Rotational Isomerism in Fluorene Derivatives. XVI.[1] Conformational Equilibria of 9-Substituted 9-(2′-Bromomethylphenyl)fluorene Derivatives

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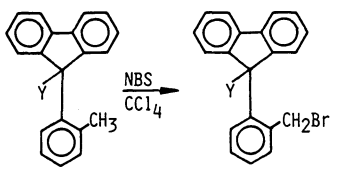
Synopsis. (Eight 9-substituted 9-(2′-bromomethylphenyl)fluorene derivatives) (**1**) were prepared. Their conformational equilibria (*ap* ⇄ *sp*) are discussed on the basis of kinetic data for internal rotation obtained by ^{1}H NMR spectroscopy.

We have recently investigated the conformational equilibria (*ap* ⇄ *sp*) of 9-(2′-substituted phenyl)fluorene derivatives having the 2′-substituents such as methyl-,[2] methoxy-,[3] methylthio-,[4] methylsulfinyl-,[4] dimethylamino-,[5] methoxymethyl-,[6] and methylamino group,[7] on the basis of their DNMR spectra. In the present paper, we wish to report on the preparation of 9-substituted 9-(2′-bromomethylphenyl)fluorene derivatives (**1**) and a study concerning the conformational equilibria of these compounds by comparing their ^{1}H NMR behavior with those of 9-substituted 9-(2′-methylphenyl)fluorene derivatives (**2**).

Results and Discussion

Preparation of 1. Fluorenes **1**, except 9-(2′-bromomethylphenyl)fluorene (**1b**), were prepared by the bromination of the corresponding 9-substituted 9-(2′-methylphenyl)fluorenes **2** with NBS in carbon tetrachloride in the presence of a small amount of BPO. Thus, 9-hydroxy- (**1a**), 9-methoxy- (**1c**), 9-methyl- (**1d**), 9-carboxy- (**1e**), 9-methoxycarbonyl- (**1f**), 9-acetyl- (**1g**), and 9-benzoyl-9-(2′-bromomethyl)fluorene (**1h**) were obtained from 9-hydroxy- (**2a**),[7] 9-methoxy- (**2c**),[8] 9-methyl- (**2d**),[2] 9-carboxy- (**2e**),[2] 9-methoxycarbonyl- (**2f**),[2] 9-acetyl- (**2g**),[2] and 9-benzoyl-9-(2′-methylphenyl)fluorene (**2h**),[2] respectively (Scheme 1). Compound **1b** was obtained by the bromination of 9-(2′-hydroxymethylphenyl)fluorene (**4**), which was prepared by the hydrolysis of 9-(2′-iodomethylphenyl)fluorene (**3**),[6] with dry hydrogen bromide. The results of the preparation of **1** and their partial ^{1}H NMR data are shown in Table 1.



2 1

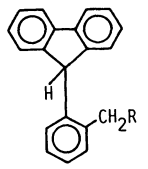
Y		Y	
a	OH	f	$COOCH_3$
c	OCH_3	g	$COCH_3$
d	CH_3	h	COPh
e	COOH		

Scheme 1.

Table 1. ^{1}H NMR Data of 9-Substituted 9-(2′-Bromomethylphenyl) fluorene Derivatives (**1**) at Room Temperature (δ, $CDCl_3$)

Compd	2′-CH_2Br	9-Substituent	6′-H
1a	4.02br.s	2.38br.s	
1b	4.96s(5.5)	5.55s(5.5)	6.42d
	3.44s(1)	5.02(1)	
1c	4.12br.s	2.76s	
1d	3.48s	1.78s	
1e	3.94br.s	—	
1f	4.06br.s	3.84s	
1g	4.16s	1.95s	
1h	4.40s	—	

a) Numerals in parentheses are ratios of signal intensities.



1b: R = Br 3: R = I
2b: R = H 4: R = OH

Conformational Equilibria of 1. Signals due to the two rotamers, *ap* and *sp*, of 9-(2′-substituted phenyl)fluorene derivatives were observed in their NMR spectra at room temperature or at low temperature owing to their high barriers for rotation about the C(9)-C(Ar) bond. For example, two singlets due to the bromomethyl group of *ap* and *sp* forms of **1b** were observed at δ 3.44 and 4.96 ($K(ap/sp)$=1/5.5) at room temperature. The geometries of the two rotamers, *ap* and *sp*, of **1b** are shown in Fig. 1.

Since the signal of bromomethyl group of compound **1d** appeared at 3.48 ppm, which was very close to that of the *ap*-form of **1b**, as a sharp singlet even at

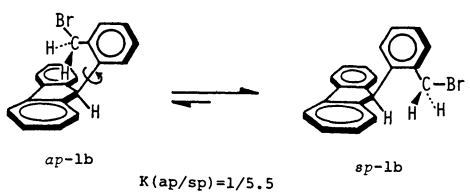


Fig. 1. The two rotamers of **1b**.

low temperature (−50 °C), this compound may exist only as the *ap*-form.

It was, however, difficult to assign the predominant conformers of the other bromomethyl series **1a**, **1c**, **1e**, **1f**, **1g**, and **1h**, by means of their ^{1}H NMR spectra at room temperature. Their DNMR spectra at low temperature (ca. −50 °C) were, therefore, measured by the usual method. The signals of the bromomethyl group in **1a**, **1c**, and **1f** were found to split at low temperature. Although the signal of **1h** broadened (T_c=−45 °C), two isomers of **1h** could not be observed until as low as −50 °C. The DNMR spectra of **1e** and **1g** could not be obtained because of their poor solubilities in $CDCl_3$ at low temperature. The equilibrium constants $K(ap/sp)$ between *ap* and *sp* forms of these compounds at room temperature or at low temperature, together with that of compound **2**,[9] are shown in Table 2. Since each *ap*- and *sp*- bromomethyl signal of **1g** and **1h** could not be observed at low temperature (−50 °C), it was assumed that these chemical shifts were the same values as those of **1b**. Then, K values of **1g** (or **1h**) were estimated from the chemical shifts of the bromomethyl group of *ap*-, and *sp*-**1b** and **1g** (or **1h**).

As shown in Table 2, though the equilibrium of **2a** was onesided in the *ap*-form, two conformers of **1a** existed in equilibrium, $K(ap/sp)$=3.9/1. In order to explain the stabillization of the *sp*-form of **1a**, we assumed the existence of intramolecular hydrogen bonding between the oxygen atom of the 9-hydroxyl group and the hydrogen atom of the 2′-bromomethyl group or the hydrogen atom of the 9-hydroxyl group and the bromine atom of the 2′-bromomethyl group in the *sp*-form (the latter hydrogen bonding has been reported in 2-haloethanol[10]). An intramolecular hydrogen bonding which controlled the equilibrium of **1a** would be influenced by a solvent effect. No expected solvent effects, which were found in the cases of 9-(2′-methoxyphenyl)-9-fluorenol[3] and 9-(2′-dimethylaminophenyl)-9-fluorenol,[5] however, were observed in the ^{1}H NMR spectra of **1a** in several solvents (DMSO-d_6, acetone-d_6, and methanol-d_4). If intermolecular hydrogen bonding between the hydrogen atom of the 9-hydroxyl group and these solvents exists, the equilibrium of **1a** would incline completely to the *ap*-form.

Table 2. Equilibrium Constant and Activation Parameter for Rotation of **1** and **2**[a]

	1			**2**[a]		
	$K(ap/sp)$ (Temp/ °C)	ΔG^*/kcal mol^{-1}		$K(ap/sp)$ (Temp/ °C)	ΔG^*/kcal mol^{-1}	
		ap→*sp*	*sp*→*ap*		*ap*→*sp*	*sp*→*ap*
a	3.9/1(−37)	13.7	12.9	*ap* only		
b	1/5.5(25)	15.5	16.5	1/1.6(25)	16.3	16.6
c	2.6/1(−50)	13.5	12.9	*ap* only		
d	*ap* only			*ap* only		
e	—[b]			—[b]		
f	1.35/1(−50)	12.9	12.7	1/1.1(−50)	12.4	12.7
g	(1/1)[b,c]			1/2.1(−50)	12.2	12.7
h	(1/2)[c,d]			1/3.5(−65)	11.7	12.4

a) Results taken from Refs. 2 and 12. b) Insoluble in $CDCl_3$ at low temperature. c) K value is estimated from the chemical shifts of the bromomethyl group of *ap*- and *sp*-**1b** and this compound. d) Coalesed at −45 °C.

Compounds **1b** and **1c** also showed a tendency to increase the *sp*-form, compared with 9-(2′-methylphenyl)fluorene (**2b**) and **2c**. Regarding compounds **1a—c**, it can be considered that a repulsive interaction between the π-electron of the fluorene ring and an unshared electron of the bromine atom of 2′-bromomethyl group or a steric repulsion between the fluorene ring and the bromomethyl group may destabilize the *ap*-form. Thus, the *ap*-forms of **1a—c** would be more unstable than those of **2a—c**.

We have already presumed that the stabilization of the *sp*-forms in **2f—h**, which are disadvantageous with respect to the steric effect, may be due to the existence of an attractive interaction between the oxygen atom of the 9-carbonyl group and the 2′-methyl group.[2] However, the *ap*-forms in **1f—h** were found to increase, compared with those of **2f—h**. It can be concluded that the equilibria of **1f—h** are controlled by a balance of the electronic repulsion and/or the steric hindrance between the 2′-bromomethyl group and the 9-carbonyl group or the fluorene ring.

Experimental

All melting points are uncorrected. The ^{1}H NMR spectra were recorded on a JEOL-MH-100 spectrometer with a JEOL model JES-VT-3 variable temperature controller (Solvent, $CDCl_3$; $SiMe_4$). Dynamic NMR spectra were analyzed by using a modified version of the computer program DNMR 3.[11] The IR spectra were measured with a IRA-1 spectrometer as potassium bromide pellets.

Bromination of 2a with NBS. Typical Procedure. To a solution of **2a** (1.0 g, 4 mmol) in CCl_4 (20 ml) was added NBS (0.7 g, 4 mmol) and a small amount of BPO, and the mixture was refluxed for 30 min. After cooling the reaction mixture the obtained succinimide was filtered off; the filtrate was then concentrated. The crude product was washed with water, dried, and recrystallized from petroleum benzine to give 9-(2′-bromomethylphenyl)-9-fluorenol (**1a**) as colorless prisms; yield 1.1 g (85%); mp 146—147 °C; IR (KBr) 3515 cm^{-1} (OH); Found: C, 68.73; H, 4.06%. Calcd for $C_{20}H_{18}OBr$: C, 68.39; H, 4.30%.

9-(2′-Bromomethylphenyl)-9-methoxyfluorene (1c). Yield 49%; colorless prisms; mp 101—103 °C; Found: C, 68.76; H, 4.75%. Calcd for $C_{21}H_{17}OBr$: C, 69.04; H, 4.69%.

9-(2′-Bromomethylphenyl)-9-methylfluorene (1d). Yield 75%; colorless prisms; mp 150—152 °C; Found: C, 72.30; H, 4.85%. Calcd for $C_{21}H_{17}Br$: C, 72.22; H, 4.91%.

9-(2′-Bromomethylphenyl)-9-fluorenecarboxylic Acid (1e). Yield 55%; colorless crystals; mp 163—164 °C; IR (KBr) 1685 cm^{-1} (C=O); Found: C, 66.25; H, 4.02%. Calcd for $C_{21}H_{15}O_2Br$: C, 66.51; H, 3.99%.

9-(2′-Bromomethylphenyl)-9-methoxycarbonylfluorene (1f). Yield 62%; colorless prisms; mp 99—101 °C; IR (KBr) 1730 cm^{-1} (C=O); Found: C, 67.05; H, 4.47%. Calcd for $C_{22}H_{17}O_2Br$: C, 67.19; H, 4.36%.

9-Acetyl-9-(2′-bromomethylphenyl)fluorene (1g). Yield 66%; colorless prisms; mp 103—105 °C; IR (KBr) 1700 cm^{-1} (C=O); Found: C, 70.30; H, 4.28%. Cacld for $C_{22}H_{17}OBr$: C, 70.04; H, 4.54%.

9-Benzoyl-9-(2′-bromomethylphenyl)fluorene (1h). Yield 78%; colorless prisms; mp 131—132 °C; IR (KBr) 1670 cm^{-1} (C=O); Found: C, 73.84; H, 4.45%. Cacld for $C_{27}H_{19}OBr$: C, 73.81; H, 4.36%.

9-(2′-Iodomethylphenyl)fluorene (3). To a solution of **1a** (1 g, 3 mmol) in acetic acid (15 ml) was added hydroiodic acid (57%, 2.1 g, 9 mmol); the mixture was refluxed for 2 h. Upon cooling to room temperature, the reaction mixture was poured into water and extracted with benzene. The benzene solution was washed with a $NaHSO_3$ solution, dried over $MgSO_4$, and concentrated in vacuo. The crude product was recrystallized from petroleum benzine to give **3** as light-yellow crystals; yield 0.52 g (47%); mp 117—119 °C; ^{1}H NMR δ=3.26, 4.75 (0.4H and 1.6H, two s, CH_2I), 4.84, 5.29 (0.8H and 0.2H, two s, 9-H), 6.12—7.78 (12H, m, $H_{arom.}$). Found: C, 62.64; H, 3.76%. Calcd for $C_{20}H_{15}I$: C, 62.84; H, 3.95%.

9-(2′-Hydroxymethylphenyl)fluorene (4). A solution of **3** (0.2 g, 0.5 mmol) in dioxane (10 ml)-water (2 ml) was refluxed for 3 h. Upon cooling to room temperature, the reaction mixture was poured into water; the deposited crude product was filtered, dried, and recrystallized from petroleum benzine to give **4** as colorless needles; yield 0.11 g (80%); mp 135—136 °C; IR (KBr); 3340 cm^{-1} (OH); ^{1}H NMR δ=3.42, 5.03 (0.6H and 1.4H, two s, $C\underline{H}_2OH$), 5.04, 5.43 (1H, two s, 9-H), 6.34 (0.7H, d, J=8 Hz, 6′-H), 7.74 (2H, d, J=7.5 Hz, 4- and 5-H), 6.7—7.5 (9.3H, m, $H_{arom.}$). Found: C, 88.18; H, 5.79%. Calcd for $C_{20}H_{16}O$: C, 88.20; H, 5.92%.

9-(2′-Bromomethylphenyl)fluorene (1b). Into a solution of **4** (0.5 g, 1.8 mmol) in acetic acid (10 ml) was bubbled dry hydrogen bromide, which was generated by a reaction of tetralin with bromine for 5 min. The reaction mixture was poured into cold water; then, precipitated crystals were filtered, washed, and dried. The product was recrystallized from petroleum benzine to give **1b** as light-yellow needles; yield 0.54 g (88%); mp 87—88 °C; Found: C, 71.82; H, 4.35%. Calcd for $C_{20}H_{15}Br$: C, 71.66; H, 4.51%.

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