Reference Data

¹³C NMR Analysis of Specifically Labeled [¹³C] Azobenzenes

HENRY J. SHINE (to whom correspondence should be addressed) and WITOLD SUBOTKOWSKI Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409, USA

¹³C NMR chemical shifts and ¹³C-¹³C couplings for six specifically labeled [¹³C] azobenzenes are reported. Coupling magnitudes depend on the position of labeling and the nature of the substituents.

KEY WORDS ¹³C NMR Specifically labeled [¹³C]azobenzenes

INTRODUCTION

During studies of heavy-atom kinetic isotope effects in benzidine rearrangements over the last few years,¹ it was necessary to prepare some specifically-labeled [¹³C]azobenzenes. ¹³C NMR spectra of the labeled compounds confirmed the positioning of the label. We have now been able to use the compounds for the measurement of ¹³C-¹³C couplings.

MATERIALS

The six specifically labeled azobenzenes and their ${}^{13}C$ enrichments are listed in Table 1;

syntheses have been reported earlier, as noted. Samples were sublimed before recording the spectra, with the exception of 2,2'-dimethoxy[$4,4'-^{13}C_2$]azobenzene, which was crystallized from absolute ethanol.

The stable form of an azobenzene is the *trans* isomer. The *cis* isomer can be obtained by ultraviolet irradiation of the *trans* isomer.⁸ The compounds listed in Table 1 were predominantly the *trans* isomers, but each contained a small amount of the *cis* isomer. The *cis* isomer content of $[1,1'^{-13}C_2]$ and $[4,4'^{-13}C_2]$ azobenzene was augmented by irradiation of their solutions in hexane.

RESULTS AND DISCUSSION

Chemical shift assignments and couplings are shown in Table 2 (trans isomers) and Table 3 (cis isomers). Data for a cis isomer were obtained from the spectrum of a mixture of the cis and trans isomers. In such a mixture the trans isomer and its ¹³C signals were dominant. Because the cis isomer was present in such low concentration some of its ¹³C signals were too weak to be detected, as noted in Table 3. This applied particularly to the signal from the C-1 position. The chemical shifts of azobenzene itself were in good agreement with literature data.9 Assignments of shifts in enriched azobenzenes were made by comparison with spectra of the unenriched corresponding compounds. 2,2'-dimethoxy[4,4'-Assignments for ¹³C₂]azobenzene were made, in part, by analogy with data for anisole.10



Table 1. Labeled azobenzenes: synthesis and ¹³C enrichment

Azobenzene	[¹³ C ₂] enrichment (%)	(%) Lit.	
[1,1'- ¹³ C ₂]	98*	2	
[4,4'- ¹³ C ₂]	846	3	
4,4'-Dichloro[4,4'-13C]	95 ^b	4	
4,4'-Dijodo [4,4,'-13C2]	98*	5	
2,2'-Dimethoxy[4,4'- ¹³ C ₂]	4 ^b	6	
[2,2',6,6'- ¹³ C ₄]	58 ^{b,c}	7	
Calculated from enrichment of stotopic enrichment determine rometry.	precursor [2- ¹³ C] acetone d by whole-molecule ma	ss spec∘	

© 1991 by John Wiley & Sons, Ltd.

The ¹³C signals of the carbon atom in position 1 were weak (except for [1,1'-¹³C₂]azobenzene), because of the long relaxation times of quaternary carbon atoms. The chemical shifts of the carbon atom in position 4 depended on the nature of the substituent at that position. Iodine atoms in trans-4,4'diiodo[4,4'-¹³C₂]azobenzene caused an upfield shift of the signal of the C-4 atom from ca. 131 ppm (for unsubstituted azobenzene) to ca. 98 ppm. This upfield trend is attributable to the heavy atom effect (a large diamagnetic shielding contribution).11 Chemical shifts of carbons in positions 2 and 3 in symmetrical azobenzenes were spaced closely together, with the exception of trans-4,4'-diiodo[4,4'- $^{13}C_2$]azobenzene. Shifts in 2,2'-dimethoxy[4,4'- $^{13}C_2$]azobenzene were different from those in the other compounds owing to o-methoxy substitution. Where a multiplet occurred in a spectrum, a signal appeared at its center, arising from the atom in the corresponding naturally occurring compound. The relative intensity of this central signal depended on the extent of enrichment. Enrichment of an azobenzene at a specific carbon atom caused small (up to 0.16 ppm) upfield shifts in the signals from other carbon atoms in the molecule, as compared with the corresponding signals in the naturally occurring compound. This effect was discernible even three bonds away.

Although ¹³C couplings can be measured with the low natural abundance of unenriched compounds and INADEQUATE experiments, the procedure is laborious and extremely time consuming. With specifically enriched compounds, particularly with the highly enriched compounds such as we have used (Table 1), spectra and coupling constants can be obtained with relative ease.

In benzenoid aromatics, ¹J couplings vary from 50 to 65 Hz^{10,12} and generally increase with the replacement of a hydrogen atom with an electronegative group. In our series of 4,4'-disubstituted-[4,4'-13C2]azobenzenes, ¹J(43) increases from 56 Hz (unsubstituted) through 61 Hz (4,4'-diiodo[4,4'-13C2]azobenzene) to 65 Hz (4,4'-dichloro[4,4'-¹³C₂]azobenzene). Also, a change of the labeling position in unsubstituted azobenzenes from the $4 - [^{1}J(43) = 56 \text{ Hz}]$ to the 1position (electronegative azo group) causes an increase in ${}^{1}J$ [${}^{1}J(12) = 67$ Hz]. Labeling in the 2-position ($[2,2',6,6'-{}^{13}C_4]$ azobenzene) leads to two different ${}^{1}J$ couplings, ${}^{1}J(21) = 64$ Hz and ${}^{1}J(23) = 57$ Hz, the higher ${}^{1}J(21)$ being attributable to the presence of the electronegative azo group at the 1-position.

Geminal ${}^{13}C{}^{-13}C$ couplings (i.e. through two bonds) have small values of up to *ca*. 3 Hz.^{10,12} In the labeled azobenzenes we did not always observe these couplings; in some

Table 2. ¹³ C NMR shifts (ppm) and ¹³ C- ¹³ C couplings (Hz) of trans-azobenzenes ^a						
Azobenzene	C-1	C-2	C-3	C-4		
Unlabeled	152.51	122.78	128.93	130.84		
	s	S	S	s		
[1,1'- ¹³ C ₂]	152.67	122.83	129.07	130.97		
	S	dd	S	Ь		
		$^{1}J(12) = 67$				
		$^{4}J(1'2) = 4$				
[4,4'- ¹³ C ₂]	152.67	122.83	128.98	130.97		
	d	d	d	s		
	$^{3}J(41) = 9$	$^{2}J(42) = 2$	$^{1}J(43) = 56$			
4,4'-Dichloro[4,4'- ¹³ C ₂]	153.24	124.18	129.35	137.22		
	ď	S	d	s		
	$^{3}J(41) = 9$		$^{1}J(43) = 65$			
4,4'-Diiodo[4,4'- ¹³ C ₂]	151.73	124.53	138.42	98.12		
	d	d	d	s		
	$^{3}J(41) = 10$	$^{2}J(42) = 2$	$^{1}J(43) = 61$			
2,2'-Dimethoxy[4,4'- ¹³ C ₂] ^c	156.94	143.05	112.64	132.28		
	s	s	ď	S		
			$^{1}J(43) = 58$			
[2,2',6,6'- ¹³ C ₄]	152.61	122.81	129.06	130.96		
	t	s	d-d	t		
	$^{1}J(21) = 64$		$^{1}J(23) = 57$	$^{2}J(24) = 3$		
			$^{3}J(63) = 8$			

^a Resolution for the $[1,1'_{-}^{13}C_{2}]$ and $[2,2',6,6'_{-}^{13}C_{4}]$ cases was 0.2 Hz per point. Resolution for other cases was 0.9 Hz per point.

^b AA'X triplet with spacing 4.4 Hz. ^c Others: 120.64, d, ¹J(45) = 56 Hz, C-5; 117.62, s, C-6; 56.41, s, OCH₃.

Table 3. ¹³ C NMR shifts (pp	m) and ¹³ (C- ¹³ C couplings	(Hz) of cis-azo	benzenes*
Azobenzene	C-1	C-2	C-3	C-4
Unlabeled ^b	153.6	120.5	128.7	127.3
	s	S	S	s
[1,1'- ¹³ C ₂]	153.41	122.48	128.69	127.32
	s	dd	s	c
		$^{1}J(12) = 64$		
		$^{4}J(1'2) = 3$		
[4,4'- ¹³ C ₂]		120.49	128.72	127.31
	d	d	d	s
		$^{2}J(42) = 2$	$^{1}J(43) = 52$	
4,4-Dichloro[4,4'-13C ₂]		121.92		133.52
	d	s	đ	s
4,4'-Diiodo[4,4'- ¹³ C ₂]		122.24	138.06	93.14
	d	d	d	s
		$^{2}J(42) = 3$	$^{1}J(43) = 61$	
2,2'-Dimethoxy[4,4'- ¹³ C ₂] ^f			111.42	128.52
	d	d	se	s
[2,2',6,6'- ¹³ C ₄]		120.48		127.45
	đ	s	đ	br.s

^a Resolution for the $[1,1'-{}^{13}C_2]$ and $[2,2',6,6'-{}^{13}C_4]$ cases was 0.2 Hz per point. Resolution for other cases was 0.9 Hz per point.

^b Ref. 9. ^c AA'X triplet with spacing 4.4 Hz.

^a AG & thplet with spacing 4.4 mills. ^a Not seen. ^e This should be a doublet but only a singlet was found from the unlabeled com-pound (low ¹³C enrichment). [†] Others: 120.18, s^e, C-5; 118.88, s, C-6; 55.55, s, OCH₃.

cases we observed a broad signal instead of the expected doublet. Vicinal ${}^{13}C{}^{-13}C$ couplings (through three bonds) have magnitudes varying up to 16 Hz^{10,12} and approximating 9 Hz in aromatics. Our results agree well with this.

An interesting case is trans-[1,1'-¹³C₂]azobenzene. Because of the close distance between the identically labeled carbon atoms, this spin system can be described as AA'X, where the AA' parts are the labeled carbons at the 1- and 1'-positions. The ¹³C signal of the C-4 atom (X part) is a triplet with a spacing of 4.4 Hz (this spectrum was recorded with a resolution of 0.206 Hz per point). Theoretically, this spacing should be equal to $(1/2)(J_{AX} + J_{A'X})$,¹³ where J_{AX} is ${}^{3}J(14)$ and $J_{A'X}$ is ${}^{6}J(1'4)$. From the spectrum of $[4,4'-{}^{13}C_2]$ azobenzene, where ${}^{3}J(41) = 9$ Hz, we can speculate that J_{AX} will have a similar value and that ${}^{6}J(1'4)$ in [1,1'-¹³C₂]azobenzene is therefore small (not larger than 0.1 Hz) and presumably of opposite sign to ${}^{3}J(14)$ (presumably negative, because ${}^{3}J$ in aromatics is generally positive).¹² The ¹³C signal of C-2 in [1,1'-¹³C₂]azobenzene is the X part of another AA'X system but, in contrast, is a dd, in which ${}^{1}J(12) = 67$ Hz and ${}^{4}J(1'2) = 4$ Hz. The contrast between this coupling and the X pattern for C-4 arises from the sizes of the coupling constants $[^{1}J(12)$ and $^{4}J(1'2)]$, which apparently do not fit the condition for an AA'X triplet, namely that $[J(12) - J(1'2)] \ll J(11')^{13}$ [we were unable to determine ${}^{3}J(11')$].

EXPERIMENTAL

¹H-decoupled ¹³C NMR spectra were recorded for solutions of ca. 10 mg of compound in 0.8 ml of CDCl₃ in 5-mm tubes at room temperature, with a Bruker-IBM AF-300 (75.469 MHz) Fourier transform NMR spectrometer equipped with an Aspect 3000 computer and using DISNMR version 87 from the Bruker Software Library. Spectra were recorded in the Fourier transform mode using a deuterium lock. Chemical shifts are expressed in ppm relative to TMS, but were measured to the central solvent peak at 77.00 ppm. Typical conditions were as follows: 64 K data points, spectral width 29412 Hz. digital resolution 0.898 Hz per point, pulse width 4.4 µs (90°), acquisition time 1.114 s, pulse delay 1-20 s and 200-4000 scans. Spectra of $[1, 1_1 - {}^{13}C_2]$ azobenzene and [2, 2'6,6'- ¹³C₄]azobenzene were also recorded with a sweep width of 6757 Hz, resulting in a digital resolution of 0.206 Hz per point.

Acknowledgments

We thank the National Science Foundation (Grant 89-19768) and the Robert A. Welch Foundation (Grant D-028) for support of this and earlier research.

References

1. For a review, see H. J. Shine, J. Phys. Org. Chem. 2, 491 (1989).

- H. J. Shine and W. Subotkowski, unpublished results.
- H. J. Shine, H. Zmuda, K. H. Park, H. Kwart, A. G. Horgan and M. Brechbiel, J. Am. Chem. Soc. 104, 2501 (1982).
- H. J. Shine and E. S. Rhee, J. Labelled Compd. Radiopharm. 21, 569 (1984).
- H. J. Shine, J. Habdas, H. Kwart, M. Brechbiel, A. G. Horgan and J. San Filippo, Jr, *J. Am. Chem. Soc.* **105**, 2823 (1983).
- H. J. Shine, K. H. Park, M. L. Brownawell and J. San Filippo, Jr, J. Am. Chem. Soc. 106, 7077 (1984).
- L. Kupczyk-Subotkowska, H. J. Shine, W. Subotkowski and J. Zygmunt, *Gazz. Chim. Ital.* **117**, 513 (1987).
- A. Vogel, *Textbook of Practical Organic Chemistry*, 4th edn, p. 208. Longman, London (1978).
- 9. Y. Kuroda and Y. Fujiwara, *J. Phys. Chem.* **85**, 2655 (1981).
- H. O. Kalinowski, S. Berger and S. Braun, Carbon-13 NMR Spectroscopy. Wiley, New York (1988).
- 11. J. Mason, J. Chem. Soc. A 1038 (1971).
- J. L. Marshall, Carbon–Carbon and Carbon–Proton NMR Couplings. Verlag Chemie, Deerfield Beach, FL (1983).
- P. E. Hansen, O. K. Poulsen and A. Berg, Org. Magn. Reson. 7, 591 (1975).

Received 19 November 1990; accepted (revised) 6 March 1991

¹H and ¹³C NMR Study of Some (E)-3'and 4'-Substituted Stilben-4-ols

THOMAS H. FISHER (to whom correspondence should be addressed) Department of Chemistry, Mississippi State University, Mississippi State, Mississippi 39762, USA

TOR P. SCHULTZ Mississippi Forest Products Utilization Laboratory, Mississippi State University, Mississippi State, Mississippi 39762, USA

A series of ten (E)-stilben-4-ols, HOPhCH \rightarrow CHPhX, with X = H, 4'-Cl, 4'-F, 4'-Me, 4'-OMe, 3'-Me, 3'-OMe, 3'-OH, 3'-F and 3',4-diOMe, were studied using one- and two-dimensional NMR techniques. Interpretation of these spectra led to definitive assignments of all carbon and hydrogen chemical shifts. ¹H chemical shift increments were quantitatively determined for the five substituents studied, and the *para* A_i value of the styryl group was found to be more deshielding than those recorded in previous reports.

KEY WORDS Stilben-4-ols ¹H and ¹³C chemical shifts

INTRODUCTION

Stilben-4-ols have been studied for their role in the natural durability of wood,¹ for growth inhibitory activity in liverwort gemmaling assays² and for their anticonvulsant properties.³ Very few ¹H NMR data have been reported on stilben-4-ols because of the complexity of the aryl region. Wyrzykiewicz *et* $al.^4$ assigned the ¹³C NMR chemical shifts for a large number of (*E*)-hydroxyazastilbenes and included stilben-2-, 3- and -4-ol in the study. In this study the complete ${}^{1}H$ and ${}^{13}C$ chemical shift assignments for a series of ten 4'- and 3'-substituted-stilben-4-ols are reported. The use of various two-dimensional (2D) NMR techniques allowed definitive assignments to be made.

EXPERIMENTAL

The synthesis and physical properties of stilben-4-ols 1-7 and 9-10 were reported previously,¹ and 3-hydroxystilben-4-ol (8) is also a known compound.³ All spectra were obtained on a General Electric QE-300 spectrometer at 22 ± 1 °C, observing ¹H and ¹³C at 300.67 and 75.61 MHz, respectively. NMR samples contained *ca.* 40 mg of each stilbenol in 0.5 ml of acetone- d_6 containing 1% of TMS. ¹H spectra were collected into 32K data sets over a spectral width of 6 kHz using a 30° pulse. ¹³C spectra were collected into 32K data sets over a spectral width of 20 kHz using a 40° pulse and were processed using