Restricted Rotation Involving the Tetrahedral Carbon. XXXVIII. Barriers to Rotation and Population Distributions of 9-(8-Methyl-1-naphthyl)fluorene and Its 1-Methyl Derivative[1]

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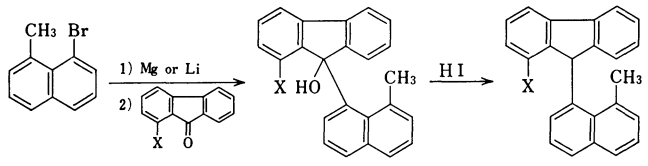
The title compounds were prepared to see the effect of an 8-methyl group on the populations and the barriers to rotation of rotamers. As expected, the substituent destablized the *syn* conformation to a considerable extent, although the extent appeared to be a little less than that of a 2-*t*-butylphenyl group. Atropisomers of 1-methyl-9-(8-methyl-1-naphthyl)fluorene were isolated. The barriers to rotation were discussed with reference to related compounds.

In one of the previous papers, we have demonstrated that the conformational equilibrium of 9-(2-*t*-butylphenyl)fluorene is lop-sided: since the ground state of the *ap* conformation is so energy-rich that it rotates slowly at room temperature, although it can be made, to form the corresponding *sp* isomer, of which isomerization to the *ap* is practically nonexistent at room temperature.[2] This finding aroused our interest in investigating the effect of an 8-methyl-1-naphthyl group in the 9-position of fluorene on the barriers to rotation and population equilibriums, because the bulkiness of a *t*-butyl group is often compared with that of an 8-methyl-1-naphthyl substituent: the compound may give stable atropisomers. It is also interesting to see how atropisomers become stable when we introduce a methyl group into 1-position of the fluorene ring, since such an operation is known to raise the barriers to rotation to a considerable extent.[3,4]

Syntheses of the compounds were carried out in the following way. Fluorenones were added to a Grignard or a lithium compound derived from 1-bromo-8-methylnaphthalene (**1**) and the resultant 9-aryl-9-fluorenols (**2** and **3**) were reduced with hydriodic acid at room temperature to afford 9-(8-methyl-1-naphthyl)fluorenes (**4** and **5**).



1 **2**: X=H, **3**: X=CH3 **4**: X=H, **5**: X=CH3

The syntheses afforded an isomer exclusively: **2** gave *syn*-**4** whereas **3** gave *anti*-**5**. Thus *syn*-**4** had to be converted to *anti*-**4** to examine the barrier to rotation. It was accomplished by taking advantage of the fact that protonation after lithiation of the 9-position proceeds from the less hindered side.[2,5]

This paper reports the findings on the equilibriums of rotamers of 9-(8-methyl-1-naphthyl)fluorene and its 1-methyl derivative in addition to the syntheses and compares the barriers and populations of rotamers, which are affected by the substituents, with related compounds.

Experimental

syn-9-(8-Methyl-1-naphthyl)fluorene (syn-*4*). A solution of 279 mg (1.26 mmol) of 1-bromo-8-methylnaphthalene (**1**)[6] in 30 mL of tetrahydrofuran was refluxed with 33 mg (1.4 mmol) of magnesium until most of the magnesium disappeared (*ca.* 3 h). Fluorenone (346 mg or 1.92 mmol) was added to the solution in the form of powder and the whole was refluxed for 2 h. The resultant mixture was treated in a usual manner and the desired product (**2**) was obtained in 28% yield. ^{1}H NMR ($CDCl_3$, δ): 1.40 (3H, s), 2.17 (1H, s), 7.0—7.8 (13H, m), 8.67 (1H, q). This compound must exist as an *anti* form from the ^{1}H NMR data.

A solution of 100 mg of **2** in 20 mL of acetic acid was mixed with 3 mL of 57% hydriodic acid and stirred for 6 h at room temperature. The solution was poured into water, treated with aqueous sodium dithionite and then with aqueous sodium hydrogencarbonate, and extracted with ether. The product was chromatographed on silica gel to afford *syn*-**4**, oil, in 90% yield. The purity was checked by a ^{1}H NMR spectrum and a high resolution mass spectrum. MS: found (M^+) 306.1399; calcd for $C_{24}H_{18}$, 306.1409. ^{1}H NMR ($CDCl_3$, δ): 3.17 (3H, s), 6.40 (1H, s), 6.62 (1/2H, d), 6.73 (1/2H, d), 7.0—7.8 (13H, m).

anti-9-(8-Methyl-1-naphthyl)fluorene (anti-*4*). A solution of 20 mg of *syn*-**4** in 0.4 mL of tetrahydrofuran was mixed with 0.5 mmol of butyllithium in hexane at room temperature. The mixture was heated at 60 °C for 3 h and was quenched with trifluoroacetic acid. The mixture was quickly treated in a usual manner and the product was purified by TLC on a silica gel plate at 0 °C. The operation afforded a mixture of *syn*-**4** and *anti*-**4** (*ca.* 3 : 7), which was directly used for the measurements of rates of isomerization. The following ^{1}H NMR data ($CDCl_3$, δ) were obtained by subtracting the signals due to *syn*-**4**: 1.32 (3H, s), 5.40 (1H, s).

anti-1-Methyl-9-(8-methyl-1-naphthyl)fluorene (anti-*5*). A mixture of 1.2 g (5.4 mmol) of **1** and 95 mg (14 mmol) of lithium in 20 mL of ether was refluxed until a reddish brown solution was obtained (*ca.* 2 h). To the solution was added 1.12 g (5.8 mmol) of 1-methyl-9-fluorenone[7] in 20 mL of benzene over a period of 20 min. The solution was refluxed for 3 h and treated in a usual manner. The product was purified by silica-gel chromatography to afford 51% oil (**3**), which existed as *anti* conformation only as judged from its ^{1}H NMR spectrum ($CDCl_3$, δ): 1.44 (3H, s), 1.54 (3H, s), 2.30 (1H, s), 6.7—7.9 (12H, m), 8.76 (1H, q).

A solution of **3** in acetic acid was treated with hydriodic acid as described above to afford *anti*-**5**, mp 126—128 °C, in 93% yield. Found: C, 93.99; H, 6.10%. Calcd for $C_{25}H_{20}$: C, 93.71; H, 6.29%. ^{1}H NMR ($CDCl_3$, δ): 1.32 (3H, s), 1.71

(3H, s), 5.36 (1H, s), 6.7—8.0 (13H, s). ^{13}C NMR ($CDCl_3$, ppm from TMS): 19.3, 21.5, 59.8, 118.0, 120.2, 123.8, 126.8, 127.0, 127.7, 129.0, 129.4, 129.6, 130.4, 133.1, 134.4, 134.9, 135.0, 135.6, 135.9, 139.8, 146.3, 148.9.

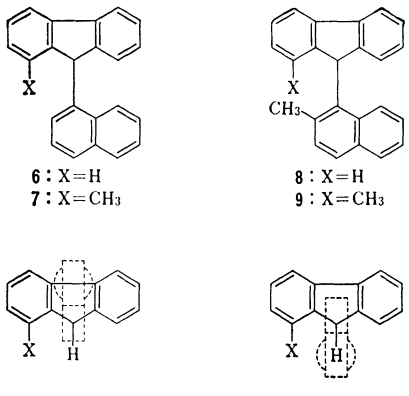
syn-*1-Methyl-9-(8-methyl-1-naphthyl)fluorene* (syn-**5**). An equilibrium mixture of *syn* and *anti* forms of **5** was obtained by the kinetic study described below. The solution was evaporated and the residue was crystallized from dichloromethane–hexane. Mp 123—125 °C. Found: C, 93.66; H, 6.04%. Calcd for $C_{25}H_{20}$: C, 93.71; H, 6.29%. ^1H NMR ($CDCl_3$, δ): 1.90 (3H, s), 3.23 (3H, s), 6.47 (1H, s), 6.8—8.0 (13H, m). ^{13}C NMR ($CDCl_3$, ppm from TMS): 19.4, 27.2, 50.7, 118.0, 120.0, 124.8, 125.3, 126.2, 126.8, 127.1, 127.4, 128.5, 128.9, 130.8, 132.1, 133.3, 134.6, 135.7, 137.3, 140.2, 141.3, 147.6, 149.8.

Spectral Measurements. ^1H NMR spectra were measured on a Hitachi R-20B spectrometer and ^{13}C NMR with a JEOL FX-60 spectrometer. ^{13}C NMR spectra of *syn*- and *anti*-**5** were obtained at −20 °C to avoid isomerization of the latter during the measurement. A high resolution mass spectrum was obtained with a JEOL JMS-D-300 spectrometer.

Measurements of Rates of Rotation. Kinetic measurements were carried out with solutions of chloroform-*d*. Measurements which were necessary for both determination of the rates of rotation and equilibrium constants were carried out using ^1H NMR spectra where appropriate. In the cases where one isomer was so predominant that the errors involved in the measurements by the NMR spectra were large, a Waters HPLC instrument which was equipped with a UV detecter was used for the analysis. The correspondence of the peak areas in HPLC to the real populations was checked by comparing those with the populations obtained by the NMR spectra, where the latter was applicable. The correspondence was found to be satisfactory without considering the difference in absorption strengths per molecule of the isomers. The kinetic data were treated as a reversible unimolecular reaction to afford satisfactory results. The errors in rate constants are given for 95% confidence intervals in the least squares method, adopting t-distribution.

Results and Discussion

The first problem we wish to discuss is the nomenclature of the conformers concerned. If the fluorene ring is unsubstituted or symmetrically substituted, there is no problem in designating the rotational isomers by the present IUPAC rule E.[8] Namely we do have *ap* and *sp* isomers of 9-(8-methyl-1-naphthyl)fluorene (**4**) and they involve no ambiguities. The same is true for 9-(1-naphthyl)fluorene (**6**) and 9-(2-methyl-1-naphthyl)-fluorene (**8**). However, as soon as a methyl group is introduced into the 1-position of fluorene, we come across a difficulty. One may designate the conformation of 1-methyl-9-(8-methyl-1-naphthyl)fluorene (**5**), which corresponds to the *ap* conformation of **4**, as $\pm sc$. However, there is another conformation which is $\pm sc$ in this case: if we consider a conformation in which the 8-methyl-1-naphthyl group eclipses the bond connecting C_9 and an aromatic carbon of which ring bears no substituent, the conformation is also $\pm sc$ if the prefered side, in the sequence rule,[9] of the naphthyl moiety is close to the 1-methyl group. This type of ambiguity arises always when a conformation involves at least one chiral center. We must specify the configuration of the chiral center, in addition to the conformation, to avoid ambiguities. Thus the conformation becomes $[-sc(R)]+[+sc(S)]$.[10] In practice, however, comparing the *ap* form of **4** and $[-sc(R)]+[+sc(S)]$ form of **5** may be too complicated in writing and may cause confusion. Therefore, in designation of conformations concerned, we prefer to commonly use "*syn*" for the conformation in which a prefered group in the sequence rule is synclinal to the C_9–H bond (C_9–OH in the case of **2** and **3**). This nomenclature is conventional but is more convenient in the present case.



6: X=H
7: X=CH3
8: X=H
9: X=CH3

ap or $-sc(R)$ *sp* or $+ac(R)$

(Only one enantiomer is shown when X is CH_3.)

9-(8-Methyl-1-naphthyl)-9-fluorenols. The assignment of the conformation is straightforward, because the methyl group substituting the naphthyl moiety is expected to give a signal at a high magnetic field in the ^1H NMR spectrum if it is *anti* and that, in the *syn*, it must give a signal at a lower field. It is interesting to note that the *anti* isomer overwhelms in **2** and **3** in contrast to the fact that, in 9-(2-*t*-butylphenyl)-9-fluorenol, the *syn* isomer is overwhelming.[2] The distribution of conformers in **2** and **3** is similar with the cases of other 9-(2-alkylphenyl)-9-fluorenols. Probably the repulsive interaction between the *t*-butylphenyl group and the fluorene ring is much more severe than that between the 8-methylnaphthyl group and the fluorene. This is reflected in the equilibrium constants of the hydrocarbons also (*vide infra*).

It is well documented that substitution of the 9-hydrogen in 9-arylfluorenes by other groups decreases the barrier to rotation.[11] Thus it is not possible to isolate rotational isomers of 9-(2-methyl-1-naphthyl)-9-fluorenol (**10**), although rotamers of its parent hydrocarbon (**8**) were isolated.[2,12] However, Ford *et al.* reported that the introduction of a methyl group into the 1-position of the fluorene ring of **10** caused the increase in the rotational barrier (in **11**) and suggested that the barrier would be over 26 kcal/mol (1 kcal= 4.18 kJ):[3] the value is high enough for isolation of rotamers at room temperature. Indeed, Kajigaeshi *et al.* were able to isolate one of the rotamers of a benzo-annelated derivative of **10**, the barrier ($\Delta G^{\ddagger}_{323}$) being 24.6 kcal/mol.[13]

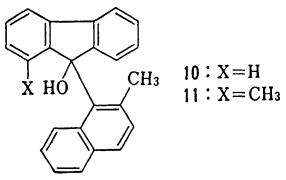
We found a similar situation for **3**, though to a lesser degree of enhancement of the barrier. The ^1H NMR spectra of the compound suggested the presence of a negligible amount of the *syn* isomer and overwhelming population of the *anti* isomer at room temperature.

TABLE 1. KINETIC AND THERMODYNAMIC DATA FOR THE ROTATION ABOUT THE C_9–C_{Ar} BOND OF 9-(1-NAPHTHYL)FLUORENES AND 9-(2-*t*-BUTYLPHENYL)FLUORENE

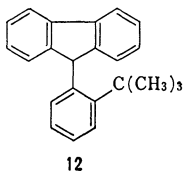
Comopund	Substituent		Rate Constant for Rotation (*anti*→*syn*)[a] ($\times 10^5$ s^{-1})	$\Delta G^{\ddagger}$[a] kcal mol^{-1}	Equilium Constant[a] (*syn*/*anti*)	Reference
	Fluorene	Naphthalene				
12	—	—	39(272)	20.1(307)[b]	>100(273)	2
4	H	8-CH_3	5.6±4.2(307) 170±20(327)	23.9(307)	25[c]	This work
5	1-CH_3	8-CH_3	0.80±0.03(307) 11.5±0.7(327)	25.2(307)	33[c]	This work
6	H	H		17.4(307)[b] 17.7(307)[b]	2[d] 2(303)	18 12
7	1-CH_3	H		21.4(433)	2[e]	4
8	H	2-CH_3		29.2(393)	1(373)	12
9	1-CH_3	2-CH_3		33.3(429)	1(429)	3

a) Numericals in parentheses are temperatures in Kelvin. b) Calculated from available data. c) These values were independent of temperatures examined. d) At room temperature and below. e) At room temperature.

However, on raising the temperature, we found that the signal due to the methyl group broadened considerably at about 120 °C to suggest that coalescence of two signals took place. The barriers to rotation in **3** is not certain, because we could not detect the signal due to the *syn* isomer, but is of the order of 20 kcal/mol.



10 : X=H
11 : X=CH_3



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Populations of 9-(8-Methyl-1-naphthyl)fluorene Rotamers. Assignment of the conformations was carried out both from the ^1H NMR features as described above and from the mode of protonation. It is interesting to note that the unstable *anti* form of **5** was prepared preferentially, whereas the stable *syn*-**4** was the sole product in the preparation of **4**. This must be caused because **5** gave the kinetially controlled product owing to its high barrier to rotation whereas **4** gave the thermodynamically controlled product due to its low barrier to rotation. Although the mechanisms of the reaction are not well understood, the reaction conceivably proceeds *via* an iodide followed by a reaction with complex iodide anions.[14] In both cases, a bulky iodide ion is involved in the reaction and the approach from the less hindered side is favored to produce *anti*-**5**.

Equilibrium constants between the rotamers of **4** and **5** are summarized in Table 1 together with those of related compounds. From the molecular models, the 8-methyl group is expected to give severe steric interaction with the fluorene ring when the molecule has the *anti* conformation. This effect is apparent if one compares the equilibrium constants of **4** and **5** with those of the compounds which do not possess a methyl in the 8-position but do or do not carry a methyl in a position other than 8 of the naphthyl group. The ground states of **4** and **5** are raised to a considerable extent.

If one compares the equilibrium constants of **4** and **5** with that of 9-(2-*t*-butylphenyl)fluorene (**12**), however, one notices an interesting point. That is, although the steric effect of the *t*-butyl group given to the *o*-position of a phenyl group is often compared with that of the 8-methyl group given to the 1-position of naphthalene and the latter is often referred to be larger than the former because of rigidity, the data in Table 1 suggest that the ground state of the *anti* conformations of **4** and **5** are, relatively speaking, more stable than that of *anti*-**12**.

This is also reflected to the ^{13}C–^1H coupling constants of the NMR spectra: the coupling constants are 115.4 Hz[2] and 120.2 Hz for the *anti* forms of **12** and **5**, respectively. The coupling constants in the *syn* conformations of 9-(2-alkylphenyl)fluorenes are reported to be 128±1 Hz[2] and the *syn* form of **5** is no exception. The ^{13}C–^1H coupling constant is known to reflect the *s*-character of the carbon orbital:[15] the smaller coupling constant is due to higher *p*-character of the bonding orbital concerned. The geometry of the 9-carbon of the fluorene ring is more flattened than others in the *anti* conformation due to the steric compression between the fluorene ring and the *t*-butyl or 8-methyl group. The ^{13}C chemical shift data support the idea that the C_9 configuration has moved toward the trigonal in the *anti*-conformation of **5**: the chemical shift of the C_9 in *anti*-**5** is 9.1 ppm down field relative to that in *syn*-**5**. Therefore the anomaly in the *anti* conformations must be attributed to the steric strain rather than the electronic effect.

The smaller J_{C-H} of the *t*-butyl compound (**12**) than **5** may be taken as a reflection of the fact that the *anti* conformation of **12** has more severe steric interaction than *anti*-**5**. The reason for these phenomena is not apparent at present but may be connected to the fact that the 8-methyl-1-naphthyl group is thinner than the 2-*t*-butylphenyl group.

The effect of the 1-methyl group in the fluorene ring on the equilibrium constants seems to be very small. The difference between **4** and **5** may not be taken significant. This is in agreement with others[4,16] which generally show no difference in the equilibrium constants between a parent compound and a 1,4-dimethyl derivative. There is but one case, 9-(2-methylphenyl)-fluorene and its 1,4-dimethyl derivative, which shows a significant dependence of the equilibrium constant

on the 1-methyl group.[2,17]

Rotational Barriers. Kinetic data of internal rotation (*anti*→*syn*) of **4** and **5** are shown in Table 1 with those of related compounds. It is interesting to note that the introduction of a methyl group into the 8-position of the 1-naphthyl group raised the barrier to a considerable extent relative to the parent hydrocarbon (**6**). Since the ground state of *anti*-**4** is of high energy relative to *anti*-**6**, the high barrier for *anti*-**4** must be attributed to the steric repulsion involving the C–H group in the 1-position of the fluorene and the 8-methyl group in the transition state for rotation.

The effect of the 8-methyl group on the transition state seems to be larger than that of the 2-methyl in the naphthyl moiety, from the molecular model considerations. It seems to be reflected to the relatively high barriers to rotation of *anti*-**4** with respect to that of 9-(2-methyl-1-naphthyl)fluorene (**8**), when the very unstable ground state of *anti*-**4** is considered. Introduction of a methyl group into the 1-position of the fluorene ring caused the increase in barriers of *ca.* 3 kcal/mol and *ca.* 4 kcal/mol for the pairs of **6** : **7** and **8** : **9**, respectively, whereas the increase for the pair of **4** : **5** is 1.3 kcal/mol. The relative unimportance of the 1-methyl in *anti*-**5** in determining the barrier height may be attributed to two factors. The first is the rise of the ground state of *anti*-**5**: this will make the difference in energies between the *anti* and the transition state smaller. The second is the geometry of the transition state. The molecular model indicates that **5** can assume a transition state for rotation in which the 8-methyl group of the naphthyl avoids the 1-methyl of the fluorene. Then the transition state for rotation of **5** is very similar with that of **4**, unlike the case of a pair of **8** and **9**. The situation is rather close to that of **6** and **7** pair. Combination of these factors can give the smallest difference in barriers to rotation in the pair of **4** and **5**, if the difference is compared with others in Table 1.

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