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Restricted Rotation Involving the Tetrahedral Carbon. XXXIV. Stable Rotamers of 9-Arylfluorenes Carrying Oxygen-substituents in the Ortho Position of the Aryl Group[1,2]

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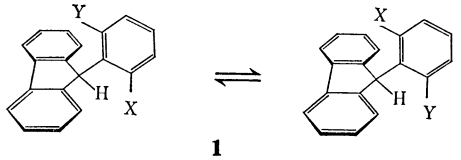
9-(2-Hydroxy-1-naphthyl)fluorene, 9-(2-hydroxy-4,6-dimethylphenyl)fluorene, and their methyl ethers have been prepared. They give stable rotamers, *sp* and *ap*, at room temperature. *ap* forms of the hydroxylic compounds are favored over the *sp* and contrary is true for the methyl ethers. These results are attributed to the stabilization of the *ap* form of the hydroxylic compounds due to intramolecular OH···π interaction. Barriers to rotation are *ca.* 105 kJ mol^{-1}.

9-Arylfluorenes (**1**) are unique systems which exhibit high barriers to rotation about the C_9–C_{ar} bond.[3] In some special cases they give stable rotational isomers, *sp* and *ap*, at room temperature.[4] As for the equilibrium between rotamers, the bulkiness of substituents X and Y are known to be primarily important.[5] That is, the predominant conformation is the one in which a bulkier substituent proximates the hydrogen in 9 position. Since the substituent X or Y in each



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rotamer is quite close to the fluorene ring, electronic interaction may occur, if a substituent has a proper character, to affect the equilibria and barriers to rotation. In fact, we have found that the charge-transfer interaction has taken place between the fluorene ring and the aroyl moiety in aroates of 9-(2-hydroxy-1-naphthyl)fluorene.[6] Thus, 9-arylfluorene is a good model for investigation of the interaction between two groups. We wish to report in this paper the syntheses of the compounds **4**—**7**, which carry oxygen-substituents in an ortho position of the aryl group and thermodynamic and kinetic parameters involving the rotational isomers. The effects of the oxygen-substituents on the thermodynamic and kinetic values will be discussed in terms of molecular interactions.

Experimental

Spectral Measurement. ^{1}H NMR spectra were determined either on a Hitachi R-20B spectrometer operating at 60 MHz or on a Varian EM 390 operating at 90 MHz. The chemical shifts of the characteristic signals of 9-arylfluorenes are given in Table 1. IR spectra were obtained on a Hitachi EPI G-3 spectrometer.

Syntheses. The syntheses of methyl ethers (**4** and **6**) were carried out by the Grignard reaction between 9-fluorenone and an appropriate arylmagnesium bromide followed by reduction with hydriodic acid at room temperarure. The hydroxylic compounds (**5** and **7**) were prepared either by demethylation of the methyl ether or by a series of similar reactions used for the syntheses of the methyl ethers.

9-(2-Methoxy-4,6-dimethylphenyl)-9-fluorenol (2). To a vigorously stirred tetrahydrofuran solution of 2-methoxy-4,6-dimethylphenylmagnesium bromide, prepared from 1.02 g (0.047 mol) of 1-bromo-2-methoxy-4,6-dimethylbenzene[7] and 1.20 g (0.049 mol) of magnesium, was added 5.41 g

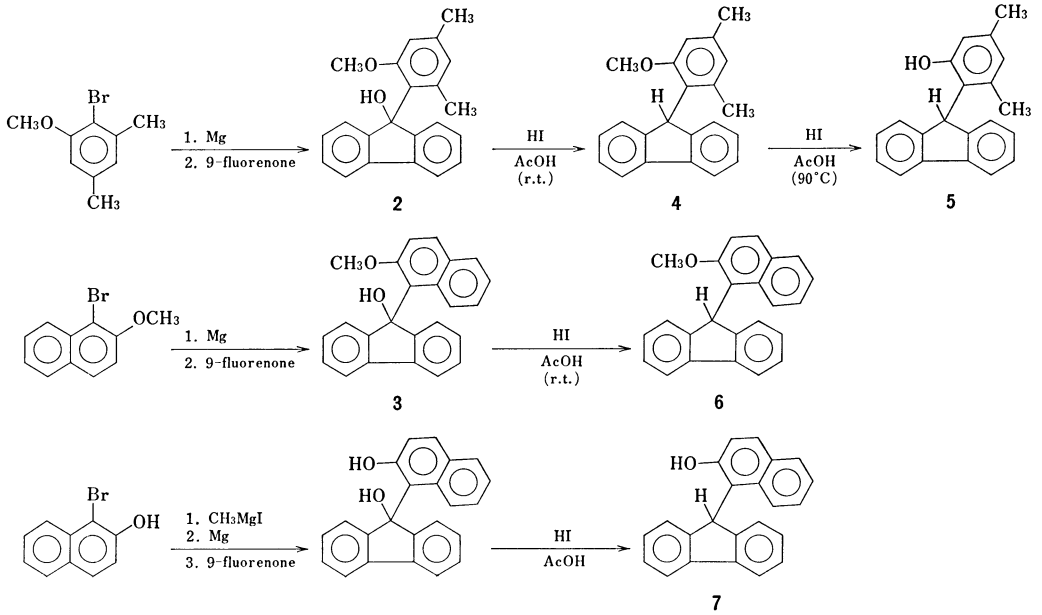


Table 1. ^{1}H NMR data of 9-arylfluorenes ($CDCl_3$, δ)

Compound	Form	2′-OCH_3	2′-OH	4′-CH_3	6′-CH_3	3′-H	5′-H	8′-H	9-H
4	*sp*	3.92	—	2.30	1.10	6.75	6.44	—	6.03
	ap	2.90	—	2.28	2.65	6.40	6.60	—	5.23
5	*sp*	—	5.0	2.20	1.10	6.51	6.36	—	5.89
	ap	—	3.6	2.22	2.62	6.35	6.72	—	5.38
6	*sp*	4.10	—	—	—	—	—	6.36	6.30
	ap	3.02	—	—	—	—	—	8.47	5.88
7	*sp*	—	5.8	—	—	—	—	6.38	6.18
	ap	—	4.1	—	—	—	—	8.40	6.02

(0.03 mol) of 9-fluorenone at 0 °C. The reaction mixture was stirred for 3 h at room temperature and was then heated with stirring for 1 h. The mixture was cooled and treated with aqueous ammonium chloride. The organic layer was dried over sodium sulfate. After evaporation of the solvent, the product was purified by chromatography on silica gel. Elution with benzene gave a pure product, mp 93.0—94.5 °C, in 78% yield based on 9-fluorenone. Found: C, 83.22; H, 6.37%. Calcd for $C_{22}H_{20}O_2$: C, 83.51; H, 6.37%. ^{1}H NMR ($CDCl_3$, δ): 1.27 (*sp*-6′-CH_3), 2.92 (*ap*-6′-CH_3), 2.27 (*sp*- and *ap*-4′-CH_3), 2.85 (*ap*-OCH_3), 4.05 (*sp*-OCH_3), 6.49 (*sp*-5′-H), 6.80 (*sp*-3′-H). The population ratio (*ap*/*sp*) was 1/9.7 in $CDCl_3$ at 34 °C.

9-(2-Methoxy-4,6-dimethylphenyl)fluorene (4). To a solution of 1.2 g (3.8 mmol) of **2** in 50 mL of acetic acid was added 10 mL of 57% hydriodic acid. The solution was stirred for 5 h at room temperature, poured into water, and then extracted with ether. The ether layer was washed with aqueous sodium hydrogencarbonate and then with aqueous sodium hydrogensulfite, and dried over sodium sulfate. After evaporation of the solvent, the products were separated by chromatography on alumina. Elution with hexane gave a pure *sp* form, mp 128—129 °C, in 55% yield. Found: C, 88.04; H, 6.59%. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71%. The chloroform solution of the *sp* form was heated for 5 h to make an equilibrium mixture and the *ap* form thus formed was separated by preparative thin layer chromatography on silica gel. The R_f value of the *ap* form was smaller than that of the *sp* form. The mp of the *ap* form was 131—133 °C. The identity of the *ap* form was established by the spectral data and the equilibration experiment: heating the *ap* afforded the same mixture of *sp* and *ap* forms which was obtained by heating the *sp* form.

9-(2-Hydroxy-4,6-dimethylphenyl)fluorene (5). To a solution of 1.10 g (43.7 mmol) of **4** in 50 mL of acetic acid was added 10 mL of 57% hydriodic acid. The solution was stirred for 5 h at 90 °C and then treated similarly as in the synthesis of **4**. The products were chromatographed on silica gel and eluted with benzene-hexane. The *ap* isomer was obtained as easily eluted fractions. Recrystallization from benzene-hexane gave pure *sp*, mp 144—145 °C, and *ap*, mp 102—104 °C. Found: (*sp*): C. 87.79; H, 6.20%. Calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34%. The identity of the *ap* form was established as described above.

9-(2-Methoxy-1-naphthyl)-9-fluorenol (3), mp 130—131 °C, was prepared by treating 2-methoxy-1-naphthylmagnesium bromide with 9-fluorenone in tetrahydrofuran. The yield was 85% based on the fluorenone. Found: C, 85.37; H, 5.34%. Calcd for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36%. ^{1}H NMR ($CDCl_3$, δ): 2.4 (*ap*-OH), 3.00 (*ap*-OCH_3), 4.19 (*sp*-OCH_3), 9.72 (*ap*-8′-H). The population ratio (*ap*/*sp*) was 1/3.4 in $CDCl_3$ at 34 °C.

9-(2-Methoxy-1-naphthyl)fluorene (6). To a solution of 2.1 g (6.2 mmol) of **3** in 70 mL of acetic acid was added 15 mL of 57% hydriodic acid. The solution was stirred for 5 h at room temperature and then treated similarly as in the case of **4**. The products were separated by chromatography on silica gel. Elution with hexane gave a pure *sp* form, mp 121—122 °C, in 72% yield. Found: C, 89.26; H, 5.55%. Calcd for $C_{24}H_{18}O$: C, 89.41; H, 5.63%. The chloroform solution of the *sp* form was refluxed for 5 h to make an equilibrium mixture and the *ap* form thus formed was separted by thin layer chromatography on silica gel. The *ap* form was eluted after the *sp* form and was then recrystallized from benzene-hexane, mp 125—126 °C. Found: C, 89.42; H, 5.70%. Calcd for $C_{24}H_{18}O$: C, 89.41; H, 5.63%.

9-(2-Hydroxy-1-naphthyl)fluorene (7). To a vigorously stirred tetrahydrofuran solution of 4.5 g (20 mmol) of 1-bromo-2-naphthol was added an ether solution of methylmagnesium iodide, prepared from 3.6 g (25 mmol) of methyl iodide and 0.65 g (27 mmol) of magnesium in ether. The reaction mixture was stirred for 10 min. The resulting suspension of the magnesium salt of 1-bromo-2-naphthol was put into a dropping funnel and was added dropwise to 0.48 g (20 mmol) of magnesium in tetrahydrofuran at the refluxing temperature. After the addition was completed, the reaction mixture was heated with refluxing for 2 h, cooled to room temperature, and then 2.16 g (12 mmol) of 9-fluorenone was added in small portions. The solution was refluxed for 1 h, cooled, and treated with aqueous ammonium chloride. The organic layer was dried over sodium sulfate and the solvent was evaporated completely *in vacuo*. The resulting oil was dissolved in 100 mL of acetic acid and 20 mL of 57% hydriodic acid was added. The mixture was stirred for 5 h at room temperature and then treated similarly as in the case of **4**. The products were separated by chromatography on silica gel. Elution with benzene gave 0.3 g (8%) of *ap*, mp 176—177 °C, and then 1.5 g (41%) of *sp*, mp 88—89 °C. Found (*ap*): C, 89.82; H, 5.06%. Calcd for $C_{23}H_{16}O$: C, 89.58; H, 5.23%. The identity of the *sp* form was established by equilibration.

Kinetics. A $CDCl_3$ solution of the *sp* form of **4** was put in an NMR sample tube and was heated at a given temperature. New signals attributable to the *ap* form gradually increased in their intensities. Since the features are the large chemical shift differences between two methoxyl signals ($\Delta\delta$=*ca.* 1.0 ppm), the increase and decrease in intensities of these signals were monitored. The rates of isomerization were obtained at 4 different temperatures by assuming the unimolecular reversible process. Putting these rate constants into Eyring's equation, we could obtain the activation parameters for rotation. The rates for rotation were similarly obtained with **5** and **6** by monitoring the change in intensities of 6′-methyl and 2′-methoxyl signals, respectively. In the case of **7**, the change in intensities of hydroxyl signals were monitored since the proton exchange between these hydroxyl groups was found to be frozen on

Table 2. Kinetic Parameters for the Internal Rotation and Equilibrium Constants at 56.3 °C for 9-Arylfluorenes

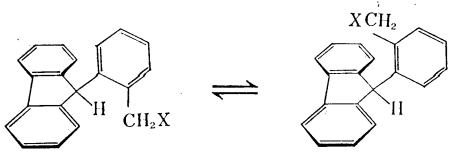
Compound	Process	ΔH^*/kJ mol^{-1}	ΔS^*/J K^{-1} mol^{-1}	ΔG^*_{329}/kJ mol^{-1}	K
4	*sp*→*ap*	102.0±0.4	−7.9±0.4	104.6±0.4	1/3.30
	ap→*sp*	96.1±0.4	−14.5±0.4	100.9±0.4	
5	*sp*→*ap*	93.6±0.4	−29.7±1.3	103.4±0.4	1.80
	ap→*sp*	96.1±0.4	−27.2±0.8	105.0±0.4	
6	*sp*→*ap*	101.2±0.8	−21.7±2.9	108.3±0.4	1/3.56
	ap→*sp*	94.9±0.8	−30.5±2.5	110.0±0.4	
7	*sp*→*ap*	92.8±0.8	−45.1±1.7	107.7±0.4	2.30
	ap→*sp*	96.1±1.2	−42.2±3.8	110.0±0.4	

the NMR time scale.

Results and Discussion

Assignment of Stereochemistry. For the two rotamers isolated, stereochemistry was assigned with the use of ^{1}H NMR spectroscopic features as were used previously.[4] The features are a high field signal due to the 2′-substituent (OH or OCH_3) and a low field signal due to the 6′-CH_3 of **4** and **5** or the 8′-H of **6** and **7** for the *ap* form. The contrary is true for the *sp* isomers: a high field signal due to 6′-CH_3 of **4** and **5** or the 8′-H of **6** and **7** and a low field signal due to OH or OCH_3. The protons of the hydroxyl or methoxyl group is a little far from the fluorene ring but the chemical shift differences were large enough for the assignment of the structures. The chemical shifts of the characteristic protons are given in Table 1.

Conformational Equilibria. Equilibrium constants are given in Table 2 together with kinetic parameters for rotation about the C_9–C_{ar} bond. The interesting features of the data are that, in both naphthyl and phenyl series, the *ap* forms of the phenolic compounds (**5** and **7**) are favored over the corresponding *sp* forms by *ca.* 2 kJ mol^{-1} at 56.3 °C. The *ap* forms of the methyl ethers (**4** and **6**), on the contrary, are less stable than the *sp* forms by *ca.* 3 kJ mol^{-1} at the same temperature. This is rather unusual, since a hydroxyl group is considered to be almost equal to a methoxyl group in the effective size.[8] The facts that the equilibrium constants (*ap*/*sp*) of 9-(2-methylphenyl)- (**8a**) and 9-(2-ethylphenyl)fluorene (**8b**) are 1/1.6 and 1/3.3, respectively, supplement the anomaly of the results observed with **4**—**7**.[5] The reason for this anomaly



8 a) X=H b) X=CH_3

is probably the stabilization due to intramolecular OH···π interaction, involving the hydroxyl group and the fluorene ring. Thus the infrared spectra were measured and the results are given in Table 3. Clearly, the OH···phenyl interaction[9] is indicated for the *ap* forms, whereas the *sp* form is present as a free phenol in dilute solutions in carbon tetrachloride. We then measured the IR spectra by imitating the conditions of the NMR measurement: chloroform as a solvent and concentrations of *ca.* 0.3 mol L^{-1}. Although the bands are shifted a little due to the solvent effects, the *ap* forms give the monomer OH···π bonded absorption only. As for the absorption of the *sp* forms, compound **5** gives only the free OH band. Compound **7**, in contrast, shows a shoulder, probably due to the dimer.[10] Although the reason for the absence of the dimer band in *sp*-**5** is unknown at present, the absence of the dimer in the *ap* forms can be ascribed to the steric effect, since sterically crowded phenols are known to exhibit monomer bands only even at a high concentration.[11] The IR study described above clearly shows that the OH···π interaction is the main origin for the stabilization of the *ap* forms of the phenolic compounds.

Table 3. ν_{OH} Absorption Spectral Data

Compound	Solvent	Concentration / mmol L^{-1}	ν_{OH} / cm^{-1}
sp-**5**	CCl_4	9.4	3611
	$CHCl_3$	260	3602
ap-**5**	CCl_4	5.7	3546
	$CHCl_3$	250	3535
sp-**7**	CCl_4	9.6	3610
	$CHCl_3$	250	3600, 3558(sh)
ap-**7**	CCl_4	10	3533
	$CHCl_3$	320	3521

Barriers to Rotation. The OH···π stabilization is also reflected to the barriers to rotation as shown in Table 2: the free energies of activation for rotation of the phenolic compounds are larger by *ca.* 4 kJ mol^{-1} than those of the methyl ethers in the *ap*→*sp* processes. If we assume that the energy level of the *sp* form of the phenolic compound is equal to that of the corresponding methyl ether, then the free energy profile may be written as shown in Fig. 1 for compounds **4** and **5**. The figure indicates that the energy level of the transition state of **4** is higher than that of **5** by 1.2 kJ mol^{-1}, which may be ascribed to the difference in steric effects between methoxyl and hydroxyl groups on the transition states for rotation. We read also from the figure that the difference in free energies of *ap* forms of **4** and **5** is 5.3 kJ mol^{-1}. Since this value contains the difference in energies ascribable to the steric effects of methoxyl and hydroxyl groups in the *ap* form, the net stabilization may be *ca.* 4 kJ mol^{-1}, which conforms with the OH···π interaction energy.[12,13] The same calculation was

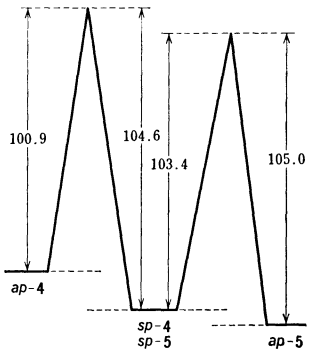


Fig. 1. Free energy profiles of **4** and **5** at 56.3 °C (kJ mol^{-1}).

applied to compounds **6** and **7** and *ca.* 3 kJ mol^{-1} was derived as the net stabilization energy of the *ap* form due to the OH···π interaction.

Comparison of the barriers to rotation of the oxygen-compounds studied here with those of the corresponding methyl or substituted methyl compound reveals that the formers exhibit lower barriers: Arrhenius activation energies for rotation of 9-(2-methyl-1-naphthyl)fluorene[14] and 9-(2-bromomethyl-6-methylphenyl)fluorene[4] are known to be 125 kJ mol^{-1} and 113 kJ mol^{-1}, respectively, for the *sp*→*ap* processes. The lowering of the barriers to rotation of compounds **4**—**7** may be attributed to lessening of the van der Waals radii of the substituents in 2′ position by going from a methyl to an oxygen, which directly affects the transition state for rotation. The difference in the barriers between the naphthyl and 2-methylphenyl analogs is smaller in the oxygen-compounds than the hydrocarbons (approximated by the bromomethyl compound). The reason for this phenomenon must further be studied.

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