Restricted Rotation Involving the Tetrahedral Carbon. XLIII. Buttressing Effect on Rotational Barriers in Bromine-substituted 9-(2-Methoxy-4,6-dimethylphenyl)fluorenes[1]

Masahiro Aoki, Mikio Nakamura,† and Michinori Ōki*

Department of Chemistry, Faculty of Science, The University of Tokyo, Bunkyo-ku, Tokyo 113

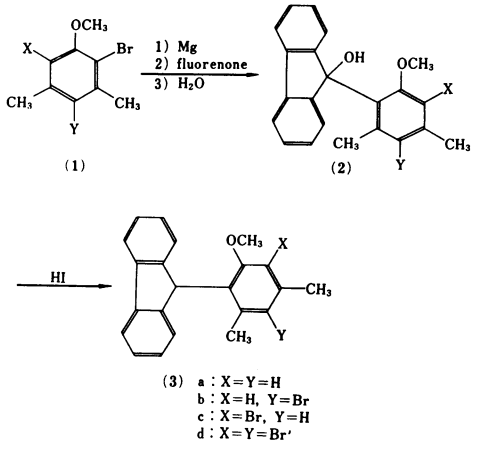
†*Department of Chemistry, School of Medicine, Toho University, Omorinishi, Ota-ku, Tokyo 143*

(Received March 30, 1982)

9-(2-Methoxy-4,6-dimethylphenyl)fluorenes carrying one or two bromo groups on the phenyl ring were prepared and the buttressing effect on the rotational barrier about the C_9–C_{ph} bond were investigated. The free energies of activation for rotation were 26.5, 25.9, and 27.2 kcal/mol at 56 °C for 3-bromo, 5-bromo, and 3,5-dibromo compounds, respectively. The buttressing effect was enhanced when the bromo group was next to the methoxyl group relative to that given to the methyl group. The results were attributed to the fact that a methoxyl group, which gives its steric effect by the oxygen atom in the normal cases, has to take conformations, not coplanar with the phenyl ring, caused by the presence of the bromo group.

Buttressing effect was found in biphenyls: barrier to rotation is raised if a substituent is introduced next to a substituent which gives direct interaction with others in the transition state for rotation. Thus in biphenyls, the barriers are enhanced by the buttressing effect.[2] However, buttressing effect does not always enhance the barrier to rotation. There is a case in which buttressing effect lowers the barrier in a triptycene system.[3] Since both triptycenes and 9-arylfluorenes are congested systems in the ground state, it is worthwhile to see whether the buttressing effect enhances the barrier to rotation in the 9-arylfluorene system. This paper reports the results of such an investigation.

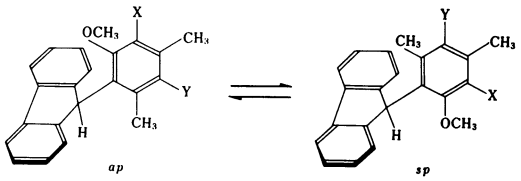
Syntheses of required compounds were carried out in the following way. 2,4,6-Tribromo-3,5-dimethylanisole (**1d**) was prepared according to a known method. 2,4-Dibromo-3,5-dimethylanisole (**1b**) had been prepared by a cumbersome method but we found that bromination of 3,5-dimethylanisole with 2 mol of bromine gave a satisfactory result. Preparation of 2,6-dibromo-3,5-dimethylphenol was described in a patent which utilizes the isomerization of a 2,4-dibromo isomer.[4] However, tracing the method revealed that it was not satisfactory for the preparative purpose. Thus we utilized a method which had been used for preparation of 2,6-dibromophenol.[5] The method, when applied to 3,5-dimethylphenol, gave a satisfactory yield of 2,6-dibromo, -3,5-dimethylphenol which was methylated to afford 2,6-dibromo-3,5-dimethylanisole (**1c**). The bromoanisoles (**1**) were converted to Grignard reagents which were allowed to react with fluorenone. The products (**2**) were reduced to give the desired monobromo or dibromo derivatives (**3**) of 9-(2-methoxy-4,6-dimethylphenyl)-fluorene.



(1) (2)

(3) a : X=Y=H
b : X=H, Y=Br
c : X=Br, Y=H
d : X=Y=Br

The assignment of the stereostructures of the products (**2** and **3**) was performed in the usual way. The *ap* forms exhibited a high field signal due to the methoxyl group in ^{1}H NMR spectroscopy relative to the *sp*, because the methoxyl group is located over the fluorene ring in the *ap*. The reverse is true for the 6-methyl protons: they give a low field signal in the *ap* conformation and a high field signal in the *sp*.



Rates of isomerization of compounds **3b—d** at various temperatures are summarized in Tables 1—3. Kinetic parameters obtained by putting the rate data into the Eyring equation are shown in Table 4 together with those for the unsubstituted compound (**3a**),[6] for comparison. The data clearly show that there is the buttressing effect operating in compounds **3b—d**. We may call now the buttressing effect which raises the

Table 1. Rates of isomerization and equilibrium constants of rotamers in 9-(5-bromo-2-methoxy-4,6-dimethylphenyl)fluorene (**3b**) in tetrachloroethene

Temp/°C	$k(sp \rightarrow ap)/s^{-1}$	$K(sp/ap)$
49.4	2.14×10^{-5}	5.71
56.5	4.73×10^{-5}	5.38
64.2	1.02×10^{-4}	5.29
69.4	1.73×10^{-4}	5.11

Table 2. Rates of isomerization and equilibrium constants of rotamers in 9-(3-bromo-2-methoxy-4,6-dimethylphenyl)fluorene (**3c**) in tetrachloroethene

Temp/°C	$k(sp \rightarrow ap)/s^{-1}$	$K(sp/ap)$
56.3	1.73×10^{-5}	5.43
64.3	4.20×10^{-5}	5.30
68.9	6.68×10^{-5}	5.21
78.4	1.73×10^{-4}	5.11

Table 3. Rates of isomerization and equilibrium constants of rotamers in 9-(3,5-dibromo-2-methoxy-4,6-dimethylphenyl)fluorene (**3d**) in tetrachloroethene

Temp/°C	$k(sp \rightarrow ap)/s^{-1}$	$K(sp/ap)$
56.3	6.13×10^{-6}	7.08
64.3	1.56×10^{-5}	6.92
69.0	2.67×10^{-5}	6.82
78.4	7.52×10^{-5}	6.70

Table 4. Activation parameters for rotation ($sp \rightarrow ap$) in 9-(2-methoxy-4,6-dimethylphenyl)-fluorene and its bromo derivatives in tetrachloroethene

Compound	Substituent 3-	Substituent 5-	$\Delta H^{\ddagger}$ / kcal mol^{-1}	$\Delta S^{\ddagger}$ / e.u.	$\Delta G^{\ddagger}_{329}$ / kcal mol^{-1}
3a[a]	H	H	24.4±0.1	−1.9±0.1	25.0
3b	H	Br	22.2±0.3	−11.3±0.8	25.9
3c	Br	H	23.2±0.0	−10.0±0.0	26.5
3d	Br	Br	25.4±0.1	−5.4±0.4	27.2

a) Chloroform-*d* solvent.

Table 5. Rates of rotation, free energy of activation for rotation and equilibrium constants of rotamers in 9-(2-methoxy-4,6-dimethylphenyl) fluorene and its bromo derivatives in chloroform-*d* at 56.5 °C

Compound	Substituent 3-	Substituent 5-	$k(sp \rightarrow ap)$ / s^{-1}	$K(sp/ap)$	$\Delta G^{\ddagger}$ / kcal mol^{-1}
3a[a]	H	H	1.74×10^{-4}	3.3	24.9
3b	H	Br	5.39×10^{-5}	3.6	25.8
3c	Br	H	1.83×10^{-5}	5.3	26.5
3d	Br	Br	6.02×10^{-6}	7.0	27.2

a) At 56.3 °C.

barrier to rotation as positive. An interesting point is that the magnitude of the positive buttressing effect is different according to the position of the bromo group. When a bromo group is introduced to the ortho position of the 6-methyl group (**3a**→**3b** or **3c**→**3d**), the barrier is enhanced by less than 1 kcal/mol (1 cal=4.18 J). In contrast, if a bromo group is introduced ortho to the methoxyl group (**3a**→**3c** or **3b**→**3d**), the barrier is raised by *ca.* 1.5 kcal/mol.

The difference in the magnitude of buttressing effect caused by the same substituent may deserve further mention here. Electronic effect[7] may be neglected because a bromo group in the 3-position of the phenyl is ortho to the methoxyl and para to the 6-methyl, whereas that in the 6-position is para to the methoxyl and ortho to the 6-methyl. Probably the most important point is that a methoxyl group has an additional bond which can be involved in forming varieties of conformations: that is the CH_3–O bond. Anisole is known to be an almost planar molecule,[8] which can be interpreted that maximum stabilization is obtained in this conformation because of delocalization of electrons. However, if both ortho positions of the methoxyl group are occupied by substituents, the planar structure is no longer stable owing to the steric effect. There are some examples known in the literature.[9] If the methoxyl group in compound **3** is not coplanar with the phenyl group, the transition state for rotation rather than the ground state will be affected, as molecular models suggest. In conclusion, there are two facets of buttressing effect: prevention of angle deformation and the increase in relative bulkiness of a group by preventing certain conformations. In the methoxyl group, both factors are operative. By preventing the planar structure of the methoxyl group with the phenyl, the buttressing effect may even play a role of lengthening the C_{ar}–O bond, although the effect of this lengthening is not well understood. In contrast, the 6-methyl group suffers the buttressing effect of the neighboring group by being prevented from its angle deformation only.

The equilibrium constants suggest that the *sp* conformation is favored in every case. The reason for this is not well understood at the moment but it is possible that the solute-solvent interaction which is more favorable in the *sp* conformation than the *ap* is one of important reasons.

The kinetic and equilibrium data were obtained with chloroform-*d* solutions to see the effect of a weak hydrogen bonding.[10] The results are shown in Table 5. The free energies of activation were almost the same for the two kinds of solutions, *viz.* tetrachloroethene and chloroform-*d*. However, it is interesting to note that the *sp* form of **3c** and **3d** which carry the 3-bromo group shows larger K values (sp/ap) than **3a** and **3b** which lack the 3-bromo. It is possible that the hydrogen bond stabilization is more effective in the *sp* forms of **3c** and **3d** because their *ap* forms are really congested.

Experimental

*2,4,6-Tribromo-3,5-dimethylanisole (**1d**)* was prepared as described in the literature.[11]

*2,4-Dibromo-3,5-dimethylanisole (**1b**).* To a solution of 14 g (0.10 mol) of 3,5-dimethylanisole[12] in 50 mL of acetic acid, was added a solution of 32 g (0.20 mol) of bromine in 30 mL of acetic acid with stirring and cooling. The mixture was poured into water and crystals were collected by filtration. Although the product contained some monobrominated compounds, recrystallization of the mixture from benzene afforded 22.5 g (76.6%) of pure **1b**, mp 108—109 °C (lit,[13] mp 108—109 °C). ^{1}H NMR ($CDCl_3$, δ): 2.39 (3H, s), 2.61 (3H, s), 3.84 (3H, s), 6.63 (1H, s).

*2,6-Dibromo-3,5-dimethylanisole (**1c**).* To a cooled solu-

tion of 14.7 g (0.20 mol) of *t*-butylamine in 250 mL of toluene, 16.0 g (0.10 mol) of bromine was added at −20——30 °C in about 10 min. To the mixture cooled at −70——75 °C was added 6.1 g (0.05 mol) of 3,5-dimethylphenol in 30 mL of dichloromethane in 5 min with vigorous stirring. The stirring was continued for 9 h at that temperature and then the mixture was allowed to warm up to room temperature. The organic layer was extracted with 10% aqueous sodium hydroxide and the extract was acidified. Extraction of the mixture with dichloromethane and evaporation of the solvent left a solid residue. Treatment of the residue with hexane separated the desired product as an insoluble part. The crude yield was 58.6%. Recrystallization of the product from hexane afforded pure 2,6-dibromo-3,5-dimethylphenol, mp 93.5—94 °C. Found: C, 34.03; H, 2.95; Br, 57.05%. Calcd for $C_8H_8Br_2O$: C, 34.32; H, 2.88; Br, 57.08%. ^{1}H NMR ($CDCl_3$, δ): 2.34 (6H, s), 5.93 (1H, s), 6.74 (1H, s).

Treatment of the phenol (2.8 g) with 0.4 g of sodium hydroxide in 30 mL of water and 0.94 mL of dimethyl sulfate afforded 52.0% **1c** as a waxy solid. This compound was directly used for the next reaction. ^{1}H NMR ($CDCl_3$, δ): 2.34 (6H, s), 3.85 (3H, s), 6.93 (1H, s).

*9-(5-Bromo-2-methoxy-4,6-dimethylphenyl)fluoren-9-ol (**2b**).* To a vigorously stirred solution of 5-bromo-2-methoxy-4,6-dimethylphenylmagnesium bromide, prepared from 14.7 g (0.050 mol) of **1b** and 1.20 g (0.050 mol) of magnesium in tetrahydrofuran, was added 7.0 g (0.039 mol) of fluorenone in portions at 0 °C. The reaction mixture was stirred for 1 h at room temperature and was then heated under reflux for 2 h. The mixture was cooled and decomposed with aqueous ammonium chloride. The organic layer was separated and dried over magnesium sulfate. After evaporation of the solvent, the products were separated by chromatography on alumina, benzene–hexane mixtures being used as eluent. **2b**, mp 147—149 °C, was eluted first and then came a mixture of **2b** and 9-(3-bromo-4-methoxy-2,6-dimethylphenyl)fluoren-9-ol, as judged by its ^{1}H NMR spectrum ($CDCl_3$, δ): *sp*, 1.32 (3H, s), 1.75 (1H, s), 2.84 (3H, s), 3.75 (3H, s), 6.52 (1H, s), 7.0—7.6 (8H, m); *ap*, 1.13 (3H, s), 1.84 (1H, s), 3.01 (3H, s), 3.64 (3H, s), 6.13 (1H, s), 7.0—7.6 (8H, m). The *sp*/*ap* ratio of the latter was 0.5. The ratio of **2b** to 9-(3-bromo-4-methoxy-2,6-dimethylphenyl)fluoren-9-ol was 3 : 1 as ^{1}H NMR spectra indicated. The yield of **2b** was 57% based on fluorenone. Found: C, 67.03; H, 4.70; Br, 19.96%. Calcd for $C_{22}H_{19}BrO_2$: C, 66.84; H. 4.84; Br, 20.21%. ^{1}H NMR ($CDCl_3$ δ) indicated that **2b** was a mixture of *sp* and *ap* rotamers (8 : 1). *sp*: 1.45 (3H, s), 2.40 (3H, s), 4.03 (3H, s), 6.82 (1H, s), 6.90 (1H, s), 7.1—7.7 (8H, m). *ap*: 2.10 (1H, s), 2.40 (3H, s), 2.85 (3H, s), 3.12 (3H, s), 6.45 (1H, s), 7.1—7.7 (8H, m).

*9-(3,5-Dibromo-2-methoxy-4,6-dimethylphenyl)fluoren-9-ol (**2d**),* mp 159—161 °C, was similarly prepared by treating 3,5-dibromo-2-methoxy-4,6-dimethylphenylmagnesium bromide, which was prepared from **1d**, with fluorenone. The yield was 43%. Found: C, 55.89; H, 3.68; Br, 33.67%. Calcd for $C_{22}H_{18}Br_2O_2$: C, 55.72; H, 3.83; Br, 33.67%. ^{1}H NMR ($CDCl_3$, δ) indicated that the compound was a 4 : 1 mixture of *sp* and *ap* forms: *sp*, 1.45 (3H, s), 2.70 (3H, s), 4.16 (3H, s), 6.57 (1H, s), 7.1—7.8 (8H, m); *ap*, 2.18 (1H, s), 2.65 (3H, s), 2.70 (3H, s), 3.10 (3H, s), 7.1—7.8 (8H, m).

*9-(3-Bromo-2-methoxy-4,6-dimethylphenyl)fluoren-9-ol (**2c**)* was similarly prepared from **1c** in 47% yield. ^{1}H NMR ($CDCl_3$, δ) indicated that the product was a 3.4 : 1 mixture of *sp* and *ap* forms: *sp*, 1.19 (3H, s), 2.36 (3H, s), 4.17 (3H, s), 6.85 (1H, s), 6.66 (1H, s), 7.1—7.8 (8H, m); *ap*, 2.06 (1H, s), 2.32 (3H, s), 2.65 (3H, s), 2.88 (3H, s), 6.93 (1H, s), 7.1—7.8 (8H, m). The product was directly used for reduction which is described below.

*9-(5-Bromo-2-methoxy-4,6-dimethylphenyl)fluorene (**3b**).* To a solution of 1.35 g (3.4 mmol) of **2b** in 50 mL of acetic acid was added 10 mL of 57% hydriodic acid. The solution was stirred for 3 h at 20 °C and poured into water. The organic materials were extracted with ether and the extract was washed with aqueous sodium hydrogencarbonate and then with aqueous sodium sulfite. The ethereal solution was dried over sodium sulfate. The solvent was evaporated and the residue was submitted to chromatography on alumina, hexane being used as an eluent. The chromatographed product was recrystallized from hexane to give pure *sp* form of **3b** in 92% yield. The melting point was 149—150 °C. Found: C, 69.83; H, 4.87; Br, 21.39%. Calcd for $C_{22}H_{19}BrO$: C, 69.67; H, 5.05; Br, 21.07%. ^{1}H NMR ($CDCl_3$, δ): 1.26 (3H, s), 2.43 (3H, s), 3.91 (3H, s), 6.02 (1H, s), 6.85 (1H, s), 7.1—7.9 (8H, m).

A rotameric mixture, which was obtained as the result of isomerization works, was submitted to TLC on alumina with hexane eluent. The *sp* form had a larger R_f value than the *ap*. Rechromatography afforded pure *ap*-**3b**, mp 132.2—133.0 °C. High resolution mass spectrum showed molecular ion peaks at 378.0675 and 380.0583, whereas $C_{22}H_{19}BrO$ requires 378.0620 and 380.0598. The relative intensities of the two peaks agreed well with those expected from the natural abundance of ^{79}Br and ^{81}Br. ^{1}H NMR ($CDCl_3$, δ): 2.38 (3H, s), 2.85 (3H, s), 2.88 (3H, s), 5.32 (1H, s), 6.45 (1H, s), 7.1—7.9 (8H, m).

*9-(3,5-Dibromo-2-methoxy-4,6-dimethylphenyl)fluorene (**3d**),* mp 149—151 °C, was prepared similarly in 35% yield. Found: C, 57.57; H, 3.75; Br, 34.62%. Calcd for $C_{22}H_{18}Br_2O$: C, 57.67; H, 3.60; Br, 34.88%. ^{1}H NMR ($CDCl_3$, δ) data indicated that the product was pure *sp*-**3d**: 1.23 (3H, s), 2.66 (3H, s), 3.99 (3H, s), 5.87 (1H, s), 7.1—7.9 (8H, m). Since the population ratio at the equilibrium was very large, the isolation of the *ap*-form was not attempted. The following ^{1}H NMR ($CDCl_3$, δ) data for the *ap* form were recorded: 2.62 (3H, s), 2.65 (3H, s), 2.87 (3H, s), 5.39 (1H, s), 7.1—7.9 (8H, m).

*9-(3-Bromo-2-methoxy-4,6-dimethylphenyl)fluorene (**3c**)* was prepared similarly. Unlike other related compounds, reduction of 0.92 g of **2c** afforded 0.30 g of *sp*, mp 136.5—137.0 °C, and 0.28 g of *ap*, mp 115.5—116.5 °C, the total yield being 66.5%. The following ^{1}H NMR data ($CDCl_3$, δ) and analytical data were obtained.

sp. Found: C, 69.59; H, 5.00; Br, 21.39%. Calcd for $C_{22}H_{19}BrO$: C, 69.67; H, 5.05; Br, 21.07%. NMR: 1.04 (3H, s), 2.36 (3H, s), 4.03 (3H, s), 5.78 (1H, s), 6.64 (1H, s), 7.1—7.9 (8H, m).

ap. High resolution mass spectrum showed molecular ion peaks at 378.0604 and 380.0581, while $C_{22}H_{19}BrO$ requires 378.0620 and 380.0598. NMR: 2.35 (3H, s), 2.63 (3H, s), 2.63 (3H, s), 2.66 (3H, s), 5.22 (1H, s), 6.97 (1H, s), 7.1—7.9 (8H, m).

Determination of Barriers to Rotation. A pure sample (*ca.* 40 mg) of *sp*-**3** was dissolved in *ca.* 0.5 mL of tetrachloroethene or chloroform-*d* and placed in an NMR sample tube. The tube was immersed in an appropriate boiling-solvent bath, temperature being checked by a thermometer, and the appearance of *ap*-**3** was followed by ^{1}H NMR spectroscopy. The data were treated by assuming a reversible first-order reaction and the rate constants were put into the Eyring equation to obtain activation parameters. The following solvents were used for the bath (solvents and approximate temperatures given): methanol–hexane azeotrope (49.4 °C), acetone (56.5 °C), methanol (64 °C), hexane (69 °C), and ethanol (78 °C).

NMR Measurement. The spectra were obtained with

either a Varian EM 390 spectrometer or a Hitachi R-20B spectrometer. Integration was carried out 8—10 times and the average was used for the kinetic measurement.

References

1) For Part XLII, see R. Saito and M. Ōki, *Bull. Chem. Soc. Jpn.*, **55**, 2508 (1982).
2) S. L. Chen and R. Adams, *J. Am. Chem. Soc.*, **56**, 1787 (1934).
3) G. Yamamoto, M. Suzuki, and M. Ōki, *Chem. Lett.*, **1980**, 1523.
4) E. J. O'Bara, Brit. Patent 1269521; *Chem. Abstr.*, **76**, 15335g (1972); See also E. J. O'Bara, R. B. Balsley, and I. Starter, *J. Org. Chem.*, **35**, 16 (1970).
5) D. E. Pearson, R. D. Wysong, and C. V. Breder, *J. Org. Chem.*, **32**, 2358 (1967).
6) M. Nakamura and M. Ōki, *Bull. Chem. Soc. Jpn.*, **53**, 3248 (1980).
7) M. Ōki and G. Yamamoto, *Bull. Chem. Soc. Jpn.*, **44**, 266 (1971).
8) H. M. Seip and R. Seip, *Acta Chem. Scand.*, **27**, 4024 (1973).
9) M. J. Aroney, M. G. Corfield, and R. J. W. Le Ferve, *J. Chem. Soc.*, **1964**, 2954.
10) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco (1960), p. 197.
11) M. Kohn and M. K. Feldmann, *Monats. Chem.*, **49**, 170 (1982).
12) G. S. Hiers and F. D. Hager, *Org. Synth.*, Coll. Vol. I, 58 (1958).
13) K. V. Awers, *Justus Liebigs Ann. Chem.*, **421**, 1 (1920).