	H	Cl

1–11

	R	R¹
12	$CH_2CH_2CO_2Me$	Cl
13	C_6H_4-p-CH_3	H
14	$CH_2COC_6H_5$	H

12–14

15

16: R = 2′-CO_2Me
17: R = 4′-Me

	R¹	R²	R³
18	OMe	OMe	Cl
19	H	H	Cl
20	H	H	H
21	H	OMe	Cl

18–21

	R¹	R²
22	n-C_3H_7	H
23	CO_2Me	Cl
24	CO_2H	H

22–24

25: R = H
26: R = Me

Scheme 1. Structures and atom identification of *N*-aralkylsulfonamides **1–15**, *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines **16–24**, and *N*-sulfonyl-2,3,4,5-tetrahydro-1*H*-2-benzazepines **25–26**.

^{13}C-NMR spectra

The ^{13}C NMR assignments of the protonated carbons are based on the analysis of the one-bond heteronuclear correlation data (HMQC). Quaternary carbons were identified from long-range correlation responses in the HMBC spectrum. For all assignments, well-established additivity rules were used.[15] In some cases, APT spectra were used to distinguish overlapping resonances of proton-bearing and quaternary carbons.

The carbon atoms C-a (**1**–**26**) and C-a″ (**16**–**26**) are α-positioned with respect to the nitrogen atom (see Scheme 1). The chemical shifts cover a range of *ca*. 10 ppm, from δ 43.2 (**8**) to 53.4 (**26**) ppm. In **1**–**3** and **16**–**24**, the C-a atom constitutes the sole methylene group between the heteroatom and the phenyl ring, and their chemical shifts (δ 46.7–47.7 ppm) prove that there is hardly any influence of the rest of the molecule on this position. The δ-values of the C-a atoms of **25** and **26** (with a seven-membered heterocyclic ring) are different from the above-mentioned ones: δ 53.1 and 45.4 ppm respectively. A deshielding of +5.8 ppm for the former and a shielding of – 1.9 ppm for the latter are observed, in comparison with the δ-value of the respective C-a in the tetrahydroisoquinoline compound **19** (δ 47.3 ppm) with a six-membered ring. A similar deshielding of about +10 ppm is observed for C-a″ (**16**–**24**, δ 43.2–44.0 ppm).

In the case of compound **15**, the signal at δ 32.7 ppm corresponds to carbon C-c. This value is relatively low as compared to other carbon atoms α-located to a phenyl ring (e.g. C-b in **4**–**7**: δ 35.6–36.5 ppm; C-d in **9** and **10**: δ 35.2 ppm and C-e in **11**: δ 35.7 ppm); shielding γ-effects of both methyl and NH groups are responsible.

The structural moiety R–NH–$(CH_2)_n$–C_6H_5 exists in 11 of the studied compounds (n = 1: **1**, **3**; n = 2: **5**, **6**, **13**, **14**; n = 3: **8**, **15**; n = 4: **9**, **10**; and n = 5: **11**). The chemical shifts of ipso- and para-carbon atoms of this phenyl ring show, approximately, a lineal dependence on the length of the chain of CH_2 groups, whereas the behavior of the ortho- and meta-carbons is erratic. The chemical shifts of the ipso-carbons show a slight increase with the number of methylene groups (n = 1, δ = 136.6–136.7, n = 2, δ = 137.6–137.8; n = 3, δ = 140.7–141.0, n = 4141.7; n = 5, δ 141.7 ppm), as a result of inductive effects. The larger increment in the δ-value going from n = 2 to n = 3 may be due to an increase in the electronic charge density at the C-c carbon (see **15**, Scheme 1) owing to a γ-effect of the N–H group. At the para-carbons, where the hyperconjugative effects prevail, the chemical shift values generally showed a slight decrease when n increases (n = 1, δ = 128.3–128.4, n = 2, δ = 126.8–127.0; n = 3, δ 126.1–126.2, n = 4, δ = 125.9–126.0 and n = 5, δ 126.0 ppm; see Table 2).

With the exception of **12**–**14**, **16**, **17**, **22**–**24**, the title compounds have a methylene group between the R′–$NHSO_2$ group and a phenyl ring. The sulfonyl group blocks any stereoelectronic influence of the amino part of the molecule, and the chemical shifts at this position (C-a′) appear in a small range of δ 56.2–58.9 ppm. Likewise, the aromatic carbons are nearly invariant as well.

Conformational analysis of the benzazepine 26

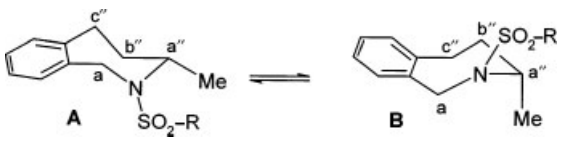
The benzazepine s **25** and **26** possess a seven-membered heterocyclic system (cf. Scheme 1). In the ^{1}H NMR spectrum of **25**, the hydrogen atoms H-a″, H-b″, and H-c″ show higher-order signals due to the existence of a conformational equilibrium (chair inversion). No attempt has been made for further evaluation. Instead, the reader is referred to Katritzky's recent communication describing this topic in detail.[16]

In compound **26**, however, the spin system of the H-a″, H-b″, and H-c″ nuclei is of first order and was interpreted in terms of the ring conformation (Scheme 2):

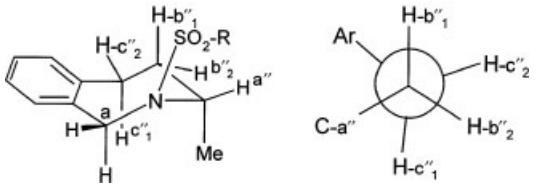
Conformational analyses of benzazepines are rare in literature; only very recently, a detailed study has been presented proving that N-substituted benzazepines strongly prefer enantiomorphic chair conformations.[16] In the case of **26**, the methyl group may be positioned either in equatorial or in axial position alternatively (Scheme 2). Two nearly equal coupling constants ^3J(H,H) $\approx$ 5.7 Hz involving H-a″ prove that it is in equatorial position since both values indicate gauche orientations between H-a″ and the two H-b″ protons. Thus, the methyl group is axial (conformer **B** in Scheme 2), probably because of severe steric interference with the sulfonyl group if it were equatorial (conformer **A** in Scheme 2). The conformational equilibrium is strongly biassed; **26** is conformationally rigid. The same evidence results from semiempirical model AM1 calculations: the axial conformer (**B** in Scheme 2) is more stable than the equatorial (**A**); $\Delta\Delta H > 5$ kJ mol^{-1}.

This stereochemical assignment is impressively confirmed by the γ-effects exerted by methyl group upon the ^{13}C chemical shifts of C-a (–7.7 ppm) and C-c″ (–4.7 ppm), as compared with **25**. These are typical diamagnetic γ-gauche effects.[17]

The ^{1}H chemical shifts and ^{1}H,^{1}H coupling constants of all ring hydrogens of **26** (Scheme 3) were assigned on the basis of the



Scheme 2. Conformational equilibrium of **26**.



Scheme 3. Structure of **26** and Newman projection along the C-b″–C-c″ bond.

Table 1. ^{1}H NMR chemical shifts and coupling constants of *N*-aralkylsulfonamides **1**–**15**[a,b]

	NH	H-a	H-b	H-c	H-d	H-a′	H-2	H-3	H-4	H-5	H-6	H-2′	H-3′	H-5′	H-6′
1	4.41; t	4.18; d	–	–	–	4.15; s	7.28; br d	7.37; br t	7.34; br t	7.37; br t	7.28; br d	7.20[c];	7.32[c];	7.32[c];	7.20[c]; 10.1;
	5.8	6.0	–	–	–		8.2	7.2	ov	7.2	8.2	10.1; 4.9; 2.3	ov	ov	4.9; 2.3
2	4.64; t	4.18; d	–	–	–	4.08; s	6.82; t	–	6.87; br d	7.30; t	6.87; br d	7.24; d	–	7.40; d	7.10; dd
	6.0	6.0					2.0		8.3	7.9	8.3	2.1		8.3	8.3
3	4.62; t	4.20; d	–	–	–	4.06; s	7.29; br d	7.37; ov m	7.34; tt	7.37; ov m	7.29; br d	7.24; d	–	7.39; d	7.08; dd
	5.9	6.0					8.1		7.4; 1.2		8.1	2.1		8.1	8.2; 2.0
4	4.25; t	3.24; qr	2.75; t	–	–	4.10; s	6.67; d	–	–	6.81; d	6.70; dd	7.43; d	–	7.41; d	7.13; dd
	6.1	6.8; 6.2	6.8				1.9			8.0	8.0; 2.0	2.1		8.3	8.2; 2.0
5	4.29; t	3.23; qr	2.78; t	–	–	4.09; s	7.15; br d	7.31; br t	7.24; tt	7.31; br t	7.15; br d	7.19[c];	7.29[c];	7.29[c];	7.19[c];
	6.0	6.9; 6.3	6.9				8.0	7.2	7.3; 1.3	7.2	8.0	10.1; 5.0; 2.3	ov	ov	10.1; 5.1; 2.2
6	4.29; t	3.27; qr	2.80; t	–	–	4.05; s	7.16; br d	7.32; br t	7.25; tt	7.32; br t	7.16; br d	7.40; d	–	7.39; d	7.10; dd
	6.0	6.8; 6.4	6.8				8.0	7.3	7.3; 1.2	7.3	8.0	2.0		8.3	8.2; 2.0
7	4.23; t	3.23; br qr	2.75; t	–	–	4.07; s	7.07; ddd	6.85; ddd	–	6.85; ddd	7.07; ddd	7.40; d	–	7.11; dd	7.40; d
	6.1	6.6	6.7				9.5; 2.7; 2.0	9.5; 2.9; 2.0		9.5; 2.9; 2.0	9.5; 2.7; 2.0	1.8		8.3; 2.0	8.4
8	4.27; t	2.99; br qr	1.80; qn	2.61; t	–	4.17; s	7.13; br d	7.29; br t	7.20; tt	7.29; br t	7.13; br d	7.28[c];	7.33[c];	7.33[c];	7.28[c];
	6.0	6.8	7.3	7.1			8.1	7.2	7.4; 1.2	7.2	8.1	ov	10.1; 5.0; 2.3	10.1; 5.0; 2.3	ov
9	4.38; t	2.99; br qr	1.62; qn	1.50; qn	2.60; t	4.12; s	7.15; br d	7.27; br t	7.18; ov m	7.27; br t	7.15; br d	7.46; d	–	7.42; d	7.19; dd
	5.9	6.9	7.0	7.1	7.4		7.0	7.3		7.3	7.0	2.0		8.3	8.3; 2.0
10	4.26; t	2.97; br qr	1.61; br qn	1.48; br qn	2.59; t	4.15; s	7.14; br d	7.28 br t	7.18; br t	7.28 br t	7.14; br d	7.28[c];	7.33[c];	7.33[c];	7.28[c];
	6.0	6.7	7.3	7.3	7.4		7.3	7.5	7.4	7.5	7.3	ov	10.0; 5.0; 2.3	10.1; 5.1; 2.3	ov
11	4.28; t	2.99; br qr	1.61; qn	1.32;	1.51; qn	4.14; s	7.15; br d	7.27; br t	7.17; br t	7.27; br t	7.15; br d	7.47; d	–	7.44; d	7.22; dd
	6.0	6.9	7.6	M	7.4		8.2	8.0	7.4	8.0	8.2	2.1		8.3	8.3; 2.1
12	4.72; t	3.24; br qr	2.83; t	–	–	3.24; t	7.15; br d	7.28; br d	–	7.28; br d	7.15; br d	–	–	–	–
	6.0	6.7	7.0			7.4	8.4	8.4		8.4	8.4				
13	4.63; t	4.18; d	–	–	–	–	7.07; br d	7.27; ov m	7.20; tt	7.27; ov m	7.07; br d	7.69; br d	7.25; ov m	7.25; ov m	7.69; br d
	6.2	6.0							7.4; 1.4			8.3			8.3
14	4.97; t	3.45; dt	2.87; t	–	–	4.49; s	7.20; ov m	7.26; br t	7.21; ov m	7.26; br t	7.20; ov m	7.91; br d	7.48; br t	7.48; br t	7.91; br d
	6.1	7.1; 6.1	7.0					7.5		7.5		7.4	7.4	7.4	7.4
15	4.33; d	3.40; sx	1.75; m	2.93; t	–	4.11, 4.13[d]	7.15; br d	7.28; br t	7.19; br t	7.28; br t	7.15; br d	7.48; d	–	7.42; d	7.21; dd
	8.3	6.5		8.0			7.1	7.4	7.5	7.4	7.1	2.0		8.2	8.3; 2.1

[a] δ(^{1}H) in ppm relative to TMS (upper trace) in $CDCl_3$; coupling constants in Hz (lower trace); letters denote signal multiplicities; s, singlet; d, doublet; t, triplet; qr, quartet; qn, quintet; sx, sextet; m, multiplet br, broad; ov, overlapped.

[b] Further ^{1}H chemical shift of the substituents and other protons: **2**, δ 3.81, s, (OCH_3); **4**, δ 3.87, s, (R^1: OCH_3); δ 3.86, s, (R^2: OCH_3); **7**, δ 3.79, s, (OCH_3); **11**, δ 2.60, t, J = 7.6 Hz (H-e); **12**, δ 2.70, t, J = 7.4 Hz, (H-b′); **13**, δ 2.42, s, (CH_3); δ 3.70, s, (CH_3); **14**, δ7.62, tt, J = 7.4, 1.2 Hz, (H-4′); **15**, δ 1.22, d, J = 6.6 Hz, (CH_3).

[c] AA′XX′ spin system.

[d] AB spin system, J_{AB} = 13.9 Hz.

Table 2. ^{1}H NMR chemical shifts and coupling constants of *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines **16–24** and *N*-sulfonyl-1,3,4,5-tetrahydro-1*H*-2-benzazepines **25–26**[a,b]

	H-a	H-a′	H-b′	H-a″	H-b″	H-2	H-3	H-4	H-5	H-2′	H-3′	H-4′	H-5′	H-6′
			–											
16	4.45; s	–	–	3.54; t	2.91; t	7.07; br d	7.15; ov m	7.16; ov m	7.09; br d	–	7.50; dd	7.56; ddd	7.60; ddd	7.89; dd
				5.9	5.9	9.1			9.3		7.4; 1.5	7.5; 1.7	7.4; 1.5	7.4; 1.6
17	4.24; s	–	–	3.35; t	2.92; t	7.02; br d	7.13; ov m	7.14; ov m	7.07; br d	7.72; d[c]	7.32; d[c]	–	7.32; d[c]	7.72; d[c]
				5.9	5.9	8.9			8.9	8.2	8.2		8.2	8.2
18	4.28; s	4.16; s	–	3.48; t	2.74; t	6.43; s	–	–	6.59; s	7.38; d	–	–	7.38; d	7.19; dd
				6.0	5.9					2.1			8.2	8.3; 2.0
19	4.39; br s	4.17; s	–	3.47; t	2.83; t	6.99; br d	7.18; ov m	7.19; ov m	7.13; br d	7.41; d	–	–	7.36; d	7.18; dd
				6.0	6.0	8.8			8.8	2.0			8.3	8.3; 2.1
20	4.35; br s	4.21; s	–	3.42; t	2.80; t	6.97; br d	7.17; ov m	7.19; ov m	7.10; br d	7.28; br s	7.28; br s	–	7.28; br s	7.28; br s
				6.0	5.9	8.7			8.7					
21	4.34; br s	4.16; s	–	3.47; t	2.76; t	6.49; d	–	6.77; dd	7.03; d	7.40; d	–	–	7.37; d	7.18; dd
				6.0	6.0	2.5		8.4; 2.6	8.05	2.0			8.2	8.3; 2.0
22	4.49; s	2.96; t	1.82; q[c]	3.59; t	2.95; t	7.07; br d	7.18; ov m	7.20; ov m	7.14; br d	–	–	–	–	–
		7.5	7.7	6.0	6.1	8.8			8.8					
23	4.44; s	3.32; t	2.82; t	3.57; t	2.91; t	7.08; d	–	7.17; dd	7.08; d	–	–	–	–	–
		7.4	7.4	5.9	5.9	2.2		8.2; 2.1	8.1					
24	4.49; s	3.30; t	2.97; t	3.60; t	2.96; t	7.08; br d	7.19; ov m	7.20; ov m	7.15; br d	–	–	–	–	–
		7.4	7.4	5.9	5.9	8.9			8.9					
25	4.45, br s	3.84, s	–	3.60; br t	1.49, m	7.22; ov m	7.25; ov m	7.25; ov m	7.19; br d	6.95; d	–	–	7.32; d	6.94; dd
				5.1					7.2	2.1			8.7	8.7; 2.1
26	4.48, s	3.80, s	–	4.14, sx.	1.49 and 1.68[d]	7.20; ov m	7.20; ov m	7.25; ov m	7.17, br d	6.86, d	–	–	7.26, d	6.87, dd
				6.5, 5.7					7.3	2.0			8.2	8.1, 2.0

[a] δ(^{1}H) in ppm relative to TMS (upper trace) in $CDCl_3$; coupling constants in Hz (lower trace); letters denote signal multiplicities: s, singlet; d, doublet; t, triplet; qr, quartet; qn, quintet; sx, sextet; m, multiplet; br, broad; ov, overlapped.

[b] Further ^{1}H chemical shift of the substituents and other protons: **16**, δ 3.93, s, (CH_3); **17**, δ 2.42, s, (CH_3); **18**, δ 3.86, s, (R^1: OCH_3), δ 3.83, s, (R^2: OCH_3); **21**, δ 3.77, s, (CH_3); **22**, δ 0.89, t, J = 7.1 Hz, (CH_3); δ 1.25–1.43, m, (H-c′ and H-d′); **23**, δ 3.67, s, (CH_3); **24**, δ *ca* 2.2, br s, (OH); **25**, δ 2.92 dd with long-range coupling J = 7.0, 4.3 Hz (H-c″); **26**, δ 3.08, br dd, J = 15.5, 11.0 Hz, (H-c$''_1$); δ 2.59 ppm, ddd, J = 15.6, 8.8, 1.2 Hz, (H-c$''_2$).

[c] With long-range coupling.

[d] Diastereotopic signals (see text): δ 1.49, br ddd, J = 14.4, 11.0, 5.7 Hz, (H-b$''_1$) δ 1.68, dddd, J = 14.4, 8.8, 5.7, 1.3 Hz, (H-b$''_2$).

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Table 3. ^{13}C chemical shifts of *N*-aralkylsulfonamides **1–15**; *N*-sulfonyl-1,2,3,4-tetrahydroisoquinolines **16–24** and *N*-sulfonylbenz[*c*]azepines **25–26**[a,b]

	C-a	C-a″	C-b	C-b″	C-c	C-d	C-1	C-2	C-3	C-4	C-5	C-6	C-a′	C-b′	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	CO	CH_3
1	47.7		–				136.7	128.1	129.0	128.3	129.0	128.1	58.8		127.7	131.9	129.0	135.0	129.0	131.9		
2	47.6		–				138.2	113.8	160.1	113.7	130.1	120.3	58.4		129.3	132.4	132.9	133.3	130.7	129.9		55.3
3	47.7		–				136.6	128.2	129.1	128.4	129.1	128.2	58.4		129.3	132.4	132.9*	133.3*	130.7	129.9		
4	45.0		36.2				130.0	111.6	149.3	148.1	112.0	120.7	57.8		129.5	132.4	132.9	133.2	130.7	129.8		56.0
5	44.8		36.5				137.7	128.8	128.8	126.9	128.8	128.8	58.1		127.8	131.8	129.0	134.9	129.0	131.8		
6	44.8		36.5				137.6	128.8	128.9	127.0	128.9	128.8	57.8		129.4	132.4	132.9	133.2	130.7	129.8		
7	45.0		35.6				129.5	129.0	114.3	158.7	114.3	129.8	57.7		129.4	132.4	132.9	133.2	130.7	129.8		55.3
8	43.2		32.7		31.9	32.7	140.7	128.3	128.6	126.2	128.6	128.3	58.1		127.9	131.9	129.1	135.0	129.1	131.9		
9	43.6		29.8		28.1	35.2	141.7	128.4	128.4	126.0	128.4	128.4	57.7		129.6	132.4	132.9	133.2	130.7	129.9		
10	43.6		29.9		28.1	35.2	141.7	128.4	128.4	125.9	128.4	128.4	58.1		127.9	131.9	129.0	134.9	129.0	131.9		
11	43.7		30.8		26.1	30.3	141.7	128.4	128.4	126.0	128.4	128.4	57.7		129.6	132.4	132.9	133.2	130.8	129.9		
12	44.3		35.9				136.4	130.3	128.9	132.7	128.9	130.3	47.7	28.6							171.0	52.3
13	44.2		35.8				137.7	128.7	128.7	126.8	128.7	128.7	–		137.0	127.1	129.7	143.4	129.7	127.1		21.5
14	44.9		36.4				137.8	128.9	128.9	126.8	128.9	128.9	57.8		135.6	128.9	128.8	134.5	128.8	128.9	190.0	
15	50.5		39.4		32.1		141.0	128.3	128.5	126.1	128.5	128.3	58.9		129.6	132.5	132.8	133.2	130.7	130.0		22.2
16	47.2	43.5		28.8		–	131.8	126.3	126.4	126.8	128.9	133.6	–	–	135.8	133.3	128.5	132.4	130.2	129.0	168.4	53.1
17	47.5	43.7		28.9		–	131.7	126.3	126.4	126.7	128.8	133.4	–	–	133.1	127.7	129.7	143.7	129.7	127.7		21.5
18	47.1	43.8		28.4		–	147.9	108.7	123.7	125.0	111.7	148.2	56.5		129.1	132.4	132.8	133.1	130.6	129.9		56.5[c]
19	47.3	43.8		28.9		–	131.8	126.1	126.6	127.1	129.1	133.2	56.2	–	129.1	132.4	132.9	133.2	130.7	129.9		
20	47.3	43.7		29.0		–	132.0	126.1	126.5	127.0	129.0	133.3	56.7	–	127.4	131.9	129.0	134.9	129.0	131.9		
21	47.6	44.0		28.0		–	132.9	110.7	158.2	113.6	130.1	125.1	56.4		129.1	132.4	132.9	133.2	130.6	129.9		55.3
22	47.1	43.4		29.1		–	132.2	126.3	126.5	126.9	129.1	133.4	50.4	30.6	–		–	–	–	–		13.7
23	46.7	43.2		28.5		–	131.7	126.2	132.2	127.2	130.4	133.6	46.0	28.2	–	–	–	–	–	–	170.9	52.3
24	47.1	43.4		29.0		–	131.8	126.3	126.6	127.0	129.1	133.2	45.6	27.9	–	–	–	–	–	–	173.5	
25	53.1	52.3		28.3			137.5	128.8	126.7	128.6	130.0	141.9	58.3		129.2	132.4	132.6	132.9	130.4	129.8		
26	45.4	53.4		32.9			137.1	128.5	126.4	128.2	130.1	141.2	58.3		129.2	132.3	132.4	132.8	130.3	129.8		19.0

[a] $\delta(^{13}C)$ in ppm relative to TMS in $CDCl_3$.
[b] Further ^{13}C chemical shift of the substituents and other protons: **11**, δ 35.7, (C-e); **22**, δ 22.9, (C-e′), δ 22.2, (C-d′); **25**, δ 34.7, (C-c″); **26**, δ 30.0 ppm, (C-c″).
[c] Two close methoxy signals.

above stereochemical evidence and under the assistance of respective COSY peaks; torsion angles ϕ are estimated from X-ray diffraction (see below):

H-a″, δ 4.14 ppm, ^3J(H-a″, H-b$_1$″) = 5.7 Hz, ^3J(H-a″,H-b$_2$″) = 5.7 Hz ($\phi = +53°$ and $-63°$, respectively); H-b$_1$″ (axial), δ 1.49 ppm, ^2J(H-b$_1$″,H-b$_2$″) = 14.4 Hz, ^3J(H-b$_1$″,H-c$_1$″) = 11.0 Hz ($\phi = 163°$), ^3J(H-b$_1$″,H-c$_2$″) = 0–1 Hz ($\phi = -80°$); H-b$_2$″ (equatorial), δ 1.68 ppm, ^3J(H-b$_2$″,H-c$_1$″) = 1.3 Hz ($\phi = -81°$), ^3J(H-b$_2$″,H-c$_2$″) = 8.8 Hz ($\phi = +36°$); H-c$_1$″ (axial), δ 3.08 ppm, ^2J(H-c$_1$″,H-c$_2$″) = 15.5 Hz; H-c$_2$″ (equatorial), δ 2.59 ppm. The three-bond coupling between H-a″ and the methyl protons is 6.5 Hz. The two diastereotopic H-a atoms are nearly isochronous (δ 4.48; AB-quartet, $\Delta\delta < 0.01$ ppm); nevertheless, it was possible to estimate the geminal coupling constant to be *ca*. 16 Hz. All vicinal coupling magnitudes are in accordance with expectations on the basis of the Karplus rule.[18]

A single-crystal X-ray structure analysis of *N*-[((3′,4′-dichlorophenyl)methyl)sulfonyl]-3-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepin **26** strongly confirms the prevalence of conformer **B** in the equilibrium. As can be seen in Fig. 1, the methylated benzazepine ring adopts a chair conformation in the solid state as well. The crystallographic data are collected in Table 4. Atomic distances, bond angles, and torsion angles meet the expectation and can be requested from the correspondence author as supplementary material. The crystal structure is centrosymmetric, i.e. it contains enantiomorphic forms of the molecule. Supplementary crystallographic data of CCDC 270593 can be obtained free of charge

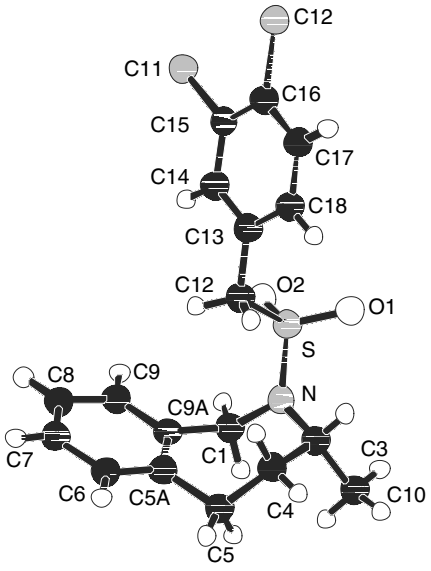

Figure 1. Structure of **26** as determined by single-crystal X-ray diffraction. The atom designation (except for hydrogen) and numbering in the X-ray structure are given in the figure.

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Spectral Assignments and Reference Data

Table 4. Crystallographic data of *N*-[((3′,4′-dichlorophenyl)methyl) sulfonyl]-3-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepin **26**

Empirical formula	$C_{18}H_{19}Cl_2NO_2S$
Formula weight	384.30
Crystal system	monoclinic
Space group	$P2_1/n$ (No. 14)
Unit cell dimensions	$a = 6.5483(15)$ Å
	$b = 27.197(5)$ Å
	$c = 10.241(2)$ Å
	$\beta = 92.49(3)^\circ$
Volume	1822.1(7) Å^3
Z	4
Temperature	293 K
Calculated density D_x	1.401 g cm^{-3}
Absorption coefficient μ (MoK$_\alpha$)	0.481 mm^{-1}
Crystal size	0.74 × 0.70 × 0.37 mm
Radiation	MoK$_\alpha$, 0.71073 Å
θ_{min}, θ_{max}	2.13°, 26.10°
Index range	$-8 \le h \le +8$; $-33 \le k \le +33$; $-12 \le l \le +12$
Reflections collected/unique	22617/3521 [$R_{int} = 0.049$]
R indices	$R^1 = 0.0346$, $wR^2 = 0.1017$
Largest difference peak and hole	0.34 and −0.33 e Å^{-3}
Structure solution and refinement	SHELXS-97, SHELXL-97[a]

[a] See Ref. 19.

via 'www.ccdc.cam.ac.uk/conts/retrieving.html' or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, fax (+44) 1223-336-033, e-mail deposit@ccdc.cam.ac.uk. A selection of those data can be requested from the correspondence author.

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