Nuclear Magnetic Resonance Study of the Effect of the Hydrogen Bond on the Internal Rotation of Biphenyls

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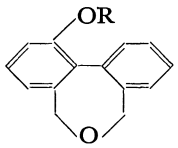
Internal rotation about the pivot bond of several biphenyl derivatives has been studied by means of the nuclear magnetic resonance technique using non-identical chemical shifts of the two methyls in the isopropyl group which is located close to the center of dissymmetry. The results with the 2-methoxy and 2-hydroxy derivatives are compared. The solvent effect is marked in 2-hydroxy derivatives. These results, together with the substituent effect, indicate that the fact that the energy of activation for rotation about the pivot bond of the 2-hydroxy derivatives is a little higher than the corresponding methyl ether may be attributed to the stabilization of the ground state resulting from the presence of intramolecular O–H···π interaction. The infrared data agree with the above conclusion.

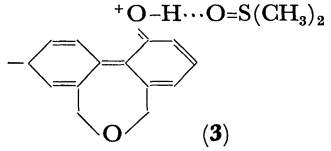
In recent years it has become very common to use the nuclear magnetic resonance technique in investigating the internal rotation. Originally, a biphenyl derivative had to be resolved into optical isomers in order to investigate the rotation about the pivot bond, because polarimetry was a sole method for the investigation. Nowadays, however, it is also possible to study the internal rotation of biphenyls by means of NMR,[1-5] and it has been confirmed that the process which is observed by polarimetry and that studied by NMR are the same.[5,6] These investigations have revealed that the solvent effect on the internal rotation in biphenyl is very small, if present at all.[4,5,7]

However, a paper[8] from this laboratory has shown that a distinct solvent effect was observed in the internal rotation of 1-hydroxy-5,7-dihydro[*c*,*e*]oxepin (**1**). This compound shows an energy of activation for the internal rotation in dimethyl sulfoxide smaller by *ca.* 1 kcal/mol than that in deuteriochloroform. This phenomenon is not observed with the corresponding methyl ether (**2**). Thus, the hydrogen bond must be playing an important role in decreasing the energy of activation for **1**.



(**1**): R=H
(**2**): R=CH_3

Two possibilities may be pointed out with regard to the decrease in energy of activation by the formation of the hydrogen bond. The first is the possibility that the transition state of the inversion of biphenyls is stabilized in dimethyl sulfoxide because of the decrease in the electronegativity of oxygen on formation of the hydrogen bond, with a concomittant increase in the electron density at the position 1 or with an increase in the contribution of the resonance structure (**3**). The second is the stabilization of the ground state due to the presence of the intramolecular O–H···π interaction, which may be very little in dimethyl sulfoxide because of the strong proton-accepting ability of the sulfoxide. The first possiblity will lower the transition state in dimethyl sulfoxide relative to that in deuteriochloroform, whereas the second possibility will lower the ground state in deuteriochloroform relative to that in dimethyl sulfoxide. In either case, the energy of activation will be lowered.



(**3**)

In the above discussion, the effect of the intermolecular hydrogen bond in **1** is disregarded, though it could be important at the concentration used for the NMR study. However, as will be seen later, the IR study indicates that the effect may be disregarded.

We wish here to report on the effect of the substituents on the internal rotation of biphenyls as studied by NMR, and to present a basis on which it can be concluded that the internal O–H···π interaction is an important factor in lowering the energy of activation for rotation about the pivot bond.

Syntheses

After several attempts at synthesizing some substituted derivatives of **1**, it was found that introducing a desired substituent at a desired position of **1** was very difficult. Therefore, we decided to use some isopropyl derivatives which have been shown[9] to give rise to magnetically non-equivalent methyl groups when the rotation about the pivot bond is slow on the NMR time scale.

The syntheses of many of the necessary methoxy

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3) R. J. Kurland, M. B. Rubin, and W. B. Wise, *J. Chem. Phys.*, **40**, 2426 (1964).
4) I. O. Sutherland and M. V. J. Ramsay, *Tetrahedron*, **21**, 3401 (1965).
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6) A. Mannschreck, A. Mattens, and G. Rissmann, *J. Mol. Spectrosc.*, **23**, 15 (1967).
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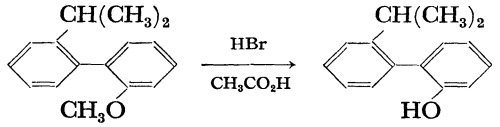
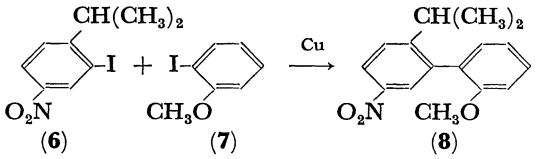
compounds have previously been reported.[9] In such cases, the methoxy compounds (**4**) were demethylated by refluxing in acetic acid with hydrogen bromide to give the corresponding hydroxybiphenyl derivatives (**5**):

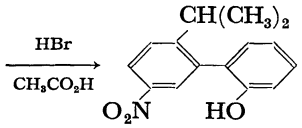


(**4**) (**5**)

Treating 2-isopropyl-5-nitroiodobenzene (**6**) and 2-methoxyiodobenzene (**7**) under the Ullmann conditions yielded 2-isopropyl-5-nitro-2′-methoxybiphenyl (**8**), which was then demethylated as above to give **9**:



(**6**) (**7**) (**8**)



(**9**)

Experimental

Measurements. The NMR spectra were measured on a spectrometer, either a Japan Electron Optics JNM C-60H and JNM C-60HL, a Hitachi R 20A, or a Varian Associates A-60 spectrometer. The solvents were dimethyl-d_6 sulfoxide or tetrachloroethane, and the concentration was *ca.* 0.3 mol/*l* or *ca.* 8% (w/w). Cyclooctane was used as the internal standard. The calibration of the coalescence temperature was determined by studying the chemical-shift difference between methylene and hydroxyl protons of ethylene glycol. This calibration was applied to the other range of temperature, and the error was estimated to be ±2°C.

In cases where the coupling constant is smaller than the chemical shift at the lower temperature, the quartets due to the magnetically non-equivalent methyls in isopropyl group coalesce when the temperature is raised, the chemical shift gradually decreases, and a broad single-peaked curve is obtained at the coalescence temperature (T_c). When the temperature is raised by 1°C from the T_c, two broad peaks are observable, indicating that the T_c is fairly dependable. On the other hand, in the cases where the coupling constant is larger than the chemical shift, the two peaks in the higher field and the two peaks in the lower field coalesce when the temperature is raised.

Various approximating methods have been presented to derive the kinetic data from the temperature-dependent NMR information. In this study, the following two equations were used to obtain the data:

$$\frac{1}{\tau} = \frac{\pi(\delta\nu_0)}{2(w-w_0)} \quad (1)$$

where τ is the average half-life time; $\delta\nu_0$, the difference in chemical shifts when the exchange is negligible; w, the half-band width at a given temperature, and w_0, the half-band width when the exchange is fast.

$$\frac{1}{\tau} = \frac{\pi(\delta\nu_0)}{\sqrt{2}} \quad (2)$$

Equation (2) is applicable at the coalescence temperature.

The effect of the population of the conformers with respect to the isopropyl group on the difference in chemical shift was calibrated by extrapolating the linear part of the $\delta\nu_0$ *vs.* temperature correlation at low temperatures.

The half-band width of cyclooctane, which was added as an internal standard, was used as w_0 by carefully adding a definite amount of cyclooctane to the solution.

The infrared spectra were obtained on a Perkin-Elmer 112 G single-beam grating spectrophotometer. Data obtained with *ca.* 1 mmol/*l* solution in carbon tetrachloride are given in Table 5. The spectra were also obtained with a tetrachloroethane solution, the concentration being *ca.* 0.3 mol/*l*, in order to obtain data which should be useful in discussing the NMR results.

Syntheses of the Materials. The Ullmann Reaction: When a mixture of 20 g (0.1 mol) of 2-methoxyiodobenzene, 15 g (0.05 mol) of 2-isopropyl-5-nitroiodobenzene, and 15 g of copper bronze was heated at 180°C, the reaction set in; the temperature was then raised to 260°C. After it had then been cooled, 20 more grams of copper bronze was added, and the mixture heated at *ca.* 200°C for 1 hr. The mixture was cooled and extracted with acetone in a Soxhlet apparatus. The extract was concentrated and chromatographed on alumina to give 1.5 g of 2-methoxy-2′-isopropyl-5′-nitrobiphenyl, mp 84—85°C. NMR (δ from TMS in CCl_4): 1.05 (3H, d J=7); 1.15 (3H, d J=7); 2.60 (1H, septet); 3.82 (3H, s); 6.9—8.4 (7H, m).

Found: C, 70.83; H, 6.32; N, 5.13%. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16%.

2-Methoxy-5-nitro-2′-isopropylbiphenyl, mp 107°C, was similarly prepared from 2-methoxy-5-nitroiodobenzene and 2-isopropyliodobenzene, the yield being 14%. NMR (δ from TMS in CCl_4): 1.05 (3H, d J=7); 1.10 (3H, d J=7); 2.83 (1H, septet); 3.72 (3H, s); 6.8—8.3 (7H, m).

Found: C, 70.87; H, 6.55; N, 4.99%. Calcd for $C_{16}H_{17}ON_3$: C, 70.83; H, 6.32; N, 5.16%.

Demethylation of the Methyl Ethers. To a solution of 1 g of the biphenyl derivative in 10—20 m*l* of acetic acid, 15—20 m*l* of 47% aqueous hydrogen bromide and *ca.* 5 m*l* of acetic anhydride were added, after which the mixture was heated for *ca.* 5 hr. The mixture was then poured onto ice water and extracted. The recrystallization of the acidic part gave the desired 2-hydroxy-2′-isopropylbiphenyl derivative. The data are given in Table 1.

Table 1. 2-Hydroxy-2′-isopropylbiphenyls

Substituent	mp (°C)	Anal.[a] (Found)		
		C	H	N
none	55—56	85.03	7.89	
4-NO_2	81—82	70.07	5.58	5.52
5-NO_2	94	70.07	5.82	5.77
4′-NO_2	128—129	70.07	6.17	5.70
5′-NO_2	90—91	70.36	5.72	5.58

a) Calculated values for 2-hydroxy-2′-isopropylbiphenyl are C 84.87 and H 7.60%. Calculated values for the nitro derivatives are C 70.02, H 5.88, and N 5.44%.

Results

Attempts at obtaining the energy and the entropy of activation from the Arrhenius plot of the data obtained by the method described in the Experimental section revealed that a considerable amount of error cannot be

Table 2. Coalescence temperature and various data at the T_c for 2-hydroxy-2′-isopropylbiphenyls[a)]

Substituent	Solvent	T_c (°C)	$\delta\nu_0$ (Hz)	k_c (sec^{-1})	$\Delta G^{\ddagger}{}_c$ (kcal/mol)
none	DMSO[b)]	58±2	6.9±0.3	15.4±0.5	17.8±0.2
	TCE[b)]	77	2.8	6.2	19.3
4-NO_2	DMSO	58	8.1	17.8	17.6
	TCE	76	3.7	8.2	19.1
5-NO_2	DMSO	49	8.3	18.5	17.0
	TCE	65	2.5	5.6	18.7
4′-NO_2	DMSO	60	6.4	14.0	17.8
	TCE	57	5.8	12.9	17.7
5′-NO_2	DMSO	42	7.7	17.1	16.7
	TCE	55	6.1	13.4	17.6

a) The subscript c denotes the value at coalescence temperature.
b) DMSO and TCE stand for dimethyl sulfoxide and tetrachloroethane, respectively.

avoided. This error may come from the facts that the signal of cyclooctane was chosen as the standard of the half-band width and that the chemical shifts of the methyl groups change according to the change in population with the temperature, in addition to the methods of approximation used in this study. However, it is possible to minimize the error if we limit the data of the half-band width to a fairly large value and limit the temperature to a small range. Thus, we decided to use a single temperature, the highest coalescence temperature among those of the compounds studied. Table 2 shows the coalescence temperatures and the pertinent data of the phenols; in Table 4 only the rates of the internal rotation of the methyl ethers in tetrachloroethane are given, because those in dimethyl sulfoxide are quite similar. The solvent effects on the rates of internal rotation and the free energies of activation for the hydroxy compounds are given in Table 3. The errors other than the systematic are estimated to be ±0.2 kcal/mol.

Table 3. Rates and energies of activation for internal rotation about the pivot bond of 2-hydroxy-2′-isopropylbiphenyls at 77°C

Substituent	in Dimethyl sulfoxide		in Tetrachloroethane	
	k(sec^{-1})	$\Delta G^{\ddagger}$(kcal/mol)	k(sec^{-1})	$\Delta G^{\ddagger}$(kcal/mol)
none	35	18.1	6	19.3
4-NO_2	45	17.9	8	19.1
5-NO_2	95	17.4	9	19.0
4′-NO_2	35	18.1	33	18.1
5′-NO_2	90	17.4	33	18.1

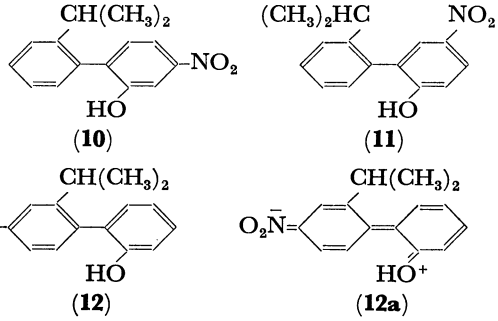
Table 4. Kinetic data of 2-methoxy-2′-isopropylbiphenyls in tetrachloroethane

Substituent	T_c (°C)	$\delta\nu_0$ (Hz)	k_c (sec^{-1})	$\Delta G^{\ddagger}{}_c$ (kcal/mol)	k_{86} (sec^{-1})	$\Delta G^{\ddagger}{}_{86}$ (kcal/mol)
none	86	7.2	16.0	19.2	16	19.2
4-NO_2	86	7.1	15.8	19.2	16	19.2
5-NO_2	70	6.3	14.0	18.4	32	18.7
4′-NO_2	79	7.2	16.0	18.8	23	18.9
5′-NO_2	69	7.7	17.1	18.3	50	18.4

Discussion

Since we have obtained only the free energy of activation, it will be safer to compare some corresponding compounds rather than to discuss the absolute values. A comparison of the data obtained with the hydroxy compounds with those of the methoxy derivatives will be made. Since it was pointed out in a previous paper[9)] that two factors—electron density and through conjugation—must be considered in discussing the internal rotation of biphenyls about the pivot bond, it is not safe to compare the data of compounds which have different substituents or which have the same substituents at different positions.

The data in Tables 2 and 3 suggest that the energies of activation for rotation of the hydroxylic compounds are not much different in dimethyl sulfoxide. Indeed, the differences are within the range of error. If the intermolecular hydrogen bonding between the phenols and dimethyl sulfoxide played an important role in lowering the energy of activation, compound **12** should show a smaller value of the energy of activation than the other compounds because the resonance structure (**12a**) is favored on forming the hydrogen bond. The experimental data, however, show an increasing tendency, although small. Therefore, the lowering of the electronegativity of the oxygen in the hydroxyl group due to the formation of the hydrogen bond is negligibly small.



From the results shown in Tables 2—4, together with the fact that the $\Delta G^{\ddagger}$'s for rotation about the pivot bond of 2-methoxybiphenyl derivatives in dimethyl sulfoxide are not very different from those in chlorinated hydrocarbons (see reference 8 and the Results of this paper), it is clear that there are some compounds which give similar $\Delta G^{\ddagger}$ values irrespective of the nature of the substituent (hydroxy or methoxy), whereas some compounds show a fairly large difference in $\Delta G^{\ddagger}$'s and k's. The methoxy compounds belong to the first category, and, among the hydroxy compounds, those which possess a nitro group in the ring not having a hydroxyl group are classified in the first category, and the others in the second. These phenomena may best be understood when the effect of the O–H···π interaction is considered.

Since those compounds which have a nitro group at the ring having a hydroxyl group may be expected to be more acidic, the intramolecular interaction is fairly strong. On the other hand, the nitro group attached to the benzene ring which is to be the proton acceptor will decrease the basicity of the π-electron system. Thus, the O–H···π interaction will be stronger and the

ground state will be more stabilized with compounds **10** and **11** than with compounds **9** and **12**. The difference in the energy of activation between these two groups is *ca.* 1 kcal/mol; this is in good agreement with the data obtained by the infrared method with 4-nitro-2-hydroxybiphenyl and 2-hydroxy-4'-nitrobiphenyl.[10]

It is an interesting phenomenon that compound **5** shows a tendency similar to that of compounds **10** and **11**. We have no good explanation for this, but wish tentatively to attribute it to the steric effect of the isopropyl group. That is, because of the steric requirement of the isopropyl group, the biphenyl derivatives studied here will have two benzene rings almost perpendicular to each other, the conformation favoring the intramolecular O–H···π interaction. Thus it may be considered that, unless the π-system is unfavorable for accepting the proton, almost all the molecules will be of the intramolecularly interacting species, leveling the effect of the O–H···π interaction to the same order of magnitude as compounds **5**, **10**, and **11**.

Table 5. Infrared spectral data of 2-hydroxy-2'-isopropylbiphenyls

Substituent		ν_{OH}(cm^{-1})	A(mol$^{-1}\cdot l\cdot$cm^{-2})
none	i[a]	3553.7	1.0×10^4
	f[a]	—	—
4-NO_2	i	3541.8	1.35
	f	—	—
5-NO_2	i	3530.0	1.4
	f	—	—
4'-NO_2	i	3570.0	0.2
	f	3602.8	1.3
5'-NO_2	i	3571.1	0.3
	f	3602.8	1.3

a) i and f denote O–H···π interacting and free species, respectively.

Support for this postulate may be obtained from the data given in Table 5. As may be seen, even the compound **5** does not show any O–H stretching absorption due to the free hydroxyl group. This indicates that introducing the isopropyl group at the 2'-position favors the intramolecular O–H···π interaction compared with 2-hydroxybiphenyl, which has shown absorption due to the free hydroxyl group.[11] Indeed, even 4-nitro-2-hydroxybiphenyl showed some free hydroxyl groups, the presence of which made the calculation of the interaction energy possible.[10] The shift (*ca.* 10 cm^{-1}) of the absorption band to a lower frequency than in the corresponding compounds lacking the isopropyl group also suggests that the O–H···π interaction is favored in the isopropyl compounds.

It may be argued that, at the concentration suitable for the NMR study, the inter- rather than the intramolecular hydrogen bond is important. Therefore, in order to justify the above discussion, infrared spectral study at that concentration is needed. The infrared absorptions in the 3μ region of compounds **5**, **9**, **11**, and **12** were thus measured at a 0.3 mol/l concentration in tetrachloroethane. Although there remains some ambiguity because of the solvent absorption, the results indicate that these compounds have no absorption below 3500 cm^{-1}; this suggests that they exist as, at least mainly, monomers. The compounds **5** and **11** have only one absorption, at *ca.* 3530 and *ca.* 3540 cm^{-1} respectively, which may be attributed to the intramolecularly interacting (O–H···π) molecular species.[12]

On the other hand, compounds **9** and **12** have two absorptions at the same wave numbers (3580 and 3560 cm^{-1}), the intensity being larger with the latter band. The band at the higher frequency may be attributed to the free form because it is at too high a frequency to be assigned to the dimer.[13] The band at the lower frequency may be assigned to the O–H···π interacting species, because the 20 cm^{-1} shift to a lower frequency is quite normal for the interaction. Thus the infrared spectral data support the above conclusion drawn from the NMR results.

There are many points to be clarified with regard to the substituent effect on the energy of activation for the internal rotation about the pivot bond of biphenyls. For example, it is not at all clear why the nitro group at the 5- or 5'-position lowers the energy of activation. We have intentionally omitted some discussions familiar to stereochemists, such as those of the buttressing effect and the difference in the sizes of hydroxyl and methoxyl groups, since the data presented here can not be discussed in detail. However, we believe that, as a first approximation, the intramolecular O–H···π interaction is an important factor in governing the energy of activation for the internal rotation of 2-hydroxybiohenyl derivatives.

10) M. Ōki, H. Iwamura, and Y. Urushibara, *ibid.*, **31**, 770 (1958).

11) M. Ōki and H. Iwamura, *ibid.*, **34**, 1395 (1961).

12) The O–H stretching absorption of the O–H···π interacting species at a 3×10^{-3} mol/l concentration in carbon tetrachloride is located close to 3550 cm^{-1}. See Table 5.

13) The absorption due to the dimer of hydroxy compounds is considered to be at *ca.* 3490 cm^{-1}.