

Spectral Assignments and Reference Data

Complete ¹H and ¹³C NMR spectral assignment of *cis-* and *trans-* 3-{2-[2-(4methylphenyl)ethenyl]phenyl]}sydnones

Kristina Butković,¹ Željko Marinić² and Marija Šindler-Kulyk¹*

¹ Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, Marulicev trg 19, 10000 Zagreb, Croatia

² NMR Center, Institute Rudjer Boskovic, Bijenicka cesta 54, 10000 Zagreb, Croatia

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¹H and ¹³C NMR spectra of *cis-* and *trans-*3-[2-[2-(4-methylphenyl)ethenyl]phenyl]}sydnones, the first stilbene-substituted mezoionic oxadiazolium rings, were fully assigned combining the information in various solvents, such as deuterated benzene, acetone and chloroform, using 2D NMR techniques. Copyright © 2004 John Wiley & Sons, Ltd.

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INTRODUCTION

Sydnones,¹ five-membered heterocycles with a sextet of electrons, belong to a class of dipolar compounds known as a 'mesoionic' and can be represented as hybrids of a number of mesomeric/ionic forms (Fig. 1). They are studied not only because of their structure, physical properties and reactivity, but also because a series of derivatives have shown various biological activities.²

Here we report the full assignment of the ¹H and ¹³C NMR spectra of stilbenyl derivatives, *cis-* and *trans-*3-{2-[2-(4-methylphenyl])ethenyl]phenyl])sydnones (1) (Fig. 2), the aromatic stilbene molecule substituted in the *ortho*-position with the mesomeric oxadiazolium ring. Although stilbene and their derivatives³ are the most extensively studied conjugated systems, this is the first example of sydnonylstilbene. They are obtained by a sequence of reactions (see Experimental).

RESULTS AND DISCUSSION

All assignments of the ¹H and ¹³C chemical shifts and coupling constants for *cis*- and *trans*-1 (Fig. 2) are given in Tables 1 and 2. To be able to make complete assignments of all carbons and hydrogens, it was necessary to use not only a single solvent such as CDCl₃ but also C₆D₆ and (CD₃)₂CO. In the case of *cis*-1, the protons H-2 to H-5 appear in CDCl₃ as a four-proton multiplet (Table 1) at 7.53–7.44 ppm. In (CD₃)₂CO only H-2 and H-5 are well resolved, but in C₆D₆ all four protons were assigned. H-2 and H-3 of *trans*-1 (Table 2) are not separable in CDCl₃ whereas in C₆D₆ and (CD₃)₂CO they are well resolved and appear as dd or dt, respectively. The resonances of the stilbene moiety were obtained from the

The resonances of the stilbene moiety were obtained from the combined information observed in 1D and 2D (COSY, HMQC, HMBC) experiments. The carbon type (C, CH, CH₃) was determined using APT experiments. In Table 3 are given $^{1}H^{-1}H$ and $^{13}C^{-1}H$ correlations, based on which the unambiguous assignment of all carbons and hydrogens was made. The typical small signal for the sydnone carbon was upfield of other aromatic carbons and the

*Correspondence to: Marija Šindler-Kulyk, Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, Marulicev trg 19, 10000 Zagreb, Croatia. E-mail: msindler@fkit.hr Contract/grant sponsor: Ministry of Science and Technology of the Republic of Croatia; Contract/grant numbers: 0125004; 0098059. corresponding proton and could be assigned without help of 2D techniques.

We conclude that the sydnone ring influences the chemical shifts on the stilbene ring mainly owing to sterric effects. It is known that *ortho*-substitution decreases the π -delocalization by changing the planarity of the system.

EXPERIMENTAL

All reagents were obtained from commercial sources and used without purification. Melting-points were recorded on an Original Kofler Mikroheiztisch apparatus (Reichert, Vienna, Austria) and are uncorrected. Silica gel (Merck, 0.05–0.2 mm) was used for chromatographic purifications.

General synthetic procedure

The starting compounds (Fig. 3), *cis*- and *trans*-2-nitro-4'-methylstilbene (2), were prepared by Wittig reaction from 2-nitrobenzaldehyde (0.020 mol) and the triphenylphosphonium salt of p-xylyl bromide (0.022 mol) in ethanol (60 ml) and addition of sodium ethoxide (0.022 mol). The isomers were separated by column chromatography $(CH_2Cl_2-light petroleum, 7:3)$ and treated separately to the sydnone derivative **1**. Reduction of **2** (0.021 mol) with zinc⁴ (0.131 mol) in acetone (40 ml) and NH₄Cl (0.053 mol) disolved in water (13 ml) under reflux gave 2-amino-4'-methylstilbene (3). Using a known method,^{5,6} amino derivative 3 (0.017 mol) was converted to amino acid 4 by substitution with ethyl bromoacetate (0.017 mol) in refluxing ethanol (12.5 ml) in the presence of sodium acetate (0.026 mol) and subsequent base-promoted hydrolysis in water. The isolated amino acid 4 (0.0041 mol) was nitrosated with NaNO2 (0.0062 mol) in water (30 ml) and addition of HCl (1:1, 1.5 ml) in an ice-cold bath, filtered, dried and, without purification, the obtained nitroso derivative 5 was refluxed in acetic anhydride (4 ml) to give sydnone derivative 1. Pure products were obtained by crystallization from ethanol. The yields and melting-points are reported in Table 4.

NMR spectroscopy

All NMR spectra were recorded with a Bruker Avance 600 spectrometer, operating at 600.13 MHz for ¹H and 150.92 MHz for ¹³C. The compounds were dissolved in $CDCl_3$, C_6D_6 and $(CD_3)_2CO$,

$$\begin{array}{c} RN + CO & \longrightarrow & RN \\ N-O & & N-O & & N=O \end{array}$$

Figure 1. Resonance structures of sydnones.







Figure 3. Structures of compounds 2-5.



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Table 1. ¹H and ¹³C NMR data for cis-1

C/H	$\delta(^{13}C)$ (ppm)			$\delta(^{1}\mathrm{H}) (\mathrm{ppm})^{\mathrm{a}}$		
	(CD ₃) ₂ CO	C_6D_6	CDCl ₃	(CD ₃) ₂ CO	C_6D_6	CDCl ₃
CH (syd)	98.11	96.74	97.11	6.96 (s)	5.79 (s)	6.42 (s)
CO (syd)	169.03	168.35	168.64	_	_	_
1	133.81	133.69	133.05	_	_	_
2	132.05	125.21	131.83 ^b	7.44 (d, 7.2)	6.69 (d, 7.8)	
3	132.79 ^b	128.33	131.50 ^b		6.65 (t, 7.8)	
4	129.68 ^b	131.27	128.51 ^b	7.60 (m, 2H)	6.70 (t, 7.8)	7.53-7.44 (m, 4H)
5	126.58	131.35	124.95 ^b	7.76 (d, 7.2)	7.01 (d, 7.8)	
6	134.59	133.57	133.40	_	_	_
7	123.36	122.33	121.76	6.55 (d, 12.0)	5.84 (d, 12.0)	6.37 (d, 12.0)
8	135.21	134.83	134.94	6.82 (d, 12.0)	6.30 (d, 12.0)	6.73 (d, 12.0)
9	134.59	133.07	132.29	_	_	_
10	129.88 ^b	129.08	128.54		6.85 (d, 8.4)	6.95 (d, 8.4)
11	129.68 ^b	129.40	129.11	7.04 (s)	6.77 (d, 8.4)	7.01 (d, 8.4)
12	138.61	138.06	138.10	_	_	_
CH ₃	21.18	21.09	21.08	2.27 (s)	1.99 (s)	2.30 (s)

^a Multiplicity and J(Hz) in parentheses.

^b Interchangeable.

Table 2. ¹H and ¹³C NMR data for trans-1

	$\delta(^{13}\mathrm{C})$ (ppm)			$\delta(^{1}\mathrm{H})(\mathrm{ppm})^{\mathrm{a}}$		
C/H	(CD ₃) ₂ CO	C_6D_6	CDCl ₃	(CD ₃) ₂ CO	C ₆ D ₆	CDCl ₃
CH (syd)	99.13	97.35	98.02	7.11 (s)	5.59 (s)	6.55 (s)
CO (syd)	169.13	168.14	168.75	_	_	_
1	133.76	132.87	132.42	_	_	_
2	127.03	125.62	125.53	7.73 (dd, 7.8,1.2)	6.55 (dd, 7.8, 1.2)	
3	129.29	127.79	128.27	7.59 (dt, 7.8, 1.2)	6.67 (dt,7.8, 1.2)	7.48-7.46 (m, 2H)
4	133.14	131.61	132.32	7.76 (dt, 7.8, 1.2)	6.89 (t, 7.8)	7.64 (m)
5	127.73	126.87	127.12	8.09 (dd, 7.8, 1.2)	7.19 (d, 7.8)	7.89 (d, 9.0)
6	134.30	133.52	133.08	_	_	_
7	120.15	119.20	118.80	7.04 (d, 16.2)	6.71 (d, 16.2)	6.80 (d, 16.2)
8	135.01	134.70	134.83	7.39 (d, 16.2)	6.78 (d, 16.2)	7.17 (d, 16.2)
9	134.66	133.62	133.45	_	_	_
10	127.98	127.27	127.03	7.48 (d, 7.8)	7.12 (d, 7.8)	7.33 (d, 8.1)
11	130.32	129.92	129.66	7.20 (d, 7.8)	6.90 (d, 7.8)	7.17 (d, 8.1)
12	139.58	139.11	139.29	_	_	—
CH ₃	21.28	21.22	21.34	2.33 (s)	2.07 (s)	2.36 (s)

^a Multiplicity and J(Hz) in parentheses.

internally referenced to tetramethylsilane, at 300 K in 5 mm NMR tubes. The digital resolution in the ¹H NMR spectra was 0.27 Hz per point and in the ¹³C NMR spectra 0.55 Hz per point. The following techniques were used: ¹H, attached proton test, ¹H–¹H COSY, HMQC and HMBC. The ¹H–¹H gradient COSY spectra were obtained in the magnitude mode with 2048 points in the F_2 dimension and 512 increments in the F_1 dimension. Each increment was obtained with eight scans, a spectral width of 8000 Hz and a relaxation delay of 1.5 s. The resolution was 3.91 and 7.82 Hz per point in the F_1 adimensions, respectively. The gradient HMQC and gradient HMBC experiments were performed with the C,H coupling value set to 145 and 8 Hz, respectively. The spectra were obtained in the magnitude mode with 2048 points

in the F_2 dimension and 256 increments in the F_1 dimension. The spectral with was 36 000 Hz in the F_2 and 8000 Hz in the F_1 dimension. All two-dimensional experiments were performed by standard pulse sequences, using Bruker XWIN-NMR software Version 3.5. For proton decoupling, Waltz 16 modulation was used.

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Table 3. ¹H, ¹H and ¹³C, ¹H correlation NMR data for *cis*-1 and *trans*-1

	HM	1BC	COSY		
$^{13}C/^{1}H$	cis-1 ^a	trans-1 ^{b,c}	cis-1 ^a	trans-1 ^c	
CH (syd)	_	CO (syd)	_	_	
CO (syd)	—	_	_	_	
1	H-5, H-3	H-5, H-3	_	_	
2	H-4	H-4	_	H-3	
3	C-1, H-5	H-5	_	H - 2, H - 4	
4	—	H-2	H-5	H-5, H-3	
5	C-7	H-7	H-4	H-4	
6	H-8, H-4	H-2	_	_	
7	H-5	H-5	H-8	H-8	
8	H-10	H-10	H-7	H-7	
9	H-11	H-11	_	_	
10	H-8, C-12	C-12	H-11	H-11	
11	CH ₃ , C-9	CH ₃	H-10, CH ₃	H-10, CH ₃	
12	CH ₃	CH ₃	_	_	
CH ₃	C-11, C-12	C-11, C-12	H-11	H-11	

 $^{^{}a}C_{6}D_{6}.$

^c (CD₃)₂CO.

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Table 4. Melting-points and yields of 1-4

Compound	Melting-point (°C)	Yield (%)
cis-1	96-98	25
trans-1	162–164	91
cis- 2	78-80	44
trans- 2	53	32
cis- 3	Oil	97
trans- 3	122–123	96
cis- 4	119–120	94
trans- 4	117-118	75

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^b CDCl₃.