Rotational Isomerisum in Fluorene Derivatives XXIII[1)] Syntheses of 1-Substituted 1'-methyl-9,9'-bifluorenyl Derivatives and Their Conformational Isomerisum

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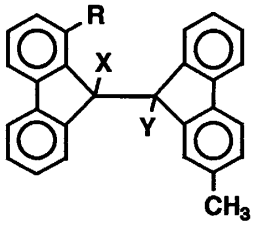
Abstract

The reaction of 1-substituted fluorenones (1-substituents: CH_3, F, Cl, Br, I, OCH_3, and Ph) with 1-methyl-9-fluorenyllithium gave a mixture of **A** (*erythro*) and **B** (*threo*)-isomers of 1-substituted 9-hydroxy-1'-methyl-9, 9'-bifluorenyls (**2**). In these cases, **2**-**B**-isomers were obtained more abundantly than **2**-**A**-isomers owing to the steric effects between 1-substituents and 1'-CH_3 group. 1-Substituted 1'-methyl-9,9'-bifluorenyls (**3**) were prepared from the reduction of **2** with HI (method i) or the reaction of 9-bromo-1-methylfluorene with 1-substituted 9-fluorenyllithium (method ii). In these cases, **3**-**B**-isomers were mainly obtained by method ii, whereas, **3**-**A**-isomers by method i. Furthermore, the restricted rotation about the C(9)-C(9') bonds in **3** were investigated by DNMR method, and we could observe some rocking motion from one *gauche* form ⓐ to the other ⓔ in **A**-isomers of 1,1'-dimethyl-9,9'-bifluorenyl (**3a**) and 1-fluoro-1'-methyl-9,9'-bifluorenyl (**3b**).

1. Introduction

In the preceding paper,[1)] it was reported that 1-substituted 2'-methyl-9,9'- bifluorenyl derivatives (**1**) were confirmed as the mixture of *erythro*- and *threo*- isomers by their ^{1}H-NMR spectra, and the restricted rotation about the C(9)-C(9') bonds of these compounds was not observed owing to their stable structures.



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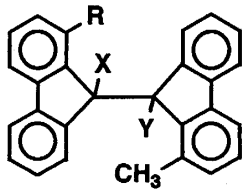

2 : X= OH, Y= H
3 : X= Y= H

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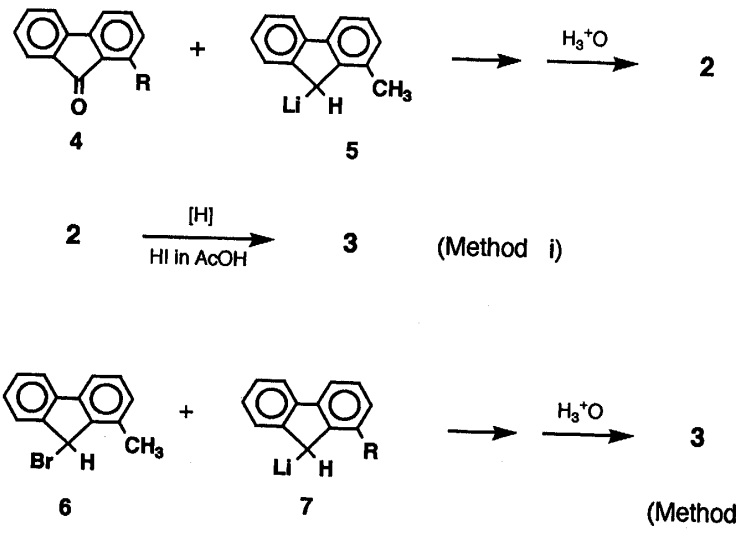
In this paper, we wish to further describe the preparation of 1-substituted 1'-methyl-9-hydroxy-9, 9'-bifluorenyl derivatives (**2**) and 1-substituted 1'-methyl-9, 9'-bifluorenyl derivatives (**3**), and discuss their rotational isomerism by means of DNMR method.

2. Results and Discussion

2. 1 Syntheses of 2 and 3

The derivatives **2** were prepared from the reactions of 1-substituted fluorenones (**4**) (1-substituents: methyl[1], fluoro[1] chloro[1], bromo[1], iodo[1], methoxyl[1], and phenyl[2]) with 1-methyl-9-fluorenyllithium (**5**) in dry benzene under nitrogen atmosphere and the subsequent decomposition reactions. The reductions of **2** with hydroiodic acid in acetic acid gave **3** (method i). The compounds **3** were also prepared from the reactions of 9-bromo-1-methylfluorene (**6**) with 1-substituted 9-fluorenyllithium (**7**) and the subsequent decompositions (method ii). Mp, yield and partial NMR data of the obtained **2** and **3** are shown in Table 1, and their analytical data are shown in Table 2.



These compounds **2** and **3** were generally obtained as a mixture of **A**- and **B**-form as shown in Table 1.

2.2 Discussion of the reaction directionality for the synthesis of 2

We confirmed **A**- and **B**-form as *erythro*- and *threo*-isomer, respectively, by their NMR spectra, according to the previously discussed procedure.[1] The NMR spectra of the **A** (*erythro*)- and **B** (*threo*)-form (shown in Table 1) could be assign on the basis of the following Newman projection formulas which were most stable conformations (Fig. 1). As an example, we showed the ^{1}H-NMR spectrum of crude **2a** in Fig. 2.

Although compounds **2** (**2a**~**2g**) were obtained as a mixture of **A**- and **B**-forms, **B**-form had been found more abundantly than **A**-form, and readily isolated by recrystallization from methanol. In compound **2a**, we found that the product ratio **A**/**B** was 1/7 as shown in Fig 2. The mechanisum of the reactions of **4** with **5** lead to **2**-**A** and **2**-**B**

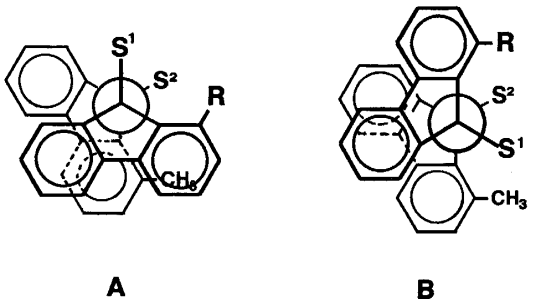
Table 1. Syntheses of **2** and **3**

Compd.	R	Yield (%)	mp (℃)	NMR: δ (ppm) in $CDCl_3$ at room temperature 1,1'-CH_3	9 or 9'-H	8,8'-H	Form	Method
2a	CH_3	91	218-221	1.54s 2.62s	5.12s	6.24d 7.67d	A	
			220-221[b]	2.86s 2.97s	5.21s	5.87d 5.90d	B	
2b	F	70	178-185	2.08s	5.16s	6.12d	A	
			246-250[b]	2.88s	5.31s	6.08d	B	
2c	Cl	67	188-203	1.57s	5.47s	6.01d	A	
			217-218[b]	2.88s	5.65s	5.95d	B	
2d	Br	72	200-218	1.55s	5.48s	5.90d 7.91d	A	
			217-220[b]	2.86s	5.60s	5.88d 5.91d	B	
2e	I	84	186-190	1.43s	5.64s	5.96d 7.91d	A	
			225-227[b]	2.95s	5.74s	5.82d 5.08d	B	
2f	OCH_3	85	164-165[a]	1.83s	5.08s	- -	A	
			216-217[b]	2.76s	5.31s	5.80d 5.80d	B	
2g	Ph	82	209-211[b]	2.31s	4.42s	5.79d 5.79d	B	
3a	CH_3	80	195-206[a]	2.04br	4.90s		A	i
		93	260-265[b]	2.85s	5.03s	5.86d	B	ii
3b	F	87	173-178	2.29br	4.84br 5.08br	6.00br	A	i
		76	234-241[b]	2.79s	4.82d 4.99d	5.75d	B	ii
3c	Cl	90	174-175[a]	1.55br	4.93br 5.40br	6.25br	A	i
		96	214-220	2.84s	5.08d 5.45d	5.90d 5.87d	B	ii
3d	Br	93	156-159[a]	1.42br	4.80br 5.50br	6.04br	A	i
		77	240-244[b]	2.87s	5.06d 5.55d	5.82dd	B	ii
3e	I	89	178-181[a]	1.34br	4.72br 5.62br	5.96br 7.98br	A	i
3g	Ph	83	185-189[a]	1.30br	4.27br 5.20br	6.00br	A	i

a) Mp of isolated **A**-form. b) Mp of isolated **B**-form.

Table 2. Analytical data for **2** and **3**

compd.	Empirilal formula	Calcd. C(%)	Calcd. H(%)	Found C(%)	Found H(%)
2a	$C_{28}H_{22}O$	89.81	5.92	89.95	5.95
2b	$C_{27}H_{19}OF$	85.70	5.06	85.49	5.09
2c	$C_{27}H_{19}OCl$	82.13	4.85	82.13	4.97
2d	$C_{27}H_{19}OBr$	73.82	4.36	73.94	4.48
2e	$C_{27}H_{19}OI$	66.68	3.94	66.53	3.98
2f	$C_{28}H_{22}O_2$	86.13	5.68	86.13	5.69
2g	$C_{33}H_{24}O$	90.79	5.54	90.59	5.56
3a	$C_{28}H_{22}$	93.81	6.19	93.97	6.15
3b	$C_{27}H_{19}F$	89.48	5.28	89.63	5.11
3c	$C_{27}H_{19}Cl$	85.59	5.06	85.91	5.14
3d	$C_{27}H_{19}Br$	76.60	4.52	76.61	4.54
3e	$C_{27}H_{19}I$	68.95	4.07	69.12	4.12
3g	$C_{33}H_{24}$	94.25	5.75	94.13	5.72



A B

Fig. 1 Most stable conformations of A- and B-forms

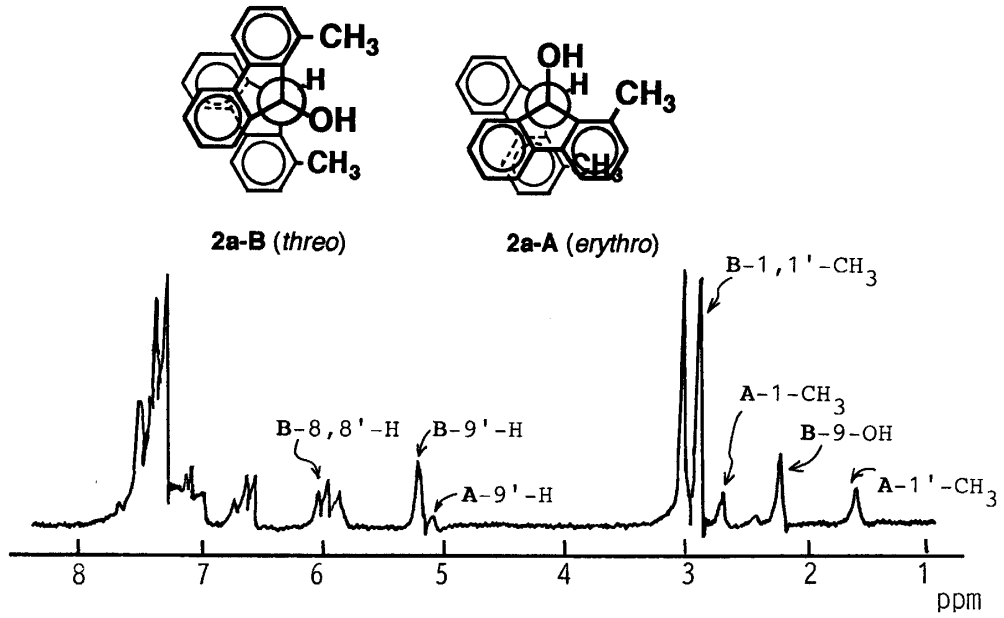


Fig. 2 ^{1}H-NMR spectrum of crude **2a** (in $CDCl_3$ at rt)

may be illustrated in Fig. 3. That is. as shown in the figure, if each R- and CH_3-groups are situated in remote positions, product should be led to **B** (*threo*)-isomer. Whereas, if R- and CH_3-groups are brought so close together, product should be led to **A** (*erythro*)-isomer.

It seems spontanenously that two fluorene molecules should be easy to approach each other from a direction which does not undergo steric hindrance. Thus, *threo*-isomer may be found more abundantly than *erythro*-isomer. Actually, in the case of R = halogen, product ratio **B/A** (**2b**; 1.2/1, **2c**; 2/1, **2d**; 2.5/1, and **2e**; 2.5/1) were influenced by the magnitudes of van der Waals radius of R. Compound **2g** (R = Ph) was obtained as only **B**-form. However, in compound **2f** (R = OCH_3), a lot of **A**-isomer was found in the crude product rather than **B**-isomer (**B/A** = 1/2). In this case, we assumed some electronic effect between OCH_3- and CH_3-groups besides the steric effect. Still, the reaction of 1,8-dimethylfluorenone[3] with **5** did not proceed at all. Furthermore, we investigated the restricted rotation about the C(9)-C(9') bonds in these compouds **2** by DNMR. However, their ^{1}H-NMR signals did not change in any temperature range.

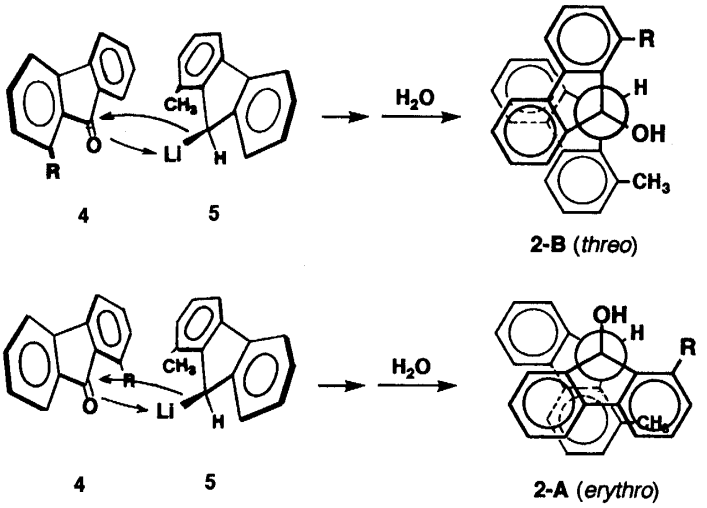


Fig. 3 Possible approaches for the reactions of **4** with **5** lead to **2-B-** and **2-A-**forms

2.3 Structure of 3 obtained by methods i and ii

We found that product ratio **A/B** of **3** considerably differed owing to the used method i or ii. That is, **3-B** (*threo*)-isomers were mainly obtained by method ii, whereas, **3-A** (*erythro*)-isomers were mainly obtained by method i. As an example, we show the ^{1}H-NMR spectrum of **3a** obtained by method i and method ii in Fig. 4.

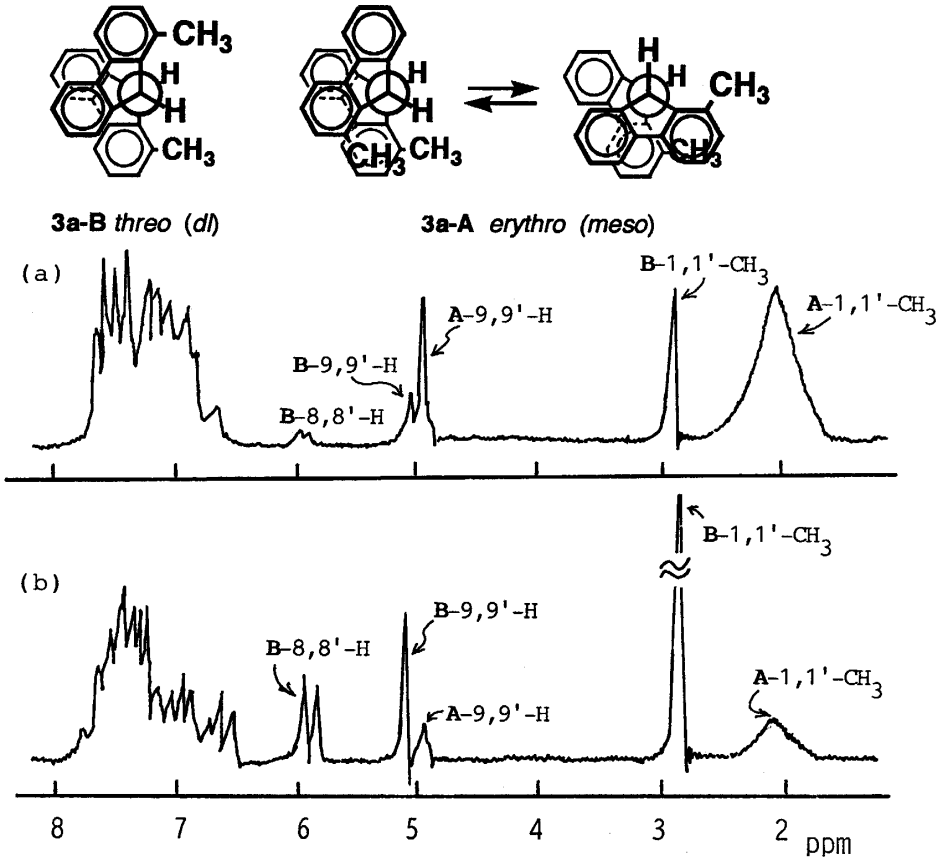


Fig. 4 ^{1}H-NMR spectrum of **3a** obtained by method i (a) and method ii (b)

In the case of method ii, we thought that two fluorene molecules approached each other from a direction which does not undergo steric hidrance as described for the reaction of **4** with **5** (Fig. 5). In the case of method i, both **2-A** and **2-B** have been mainly reduced into **3-A** isomers, together. Strange to say was that main reduction products from **2-B** were **3-A**. It is necessary to investigate in future a reduction mechanisum of **2** by use of hydroiodic acid.

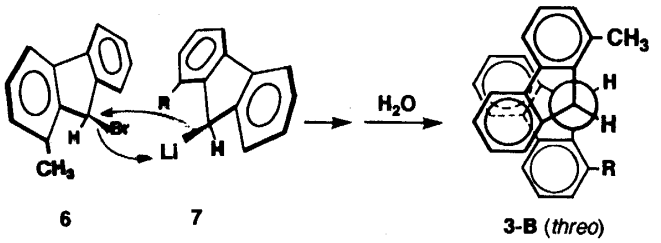


Fig. 5 Favarable approach for the reactions of **6** with **7** lead to **3**-B (*threo*)-*form*

2.4 Restricted rotation about C(9)-C(9') bonds in 3

Because ^{1}H-NMR spectrum of CH_3 in **3a-A** has been observed as broad signal at room temperature as shown in Fig.4, it can be considered that this compound already undergo the restricted rotation about the C(9)-C(9') bond at room temperature. Then, we observed the 1'-CH_3 signals in **3-A** at various temperature. The observed DNMR spectra of **3a-A** (*meso*)-isomer are shown in Fig.6 as a typical example.

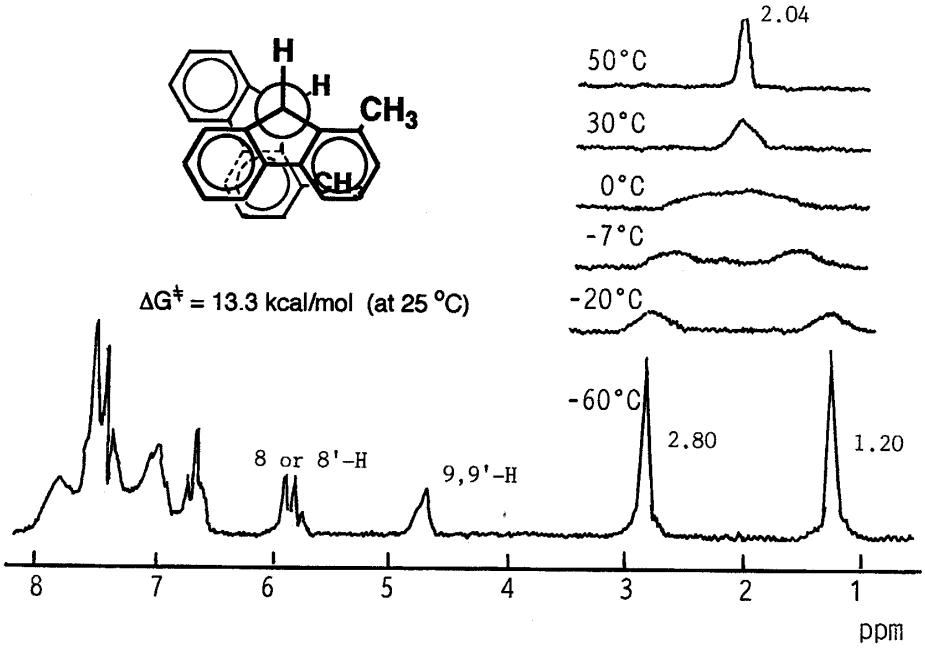


Fig. 6 Observed DNMR spectra of **3a-A** (*meso*) isomer in $CDCl_3$

In Fig.6, the 1(or 1')-CH_3 signal (δ 2.04 br.) which is observed at room temperature gradually broaden when the temperature is lowered, and is completely split into two equivalent singlets (δ 2.80 and 1.20) at -60 ℃. The broad signal at room temperature become sharp peak when the temperature is raised. In compound **3b-A**, CH_3 signal (δ 2.29 br.) at room temperature is split into two nonequivalent singlets (δ 2.78 and δ 1. 30) at -60 ℃. That is, two different conformers which are caused by restricted rotation about the C(9)-C(9') bond can be observed at low temperature.

Fig. 7 shows the conformations concerned with rotation about the C(9)-C(9') bond in **3-A**, and their interconversion processes by Newman projection formulas. The conformations ⓑ , ⓓ, and ⓕ should be unstable forms because of their *eclipsed* geometries. An examination of the molecular model suggests that *anti* conformation ⓒ is considerable unstable on account of the steric interaction between the 1-substituent (R) and 8'-proton as well as the 8-proton and 1'-CH_3 in the two fluorene

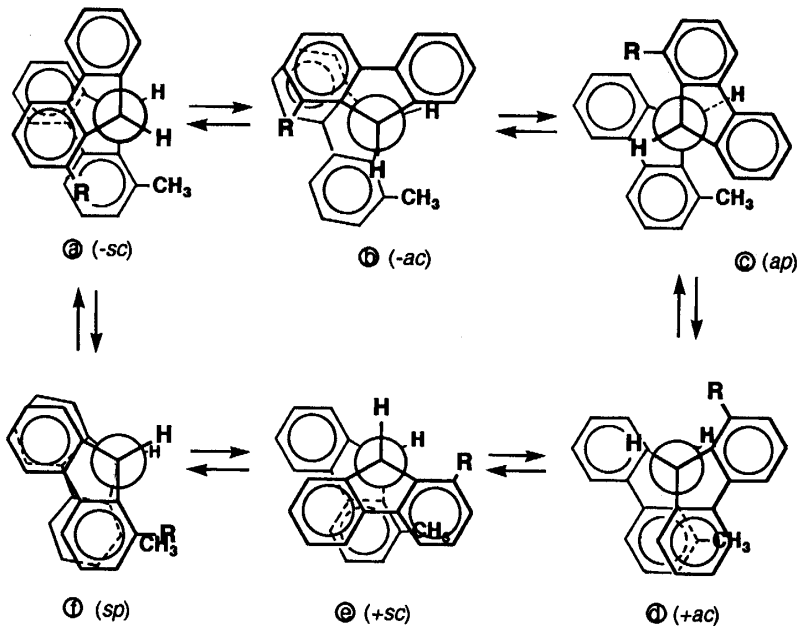


Fig. 7 Stereoisomerism process of **3-A** by rotation about the C(9)-C(9') bond

moieties. Concequently, the observed conformations at low temperature are attributed to the *gauche* forms ⓐ and ⓔ. In this case, it is reasonable to assume that 1'-CH_3 in conformation ⓐ which is located in a deshielding zone of the other fluorene moiety gives ^{1}H-NMR signal at low field, and the CH_3 group in ⓔ located in a shielding zone of the other's gives the signal at high field.

Thus, in compound **3b-A** (R=F), the singlet at δ=2. 78 is assigned to the CH_3 signal of ⓐ and the singlet at δ=1.30 is assigned to that of ⓔ. Furthermore, the equilibrium constant K(N ⓐ/N ⓔ) for the equilibria ⓐ⇄ⓔ was found to be 2/1 from the intencity ratio of the two CH_3 signals. Interconversion between the two *gauche* conformers, ⓐ and ⓔ, can occur by two different pathways, via the fully *eclipsed* form ⓕ, or via the

anti form ⓒ. But irrespective of the pathways, the observed dynamic behavior can be viewed as a rocking motion from one *gauche* form to the other. The rotational energy profile for **3b-A** is illustrated graphically in Fig. 8. Thus, it can be concluded that the rocking motions between ⓐ and ⓔ via ⓕ (ⓐ⇄ⓕ⇄ⓔ) have been observed by the DNMR spectra. For the comparison of the stability of the conformers ⓐ and ⓔ, it can be explained on the basis of each magnitude of the steric interaction between 1-F group and the other fluorene moiety in ⓐ , and between 1'-CH_3 group and the other's in ⓔ. Because the van der Waals radius of fluorine is smaller than methyl group, the former interaction should be smaller than the latter's. Thus, the conformer ⓐ is more stable than the conformer ⓔ.

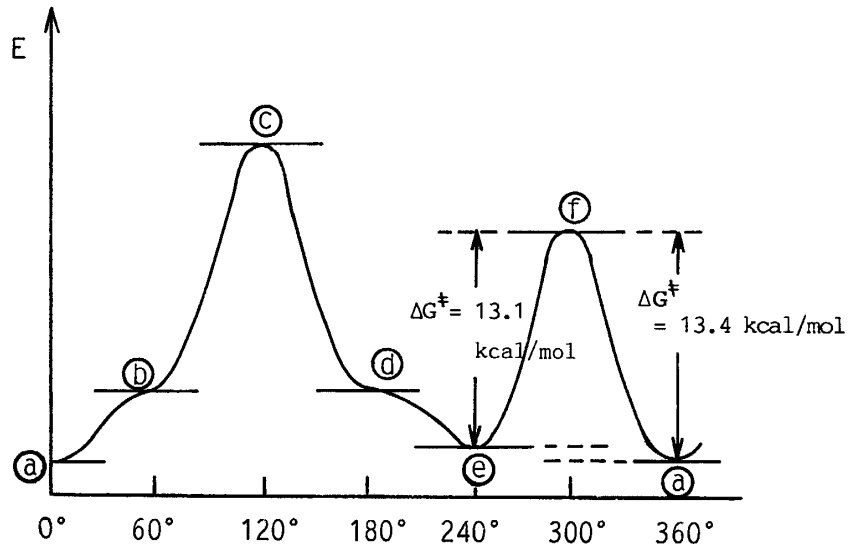


Fig. 8 Rotational energy profile for **3b-A**

The free energies of activation for the internal rotation in **3a-A** and **3b-A** obtained from the line-shape analysis of the DNMR spectra due to the methyl group are as follows: **3a-A**;ⓐ⇄ⓔ, $\Delta G^{\neq}$=13.3 kcal/mol (at 25 ℃), and **3b-A**;ⓐ→ⓔ, $\Delta G^{\neq}$=13.4 kal/mol (at 25 ℃),ⓔ→ⓐ; $\Delta G^{\neq}$=13.1 kcal/mol (at 25 ℃) as pictured in Fig. 8. Incidentally, the value of the free energy of activation for the rotation of C(9)-C(9') bond in 2-methyl-9, 9'-bifluorenyl has been estimated as follows, $\Delta G^{\neq}$=10-11 kcal/mol.[4] That is, it turned out that the energy barrier for the rotation around the C(9)-C(9') bond of 9,9'-bifluorenyl has been rose about 3 kcal/mol owing to substitute CH_3- or F-group at 1 or 1'-position of fluorene nucleus.

On the other hand, in the *erythro* isomers **3c-A**, **3d-A**, **3e-A**, and **3g-A**, only ⓔ forms were observed as the stable conformer, because ⓐ forms undertook the steric repulsion between 1-substituents and other fluorene moieties, and their CH_3-signals did not split even if temperature was lowered to -60 ℃.

Furthermore, ^{1}H-NMR signals of **3-B** (*threo*) isomers did not change in any temperature range.

3. Experimental

The ^{1}H-NMR spectra were recorded on a JEOL-MH-100 spectrometer with a JEOL model JES-VT-3 variable temperature controller. The chemical shifts are expressed in ppm, with TMS as the internal standard. DNMR spectra were analyzed by using a modified version of the computer program DNMR-3.[5] The melting points of the compounds obtanined are uncorrected.

1,1'-Dimethyl-9-hydroxy-9,9-bifluorenyl (2a). Typical Procesure for the Syntheses of 2. A solution of 1-methyl-fluorenone (**4a**) in dry benzene was added into 1-methyl -9-fluorenyllithium which was prepared from phenyllithium and 1-methylfluorene in dry ether under nitrogen atmosphere. The mixture was refluxed for 30min. After cooling, the solution was poured into dil. hydrochloric acid. Obtained organic layer was washed with water, dried with magnesium sulfate and distilled off in vacuo. Then, leaving a residue was recrystallized from methanol to give **2a**(**A/B** = 1/7) colorless prism; yield 91 %, mp 218-221 ℃. Analytical data is shown in Table 2. By recrystallization of the above crude **2a** from methanol, **2a-B**(*threo*)-isomer was isolated; mp 220-221 ℃. ^{1}H-NMR data of **2a** are shown in Table 1.

1,1'-Dimethyl-9,9'-bifluorenyl (3a). Typical Procedure for the Syntheses of 3 by Method i. Hydroiodic acid(d=1.7, 1ml) was added into a solution of **2a**(0.5 g, 0.0013 mol) in acetic acid(30 mol), and the mixture was refluxed for 1 hr. After cooling, the solution was poured into water, and then free iodine was removed with sodium sulfite. The crude product was extracted with benzene or ether, and the organic layer washed with water, then with sodium carbonate solution, and then was dried over magnesium sulfate. After the organic solution was distilled off in vacuo, the obtained residue was recrystallized from petroleum benzine to give **3a** as colorless crystals. Yield 80 %, mp 195-206 ℃ (mixture of **A** and **B**, **A/B**=3/1). ^{1}H-NMR spectrum of **3a** is shown in Fig. 4, and the data is shown in Table 1.

9-Bromo-1-methylfluorene (6). To a solution of 1-methylfluorene[6](20 g, 0.11 mol) in carbon tetrachloride(150 ml), was added *N*-bromosuccinimide(22 g, 0.12 mol) and a small amount of benzoyl peroxide, and the mixture was refluxed for 4 hr. After cooling the raction 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 **6** as colorless prisms; yield 24 g(85 %), ^{1}H-NMR ($CDCl_3$) δ=2.43(3H, s, CH_3), 5.81(1H, s, 9-CH), 6.90-7.65 (7H, m, arom. H).

Compound 3a. Typical Procedure for the Syntheses of 3 by Method ii. A solution of **6** in dry ether was added into 1-methyl-9-fluorenyllithium in dry ether under nitrogen atmosphere. The mixture was refluxed for 1 hr. After cooling, the solution was poured into dil. HCl, and the contents was extracted with ether. The ether extract was washed with water, dried over magnesium sulfate and distilled off in vacuo, leaving a residue was recrystallized from petroleum benzine to give **3a** (**A/B** = 1/3.5) as colorless crystals; yield 93 %. By fractional recrystallization of **3a** from petroleum benzine, **3a-B** (*dl*-isomer) (mp 260-265 %) was isolated. ^{1}H-NMR data of **3a-B** was shown in Table 1.

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