Carbon-13 NMR Spectra of 5-(4-Substituted Benzylidene)-2,3,4,5-tetrahydropyridines

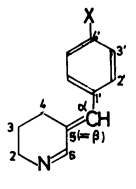
Yoshito TAKEUCHI,* Takashi BANDO, Shuji TOMODA, and Yujiro NOMURA
Department of Chemistry, College of Arts and Sciences, The University of Tokyo, Komaba, Meguro-ku, Tokyo 153
(Received December 26, 1983)

Carbon-13 chemical shifts for a series of 5-(4-substituted benzylidene)-2,3,4,5-tetrahydropyridines were determined. The substituent chemical shifts (SCS) were correlated with σ_I and σ_R° values by means of DSP and DSP-NLR analysis. It was found that as a substituent the C=C-C=N moiety is as mild as C=C and that the former can be approximated as a vinylogue of the C=N moiety. C-13 lanthanoid-induced shifts (LIS) of the parent compound were also discussed.

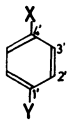
Numerous attempts have been made to correlate electronic substituent constants with C-13 chemical shifts of substituted aromatic systems.[1] Extention of these correlation to the aromatic systems with additional π-bonded side chains continue to interest several group of investigaters[2] in connection with the elucidation of the mechanism of transmission of the electronic substituent effect through the conjugated system.

Recently we prepared a series of 5-(4-substituted benzylidene)-2,3,4,5-tetrahydropyridine (**1a—1g**) by the reaction of 2,3,4,5-tetrahydropyridine trimer and appropriately substituted benzaldehydes.[3] These compounds are interesting in that the side chain C=C double bond is further conjugated with C=N double bond, and that the two double bonds are fixed in the *s-trans* conformation. In this study we compare C-13 substituent chemical shifts (SCS) of **1** with those of 4-substituted styrenes (**2**)[4] and 4-substituted phenylacetylenes (**3**),[5] in order to estimate the effect of additional conjugation by C=N bond upon the electronic property of styrene framework.

Comparison will also be made with SCS of *N*-(4-substituted benzylidene)-methylamines (**4**),[6] *N*-(4-substituted benzylidene)-*t*-butylamines (**5**)[6] and *N*-(4-substituted benzylidene)anilines (**6**),[7] and *N*-benzylidene(4-substituted aniline)s (**7**)[7] where C=N bond is directly bonded to the benzene ring.



1



2~7

2 Y=-CH=CH$_2$
3 -C≡CH
4 -CH=N-Me
5 -CH=N-t-Bu
6 -CH=N-Ph
7 -N=CH-Ph

Experimental

The preparation of benzylidenetetrahydropyridines **1a—1g** were already reported.[3]

The solutions for NMR measurements were prepared by dissolving *ca.* 50 mg of the **1a—1g** into $CDCl_3$ (1.0 ml) containing 1% tetramethylsilane (TMS) which acts as the internal standard. For LIS (lanthanoid-induced shift) study, 54 mg (0.316 mmol) of 5-(4-substituted benzylidene)-2,3,4,5-tetrahydropyridine was dissolved in $CDCl_3$ (1.0 ml), and a weighed amount of Eu(fod)$_3$ was added. The molar ratio of shift reagent/solute varied from 0.023 to 0.297.

The instrument employed was JEOL FX-90Q spectrometer operating at 22.5 MHz with a 10 mm $^1H/^{13}C$ dual probe. The spectra were obtained with proton noise decoupling for 5KHz spectral width, collection of 8K data points in the FID, and 13 μs pulse width (45°). Usually 100 scans were accumlated with a 3.5s pulse interval after each pulse. C-13 NMR chemical shifts of **1a—1g** were listed in Table 1. Assignment of C-13 NMR signals of **1a** was already reported.[8] Assignments of signals for **1b—1g** were made by comparison with the data for corresponding styrenes (**2a—2g**).[4]

Results and Discussion

The Nature of C=C-C=N Moiety. Compounds **1** may be regarded as one of aromatic systems of the general type *p*-X-C$_6$H$_4$-Y which has been extensively investigated in view of the electronic interaction between the two substituents as manifested by C-13 SCS.[9] A comparison of SCS of **1** with those of **2** is expected to depend on the difference of the interactions, one between X (variable substituents) and C=C-C=N and the other between X and C=C moiety. If the additional C=N bond does not affect the interaction to any significant extent, the correlation of SCS of **1a—1g** with those of **2a—2g** for the equivalent positions should provide a linear correlation with a slope of unity. The result of correlations is listed in Table 2.

TABLE 1. C-13 CHEMICAL SHIFTS OF 5-(4-SUBSTITUTED BENZYLIDENE)-2,3,4,5-TETRAHYDROPYRIDINES[a]

Compd.	X	C6	C5(Cβ)	C4	C3	C2	Cα	Cl′	C2′	C3′	C4′	X[b]
1a	H	163.64	131.70	21.63	25.03	49.70	136.11	135.93	129.43	128.42	128.00	
1b	NMe_2	164.31	127.96	21.62	25.25	49.35	136.84	124.06	130.99	111.82	150.01	40.14
1c	OMe	163.64	129.66	21.37	24.88	49.31	135.71	128.44	130.78	113.72	159.26	55.06
1d	Me	163.66	130.89	21.56	25.03	49.57	136.09	133.11	129.10	129.42	137.93	21.23
1e	Cl	163.28	132.08	21.45	24.92	49.57	134.79	134.35	130.69	128.61	134.35	
1f	CN	162.74	134.14	21.40	24.97	49.68	133.81	140.47	129.68	132.08	111.17	118.64
1g	NO_2	162.57	134.56	21.33	24.93	49.70	133.22	142.39	128.61	123.65	146.68	

a) δ values b) ^{13}C nuclei of substituents

Table 2. Correlation between SCS for 1 and 2[a)]

Carbon	a	b	r
C5(Cβ)	0.759	−0.443	0.993
Cα	1.932	0.885	0.975
Cl′	1.104	0.250	>0.999
C3′	1.040	0.266	0.998
C4′	1.024	−0.559	0.999

a) SCS(**1**)=a·SCS(**2**)+b; r, correlation coefficient.

Except for C2′ (meta to the substituent), a reasonable correlation (r>0.975) is always obtained. The slope of the correlation at Cl′ is larger than unity by 0.1, suggesting that the interaction of C=C-C=N moiety with X is a little larger than that of C=C moiety. The deviation of the slope from unity is much more enhanced at side-chain carbons (Cα and Cβ). This is consistent with the contribution of such a zwitterionic canonical structure as

$$\underset{\alpha\ \beta\ 6}{>C{=}C{-}C{=}N-} \cdots\cdots \underset{\alpha\ \beta\ 6}{>C^{+}{-}C{=}C{-}N^{-}-} \quad (1)$$

DSP and DSP-NLR Analysis. In order to clarify the nature of the interaction shown in Table 2, a DSP (dual substituent parameter) or a DSP-NLR (nonlinear resonance effect)[9,10] of **1** and **2** together with a variety of related systems **3**—**7** were attempted. DSP or DSP-NLR analyses were made on an identical sets of substituents, *i.e.*, NMe_2, OMe, Me, Cl, CN, and NO_2, wherever possible. In certain cases SCS data for one or two substituents were not available but from previous experiences, this will not likely to cause a serious error. According to Taft *et al.*[9] C-13 SCS of appropriate carbons of substituted aromatic system of the general type X-C_6H_4-Y where X and Y are variable and fixed substituent, respectively, can be correlated with the DSP and DSP-NLR based on the equation

$$\text{C-13 SCS} = \rho_I\sigma_I + \rho_R\sigma_R^\circ/(1-\varepsilon\sigma_R^\circ), \quad (2)$$

where σ_I and σ_R° are inductive and resonance substituent constants, respectively, and ρ_I and ρ_R are transmission coefficients determined by the least-square method. ε is null in DSP analysis by definition, while a constant for each fixed substituent Y in DSP-NLR analysis and characterizes the electron demand exerted by Y.

The results of the ayalyses for Cl′, Cα, and C5(Cβ), are summerized in Table 3. In this Table cases where f, the goodness of fit parameter, is above 0.06, the critical value for an acceptable fit, are also included for the sake of comparison. At Cl′, both ρ_I and ρ_R of **1** are larger than those of **2**, which corresponds to the slope (1.1) of the correlation given in Table 2. The ε value is small, comparable with that for **2**, to indicate that the C=C-C=N moiety is "mild" in the sense that there is no additional interaction with X through the π-frame. It is in sharp contrast with much larger ε values for **3**, **5**—**7**.

It is reported[9] that ε values in DSP-NLR analyses largely depend on the nature of terminal atoms with which Y is bonded to the benzene ring. In **1**—**6**, although the terminal atoms are all carbons, the termini can be subdivided into three types, *i.e.*, C=C, C≡C, or C=N. Our data indicate that a C=C terminal is milder than C≡C, C=N (**5**, **6**) or N=C (**7**) termini regardless of the presence of further conjugation.

A large deviation of the solpe from unity found in the correlation for Cα and Cβ given in Table 2 clearly shows that a considerable perturbation was invoked in the electronic properties of C=C bond in **1**. The slope for Cα is three times as large as that for Cβ probably because of the contribution of dipolar structure as shown in Eq. (1).

The DSP analyses of SCS for these side-chain carbons show that at Cα both ρ_I and ρ_R for **1** are larger than those for **2**. The increase is more significant for ρ_R. At Cβ, the contrary is the case. Thus, both ρ_I and ρ_R of **1** are smaller than those for **2**, and the decrease is larger for ρ_I. In view of the rather small difference between **1** and **2** of ρ_I and ρ_R at Cl′, it may be concluded that the side-chain carbon nuclei rather than the aromatic carbon atoms are much more affected by the elongation of conjugated system.

There remains one small problem. May **1** be ragarded as a vinylogue of **4**—**6**? ρ_I and ρ_R of **1** at C6 are −1.38 and −1.17, respectively, with f=0.16. The resonance effect of X is transmitted to C6 of **1** even more effectively than to Cα of **4**—**6**. Hence, **1** may be regarded as a vinylogue of such imines as **4**—**6** at least in a qualitative manner. The smaller ρ_I of **1** at C6 corresponds to the greater number of intervening bond or greater distance be-

Table 3. DSP and DSP-NLR[a)] analysis of various p-X-C_6H_4-Y_systems

Carbon	Parameter[b)]	1	2	3	4	5	6	7
Cl′	ρ_I	5.03(5.18)	4.08(4.17)	4.20(4.57)	4.09	4.21(4.58)	3.95(4.32)	4.42(4.43)
	ρ_R	21.66(20.63)	20.01(19.40)	22.58(19.80)	20.52	20.43(17.54)	20.49(17.00)	20.01(17.41)
	f	0.03(0.02)	0.02(0.01)	0.05(0.02)	0.07	0.06(0.03)	0.07(0.03)	0.01
	ε	0(−0.11)	0(−0.07)	0(−0.28)	0	0(−0.32)	0(−0.38)	0(−0.34)
Cα	ρ_I	−3.87(−3.88)	−2.83	−2.75	−3.36	−3.21	−3.83	
	ρ_R	−1.66(0.18)	0.13	−1.80	−0.17	−0.39	−0.53	
	f	0.18(0.18)	0.13	0.13	0.13	0.06	0.14	
	ε	0(−0.05)	0	0	0	0	0	
C5	ρ_I	3.14	5.30(5.28)	5.59				2.96(3.12)
(Cβ)	ρ_R	7.23	8.47(8.65)	5.80				6.63(5.90)
	f	0.09	0.05(0.05)	0.16				0.09(0.08)
	ε	0	0(0.05)	0				0(−0.36)

a) Values in parentheses. In certain DSP-NLR analyses ε values did not converge on reasonables values.
b) For definition of parameters, see Eq(1).

tween X and C-6 while larger ρ_R of **1** indicates more effective transmission of resonance effect to C-6 through π-frame as compared with that between X and Cα.

Lanthanoid-induced Shifts. Lathanoid-induced shifts of C-13 nuclei are due to the combination of contact and pseudo contact shifts. The contact term, which is much more important in conjugated systems than in saturated systems, causes in certain cases an alternating sign along the carbon chain.[11]

The contact shift arises from the delocalization of the unpaired electron of the shift reagent to the substrate atoms. It occurred to us that there might be parallelism between the extent of spin delocalization and the transmission of substituent effect through the π-frame. Thus the sign of ρ values of **1** at C6 (both negative) clearly establishes the alternating nature of the ρ signs along the π-chain Cl′–Cα–Cβ–C6. This alternation has been pointed out[5] for side-chain C-13 shifts for **2** and chalcones (two carbon unit). Our system is, to the best of our knowledge, the longest π-chain with alternating ρ signs.

With this in mind, we measured LIS of **1a** by Eu(fod)$_3$. The result is summarized in Fig. 1, where the observed LIS are plotted against the molar ratio [Eu(fod)$_3$]/[solute]. Clearly, the sign of LIS does alternate along Cl′–Cα–Cβ–C6 chain. Negative LIS for Cβ and Cl′ are associated with positive ρ values, and positive LIS for Cα and C6 with negative ρ values. This parallelism is another piece of evidence to the through conjugation in Ph–C=C–C=N moiety.

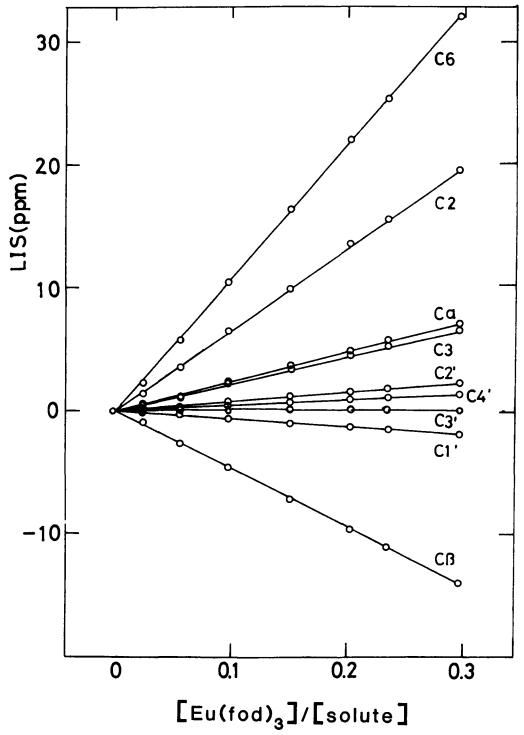


Fig. 1. Lanthanoid-induced shifts (LIS) in 5-benzylidene-2,3,4,5-tetrahydropyridine (**1a**).

Conclusion

The nature of C=C–C=N moiety in **1** as a substituent is mild and very close to the C=C moiety in respect to the magnitude of interaction with the variable substituent X attached to the same aromatic ring. The transmission of substituent effect of X to the side chain of **1** is somewhat different from that of compounds with –C=N or –N=C side-chains. The general behavior of **1** may, however, be regarded as a vinylogue of benzylideneamines. In **1**, the alternation of signs of ρ values in DSP analyses are parallel with that of LIS along Cl′–Cα–Cβ–C6 linkage. This phenomenon might be useful for theoretical treatment of the substituent effect in aromatic system.

The present work was partially suppoted by a Grant-in-Aid for Scientific Research No. 443007 from the Ministry of Education, Science and Culture.

References

1) For instance, G. E. Maciel, in G. C. Levy, ed. "Topics in Carbon-13 NMR Spectroscopy," Vol. 1, p. 53 (1974).
2) R. G. Jones and G. Allen, *Org. Magn. Reson.*, **19**, 196 (1982) and references therein.
3) Y. Nomura, T. Bando, Y. Takeuchi, and S. Tomoda, *Bull. Chem. Soc. Jpn*, **56**, 3199 (1983).
4) G. K. Hamer, I. R. Peat, and W. F. Reynolds, *Can. J. Chem.*, **51**, 897 (1973).
5) D. D. Dawson and W. F. Reynolds, *Can. J. Chem.*, **53**, 373 (1975).
6) W. B. Jennings, V. E. Wilson, D. R. Boyd, and P. B. Coulter, *Org. Magn. Reson.*, **21**, 279 (1983).
7) N. Inamoto, K. Kushida, S. Masuda, H. Ohta, S. Satoh, Y. Tamura, K. Tokumaru, K. Tori, and M. Yoshida, *Tetrahedron Lett.*, 3617 (1974).
8) Y. Nomura, T. Bando, Y. Takeuchi, and S. Tomoda, *Bull. Chem. Soc. Jpn.* **57**, 1271 (1984).
9) J. Bromilow, R. T. C. Brownlee, D. J. Craik, M. Sadek, and R. W. Taft, *J. Org. Chem.* **45**, 2429 (1980).
10) For a recent assessment of DSP analysis, see M. Charton, *Prog. Phys. Org. Chem.*, **13**, 119 (1981).
11) F. W. Wehrli and T. Wirthlin, "Interpretation of Carbon-13 NMR Spectra," Heyden & Sons, London (1978), p. 96.