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Effects of the Nitrone Group in NMR Spectra of α,*N*-Diphenylnitrones

Kinko Koyano and Hiroshi Suzuki

Department of Chemistry, College of General Education, The University of Tokyo, Komaba, Meguro-ku, Tokyo

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The NMR and UV spectra of α,*N*-diphenylnitrone and its derivatives which have a substituent at the para position of the α-phenyl group and some of which have in addition a methyl substituent at the ortho position of the α-phenyl group were measured. Examination led to the following conclusions. The NMR signal of the ortho protons of the α-phenyl group appears at a very low field. This is mainly attributed to the direct effect of the negatively charged oxygen atom of the nitrone group. Increase in the electron-donating power of the para substituent enhances this effect.

In a previous paper, we reported that the NMR signal of the ortho protons of the α-phenyl group of α,*N*-diphenylnitrone (see Fig. 1) appeared at a very low field. We ascribed this to the direct effect of the negatively charged oxygen atom of the nitrone group (–CH=NO–).[1)]

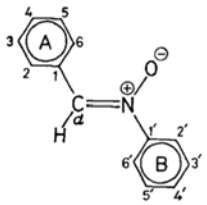

Fig. 1. α,*N*-Diphenylnitrone.

In the present paper, the NMR and UV spectra of α,*N*-diphenylnitrone and its derivatives which have a substituent at the 4-position and some of which have in addition a methyl substituent at the 2-position are examined. Special attention was paid to the effects of the nitrone group on the position of the NMR signals of the A ring protons. The conclusion of the previous paper was confirmed, and the influence of the 4-substituent on the direct effect of the oxygen atom was clarified.

Results and Discussion

The τ values of signals in the proton magnetic resonance spectra of α,*N*-diphenylnitrones in $CDCl_3$ are listed in Tables 1 and 2, and data on the longest wavelength band (referred to hereafter as the A band) in the electronic absorption spectra are shown in Table 3.

With regard to the effects of the two substituents of para-disubstituted benzenes on the chemical shift of the NMR signals of the ring protons, many

Table 1. The τ values of proton signals of 4-substituted α,*N*-diphenylnitrones in $CDCl_3$

4-Substituted α,*N*-diphenylnitrone		Position of protons					
Entry No.	4-Substituent	α	2,6	3,5	2′,6′	3′,4′,5′	4-Methyl
1	$N(CH_3)_2$	2.26	1.77(d)	3.33(d)	2.28—2 37	2.68—2.75	
2	OCH_3	2.17	1.61(d)	3.05(d)	2.26—2.33	2.61—2.67	
3	CH_3	2.16	1.73(d)	2.77(d)	2.20—2.31	2.55—2.65	7.61
4	Unsubstituted	2.12	1.58—1.69	2.54—2.64	2.22—2.44	2.54—2.64	
5	Cl	2.13	1.69(d)	2.59(d)	2.25—2.35	2.55—2.64	
6	Br	2.12	1.74(d)	2.45(d)	2.21—2.31	2.54—2.61	
7	$COOCH_3$	2.04	1.62(d)	1.98(d)	2.24—2.35	2.58—2.65	
8	CN	2.00	1.57(d)	2.32(d)	2.23—2.36	2.50—2.60	
9	NO_2	1.99	1.45(d)	1.70(d)	2.17—2.27	2.47—2.53	

When a signal is doublet (indicated by letter d), the τ value at its center is shown. $J_{2,3}=J_{6,5}=7.5$—9.3 cps. When signals are unresolved, the range in which they appear is shown.

1) K. Koyano and H. Suzuki, *Tetrahedron Letters*, **1968**, 1859.

TABLE 2. THE τ VALUES OF PROTON SIGNALS OF 4-SUBSTITUTED 2-METHYL-α,N-DIPHENYLNITRONES IN $CDCl_3$

4-Substituted 2-methyl-α,N-diphenylnitrone		Position of protons							
Entry No.	4-Substituent	α	6	3	5	2′,6′	3′,4′,5′	2-Me	4-Me
1′	$N(CH_3)_2$	2.07	0.52	3.49	3.44	2.21—2.32	2.53—2.65	7.60	
2′	OCH_3	2.03	0.51	3.23	3.16	2.20—2.32	2.50—2.62	7.61	
3′	CH_3	2.00	0.70	2.98	2.89	2.26—2.35	2.55—2.64	7.67	7.71
9′	NO_2	1.88	0.48	1.91	1.85	2.18—2.30	2.44—2.53	7.45	

The 3-, 5-, and 6-protons constitute an AMX spin system. $J_{5,6}$=about 9 cps, $J_{3,5}$=2—3 cps, and $J_{3,6}$=0 cps. When signals are unresolved, the range in which they appear is shown.

TABLE 3. THE LONGEST-WAVELENGTH BAND IN THE ELECTRONIC ABSORPTION SPECTRA OF α,N-DIPHENYLNITRONES

No.	α,N-Diphenylnitrone	In cyclohexane		In ethanol	
		λ_{max} mμ	ε_{max} $\times 10^{-4}$	λ_{max} mμ	ε_{max} $\times 10^{-4}$
1	4-$N(CH_3)_2$-	372	2.40	385	3.21
2	4-OCH_3-	334	2.05	331	2.41
3	4-CH_3-	327	2.10	319	2.35
4	Unsubstituted	320	1.86	315	2.07
5	4-Cl-	327	2.22	321	2.34
6	4-Br-	329	2.32	323	2.44
7	4-$COOCH_3$-	340	2.62	331	2.75
8	4-CN-	337	2.73	331	2.66
9	4-NO_2-	363	1.76	356	1.95
1′	2-CH_3-4-$N(CH_3)_2$-	—	—	392	3.48
2′	2-CH_3-4-OCH_3-	—	—	338	2.31
3′	2,4-$(CH_3)_2$-	329	1.87	325	2.06
9′	2-CH_3-4-NO_2-	—	—	358	1.68

workers have stated that additivity holds approximately.[2] The contributions of the substituents at the ortho and meta positions to the change in the τ value of a ring proton are denoted by S_o and S_m, respectively, and they are referred to as the ortho and meta substituent constants, respectively. The values determined by Smith[3] for CCl_4 solutions are adopted here.

4-Substituted α,N-diphenylnitrones can be regarded as para-disubstituted benzenes, in which one of the two substituents is the 4-substituent (X) and the other the N-phenylnitrone group (–CH=NO–Ph). As is shown in Fig. 2, there exists an approximately linear relationship between the τ values of the 3- and 5-protons ($\tau_{3,5}$) of 4-substituted α,N-diphenylnitrones and the ortho substituent constants of the 4-substituents (S_o(X)), and the slope of the correlation line is nearly unity. From the correlation line the τ value at S_o(X)=0 is

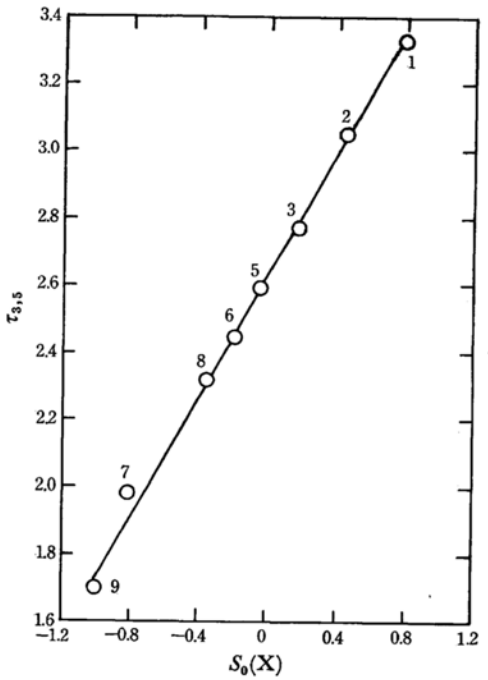

Fig. 2. The relation between the observed τ values of the 3- and 5-protons ($\tau_{3,5}$) of 4-substituted α,N-diphenylnitrones and the ortho substituent constants of the 4-substituents (S_o(X)). The numbers denote the compounds, according to the entry numbers in Table 1.

determined to be about 2.60. The difference between this value and the τ value of the protons of benzene (2.63 in $CDCl_3$), about −0.03, may be considered as the meta substituent constant of the N-phenylnitrone group, S_m(NPN). This is much smaller in absolute value than the meta substituent constant of the nitro group, $S_m(NO_2)$ (−0.21). Thus it may be said that the N-phenylnitrone group exerts only a very weak deshielding effect on the meta protons. There is also a fairly good linear relationship between the τ values of the α-protons and the Hammett σ_p values as well as Taft δ_p values[4] of the 4-substituents.

2) *Cf. e.g.*, J. W. Emsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, Oxford (1966), pp. 754—760 and 1140—1142.

3) G. W. Smith, *J. Mol. Spectry.*, **12**, 146 (1964).

4) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 1045 (1957).

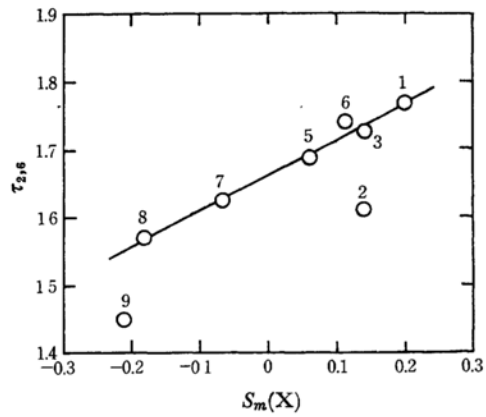

Fig. 3. The relation between the observed τ values of the 2- and 6-protons ($\tau_{2,6}$) of 4-substituted α,*N*-diphenylnitrones and the meta substituent constants of the 4-substituents (S_m (X)). The numbers denote the compounds, according to the entry numbers in Table 1.

Figure 3 shows that there is only a rough linear relationship between the τ values of the 2- and 6-protons ($\tau_{2,6}$) and the meta substituent constants of the 4-substituents (S_m(X)). The plots for the 4-methoxy and 4-nitro compounds deviate markedly from a straight correlation line. From the approximate correlation line given in Fig. 3 the τ value at S_m(X)=0 is estimated at about 1.65. If the difference between this value and the τ value of the protons of benzene, about −0.98, is tentatively considered as the ortho substituent constant of the *N*-phenylnitrone group, S_o(NPN), this substituent constant is comparable to the ortho substituent constant of the nitro group (−0.99). Thus, it might be said that the *N*-phenylnitrone group has a strong ortho substituent deshielding effect comparable to that of the nitro group.

The τ values of the 6-protons (τ_6) of the compounds having a methyl substituent at the 2-position, *viz.*, the compounds of entry numbers 1′, 2′, 3′, and 9′ in Table 2, are smaller by 0.9—1.3 than the τ values of the 2- and 6-protons ($\tau_{2,6}$) of the corresponding compounds having no methyl substituent at the 2-position, as illustrated by Fig. 4. This result is the same as that described previously for the 4-methyl compounds.[1] It is evident that the arguments are also valid in the present case. From the following facts, the most preferred conformation of the 4-substituted 2-methyl-α,*N*-diphenylnitrones seems to be a planar or nearly planar conformation in which the 6-proton is located near the oxygen atom of the nitrone group: (1) The most preferred conformation of the α,*N*-diphenylnitrones having no substituent at the ortho positions is probably a planar or nearly planar conformation;[5] (2) The values of the wavelength

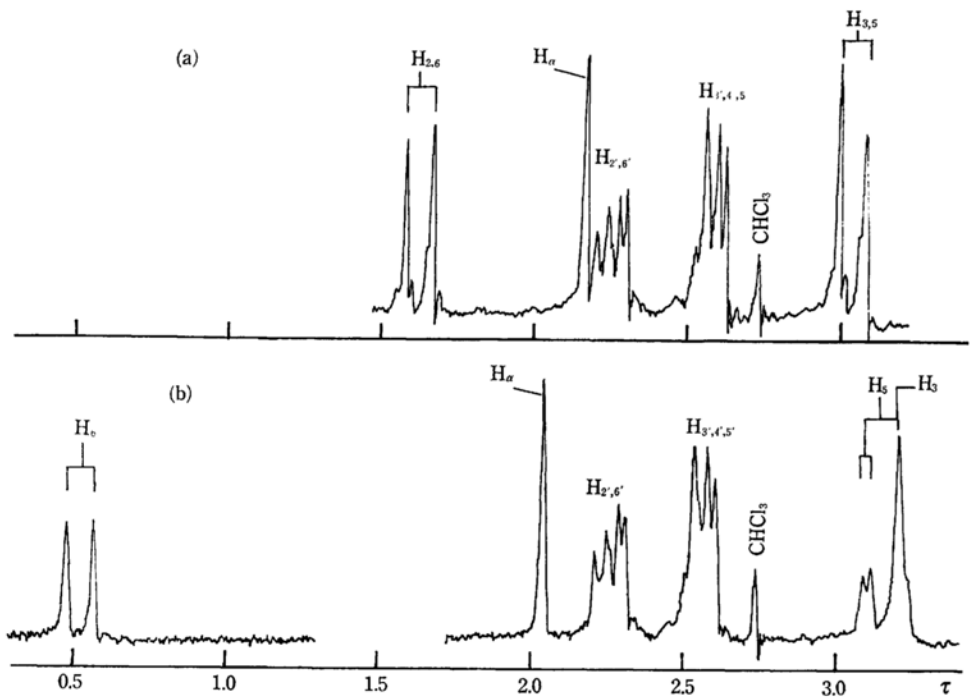

Fig. 4. The NMR spectra of (a) 4-methoxy-α,*N*-diphenylnitrone (compound 2) and (b) its 2-methyl derivative (compound 2′) in $CDCl_3$.

5) T. Kubota, M. Yamakawa and Y. Mori, This Bulletin, **36**, 1552 (1963).

and molar extinction coefficient of the A band maximum of the 4-substituted 2-methyl-α,N-diphenylnitrones are nearly equal to those of the corresponding compounds having no substituent at the 2-position (see Table 3). This seems to indicate that the most preferred conformation of the former is similar to that of the latter; (3) A scale model shows that the 2-methyl group must be sterically hindered from approaching the oxygen atom of the nitrone group. The 6-proton, being located near the negatively charged oxygen atom of the nitrone group, must be strongly affected by the oxygen atom, resulting in the marked downfield shift of its signal.

As seen in Table 2, the values of τ_6 are 0.70, 0.52, 0.51, and 0.48 for the 4-substituent (X)=CH_3, $N(CH_3)_2$, OCH_3, and NO_2, respectively. It should be noted that this order of the τ_6 values is quite different from that of the meta substituent constants of the 4-substituents.

If a 4-substituted α,N-diphenylnitrone having no substituent at the ortho positions had a fixed planar or nearly planar conformation, the 2- and 6-protons must be nonequivalent, and would show their signals at different τ values (τ_2 and τ_6). Of course, the τ value of the proton located near the oxygen atom of the nitrone group (τ_6) must be lower than that of the proton located far from the oxygen atom (τ_2). Actually, the α-phenyl group will rotate around the C_α–C_1 bond, so that the signals of the two protons coalesce. The observed values of $\tau_{2,6}$ are considered to be approximately the means of τ_2 and τ_6. Let us assume that the value of the hypothetical τ_6 of a 4-substituted compound can be calculated from the observed value of τ_6 of the corresponding 2-methyl compound by subtraction of the shift due to the substituent shielding effect of a meta methyl group, which is taken to be about 0.10. Then, from the observed $\tau_{2,6}$ values and the calculated τ_6 values, the values of the hypothetical τ_2 of 4-substituted compounds are calculated to be 3.12, 2.81, 2.86, and 2.52 for X=$N(CH_3)_2$, OCH_3, CH_3, and NO_2, respectively. These τ_2 values have a nearly linear relationship with the meta substituent constants of the 4-substituents, S_m(X).

The difference between the τ_6 value and the τ_2 value can be considered to be due to the direct effect of the oxygen atom of the nitrone group on the 6-proton. The values of this difference are −2.70, −2.40, −2.26, and −2.14 for X=$N(CH_3)_2$, OCH_3, CH_3, and NO_2, respectively. The order of these values coincides with that of the mesomeric electron-donating power of the 4-substituents. Thus, it can be said that the direct deshielding effect of the oxygen atom on the 6-proton is greater when the 4-substituent is more strongly electron-donating. This might be ascribed to the following two causes. (1) As the 4-substituent becomes more strongly electron-donating, the charge density at the oxygen atom will become larger. The inference that the π-electron density at the oxygen atom changes very sensitively by change of the 4-substituent is supported by a simple MO calculation. (2) Since the nitrone group is an electron-withdrawing group, as the 4-substituent becomes more strongly electron-donating, the conjugative interaction in the π-electron system will become stronger. As a result, the most preferred conformation will approach planarity, and its population ratio will increase. Consequently, the average distance between the 6-proton and the oxygen atom will become shorter.

Experimental

Materials. The α,N-diphenylnitrones were prepared by reaction of the adequately substituted benzaldehydes with phenylhydroxylamine in ethanol, according to the following equation:[5,6]

$$R\text{-}CHO + Ph\text{-}NHOH \longrightarrow R\text{-}CH{=}NO\text{-}Ph + H_2O$$

Their melting points (°C) were as follows (all are uncorrected): (1) 4-dimethylamino-, 140.5—141.2; (2) 4-methoxy-, 115.8—116.5; (3) 4-methyl-, 85—87; (4) unsubstituted, 113.0—113.5; (5) 4-chloro-, 153.5—154.0; (6) 4-bromo-, 161.5—162.0; (7) 4-methoxycarbonyl-, 155.5—156.0; (8) 4-cyano-, 147—149; (9) 4-nitro-, 186.0—186.5; (1′) 2-methyl-4-dimethylamino-, 142—143; (2′) 2-methyl-4-methoxy-, 97—98; (3′) 2,4-dimethyl-, 81—82; (9′) 2-methyl-4-nitro-, 153—155.

The compounds of entry numbers 1′, 2′, 3′, and 9′ are probably new compounds. The results of analysis for these compounds are as follows.

(1′) Found: C, 75.69; H, 7.22; N, 10.96%. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.02%.

(2′) Found: C, 74.61; H, 6.35; N, 5.75%. Calcd for $C_{15}H_{15}NO_2$: C, 74.66; H, 6.27; N, 5.81%.

(3′) Found: C, 79.83; H, 6.82; N, 6.47%. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%.

(9′) Found: C, 65.55; H, 4.44; N, 10.86%. Calcd for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.72; N, 10.93%.

Measurement of the NMR and UV Spectra. The NMR spectra were measured on $CDCl_3$ solutions (concentration: about 120 mg in 1 ml of solvent) at room temperature with a Japan Electron Optics Laboratory spectrometer Model JNM-4H-100 (100 MC). Tetramethylsilane was used as an internal reference.

The UV spectra were measured with a Hitachi recording spectrophotometer Model EPS-2.

6) M. J. Kamlet and L. A. Kaplan, *J. Org. Chem.*, **22**, 576 (1957); O. H. Wheeler and P. H. Gore, *J. Am. Chem. Soc.*, **78**, 3363 (1956); J. Splitter and M. Calvin, *J. Org. Chem.*, **20**, 1086 (1955).