Synthesis and NMR Study of 9'-Substituted Spiroindolinonaphthoxazine Derivatives

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A photochromic spiroindolinonaphthoxazine derivative, 1,3,3-trimethyl-9'-hydroxy-spiro[indoline-2,3'(3*H*)-naphtho[2,1-*b*][1,4]oxazine] **3** was synthesized by condensation of 1,2,3,3-tetramethylindolenium iodide **1** and 1-nitroso-2,7-dihydroxynaphthalene **2**. Further, two new derivatives, **5** and **7**, were prepared in good yields by the reactions of **3** with the hexafluoropropene trimer **4** and 4-[perfluoro(2-isopropyl-1,3-dimethyl-1-butenyl)-oxybenzoyl chloride **6**, respectively. Their unique structural features and property are discussed based on ^{1}H-, ^{13}C- and ^{19}F nmr spectral data.

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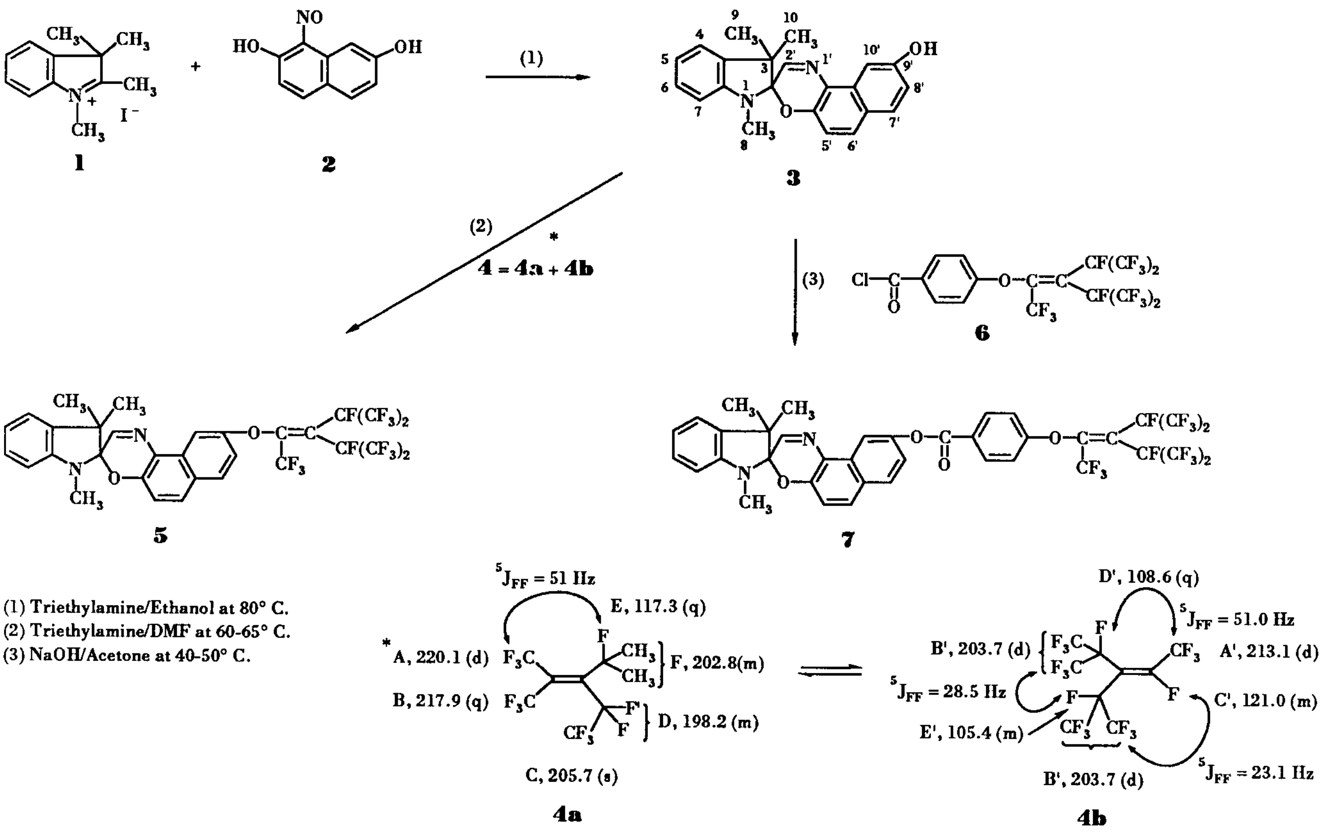
Introduction.

The photochromic phenomenon of two spiroindolinonaphthoxazine derivatives, 1,3,3-trimethylspiro[indoline-2,3'(3*H*)naphtho[2,1-*b*][1,4]oxazine] **8** (X = H) and the 5-chloro-1,3,3,-trimethyl-derivative **9** (X = Cl) was first reported by Fox in 1961 [1] and then, investigated by Brown [2]. Two reports on **8** dealing with its photochromic and thermodynamic behaviors in organic solvents [3] and with its unique behavior such as photochromism and tolerance for repetition in a polymer matrix [4], have drawn an in-

Scheme 1



(1) Triethylamine/Ethanol at 80° C.
(2) Triethylamine/DMF at 60-65° C.
(3) NaOH/Acetone at 40-50° C.

creasing attention to these kinds of compounds [5]. Many spiroindolinonaphthoxazine derivatives such as those having alkyl, alkoxy, alkoxycarbonyl, halogen and nitro substituents have been prepared [6]. Despite the large number of publications dealing with their synthesis, detailed analysis of their unique structural features, that are essential for understanding of their reactivities and photochromic phenomenon, these do not seem to be reported yet to the best of our knowledge. We wish to report herein a detailed analysis of the ^{1}H- and ^{13}C nmr spectra of the newly synthesized spiroindolinonaphthoxazine derivatives **3** [7] in comparison with the known **8**. Furthermore, two new derivatives, **5** and **7** derived by reaction of **3** with the hexafluoropropene trimer **4** and 4-[perfluoro(2-isopropyl-1,3-dimethyl-1-butenyl)oxybenzoyl chloride **6**, respectively, are discussed based on their ^{1}H-, ^{13}C-, and in particular on the ^{19}F nmr spectral data. Effects of substituent groups on chemical shifts of the ^{1}H nmr spectra are also discussed.

Results and Discussion.

A new spiroindolinonaphthoxazine **3** was obtained as colorless crystals in 50% yield by condensation of 1,2,3,3-tetramethylindolenium iodide **1** with 1-nitroso-2,7-dihydroxynaphthalene **2** under standard conditions, followed by recrystallization from ethanol (Scheme 1). The struc-

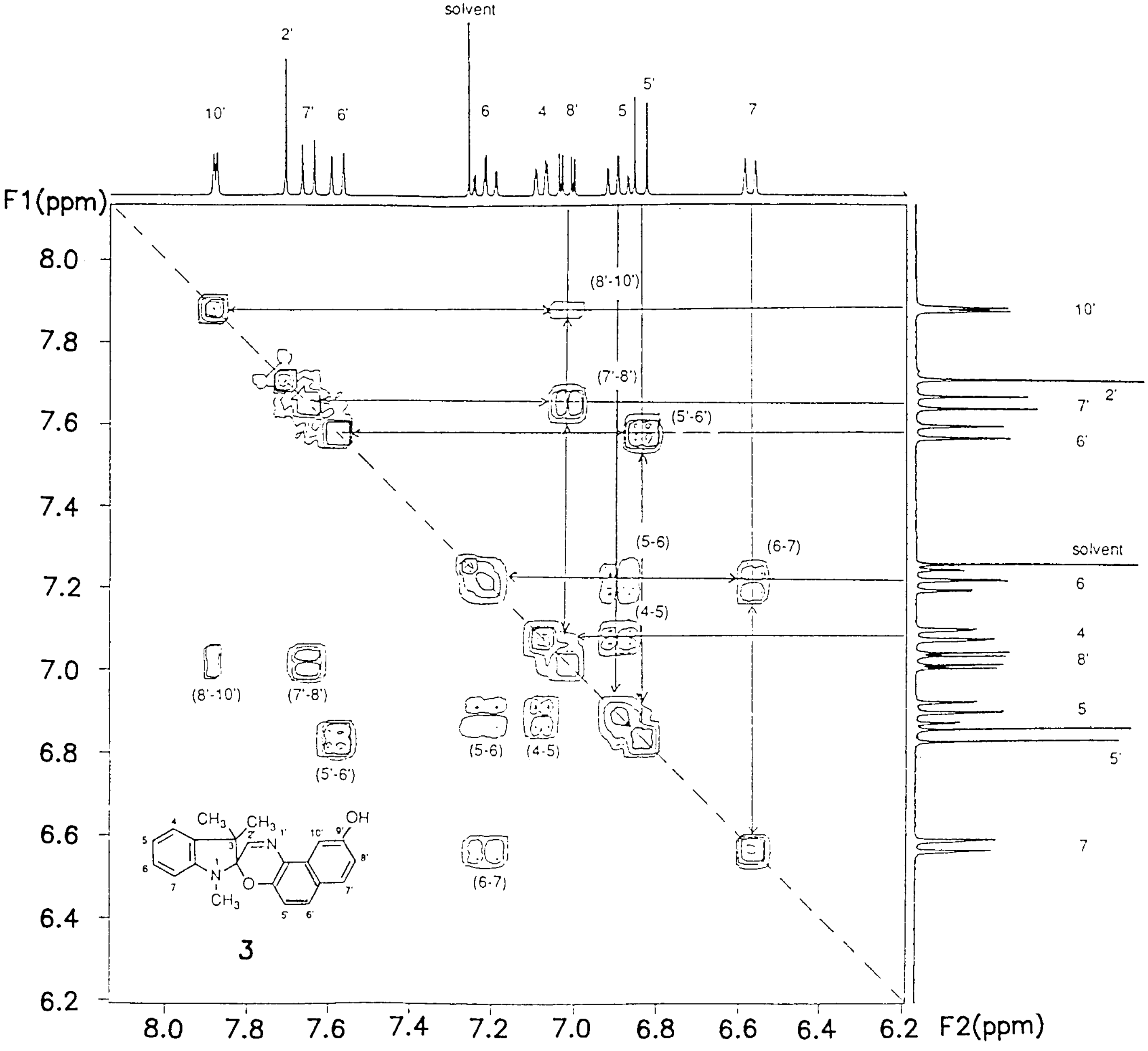
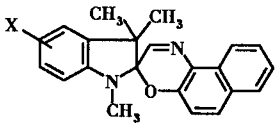


Figure 1. Contour plot of 300 MHz ^{1}H–^{1}H COSY spectrum of **3** in deuteriochloroform.

ture of **3** is supported by spectral data and analysis. The remaining of 9'-hydroxy group on the naphthalene ring of **3** was in accord with the vicinal proton-proton connectivities observed by the ^{1}H-^{1}H COSY spectrum of **3** as shown in Figure 1. The indicated assignments are straightforward for **3** by comparison with literature data [9]. The 10'-H signal appeared at δ 7.88 as a doublet ($J = 2.7$ Hz). This was due to a long range coupling with 8'-H. The 8'-H was assigned to the signal at δ 7.02 from the same long range coupling constant. Indeed there is a cross peak of 8'-H with 10'-H in Figure 1. All other protons of **3** were assignable and are summarized in Table 1 and Figure 2 in comparison with those of **8**.



8 X = H **9** X = Cl

In the Table, the chemical shift differences between **8** and **3** ($\Delta\delta$) are also shown. From the $\Delta\delta$ values, the electron-donating nature of 9'-hydroxy group is clearly reflected by the shift of 10'-H and 8'-H to higher field [10]. The 5'-H, 6'-H, 7'-H and 2'-H appeared also at higher field (see also Figure 2 for comparison with **5** and **7**). The ^{1}H-^{1}H NOESY spectrum of **3** is also investigated. On the basis of

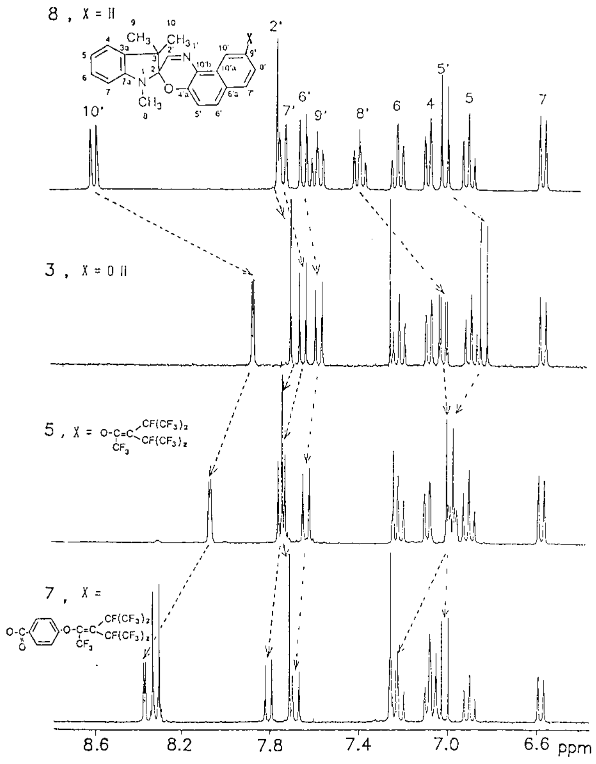


Figure 2. ^{1}H–nmr spectra (aromatic proton regions) spiroindolinonaphthoxazine derivatives.

Table 2 (1)

^{13}C NMR Spectral Data of Spiroindolinonaphthoxazine Derivatives **3, 5, 7** and **8** (Naphthoxazine Regions) [a]

Compound	2'-C	4'a-C	5'-C	6'-C	6'a-C	7'-C	8'-C	9'-C	10'-C	10'a-C	10'b-C
8	150.8	147.6	116.8	128.1	130.9	127.8	124.2	127.2	121.5	123.0	144.2
3	150.4	147.6	114.2	130.0	132.4	130.2	115.8	155.0	103.7	121.9	145.0
5	151.0	147.5	114.2	129.9	132.0	130.3	116.8	153.9	107.2	122.7	145.3
7	150.9	147.6	113.1	129.5	131.9	130.1	116.8	158.5	107.2	123.0	144.9
$\Delta\delta_3$ [b]	0.4	0	2.6	-1.9	-1.5	-2.4	8.4	-27.8	17.8	1.1	-0.8
$\Delta\delta_5$ [c]	-0.2	0.1	2.6	-1.8	-1.1	-2.5	7.4	-26.7	14.3	0.3	-1.1
$\Delta\delta_7$ [d]	-0.1	0	3.7	-1.4	-1.0	-2.3	7.4	-31.3	14.3	0	-0.7

[a] Chemical shift δ c (ppm): solvent deuteriochloroform-TMS. [b] $\Delta\delta_3=\delta_{C8}-\delta_{C3}$. [c] $\Delta\delta_5=\delta_{C8}-\delta_{C5}$. [d] $\Delta\delta_7=\delta_{C8}-\delta_{C7}$.

Table 2 (2)

^{13}C NMR Spectral Data of Spiroindolinonaphthoxazine Derivatives **3, 5, 7** and **8** (Spiroindole Regions) [a]

Compound	2-C	3-C	3a-C	4-C	5-C	6-C	7-C	7a-C	8-C	9-C	10-C
8	98.6	51.8	129.3	121.5	119.9	128.1	107.2	135.9	29.7	25.5	20.8
3	98.6	51.8	124.7	121.5	119.9	128.0	107.1	135.9	29.7	25.5	20.8
5	98.9	51.9	126.5	121.5	120.0	128.1	107.2	135.8	29.6	25.5	20.7
7	98.8	51.9	126.9	121.5	120.0	128.1	107.2	135.8	29.7	25.4	20.8
$\Delta\delta_3$ [b]	0	0	4.6	0	0	0.1	0.1	0	0	0	0
$\Delta\delta_5$ [c]	-0.3	-0.1	2.8	0	-0.1	0	0	0.1	0.1	0	0.1
$\Delta\delta_7$ [d]	-0.2	-0.1	2.4	0	-0.1	0	0	0.1	0	0.1	0

[a] Chemical shift δ c (ppm): solvent deuteriochloroform-TMS. [b] $\Delta\delta_3=\delta_{C8}-\delta_{C3}$. [c] $\Delta\delta_5=\delta_{C8}-\delta_{C5}$. [d] $\Delta\delta_7=\delta_{C8}-\delta_{C7}$.

Table 1

^{1}H NMR Spectral Data of Spiroindolinonaphthoxazine Derivatives **3**, **5**, **7** and **8** [a]

Compound	2'-H	5'-H	6'-H	7'-H	8'-H	9'-H	10'-H	4-H	5-H	6-H	7-H	8-H	9-H	10-H	Phenyl-H
8	7.75(s)	7.00 (d)	7.67 (d)	7.75 (d)	7.40 (t)	7.58 (t)	8.56 (d)	7.09 (d)	6.90 (t)	7.22 (t)	6.58 (d)	2.77 (s)	1.37 (s)	1.35 (s)	-
3	7.71(s)	6.84 (d)	7.58 (d)	7.65 (d)	7.02 (d)	-	7.88 (s)	7.08 (d)	6.89 (t)	7.22 (t)	6.57 (d)	2.77 (s)	1.37 (s)	1.35 (s)	-
5	7.75 (s)	7.01 (d)	7.65 (d)	7.76 (d)	6.99 (d)	-	8.06 (s)	7.10 (d)	6.91 (t)	7.23 (t)	6.59 (d)	2.75 (s)	1.37 (s)	1.36 (s)	-
7	7.72 (s)	7.02 (d)	7.69 (d)	7.81 (d)	7.26 (d)	-	8.37 (s)	7.10 (d)	6.91 (t)	7.23 (t)	6.59 (d)	2.75 (s)	1.37 (s)	1.36 (s)	7.08, 8.32 (d)
$\Delta\delta_3$ [b]	0.04	0.16	0.09	0.10	0.38	-	0.68	0.01	0.01	0	0.01	0	0	0	
$\Delta\delta_5$ [c]	0	-0.01	0.02	-0.01	0.31	-	0.50	-0.01	-0.01	-0.01	-0.01	-0.02	0	-0.01	
$\Delta\delta_7$ [d]	0.03	-0.02	-0.02	-0.06	0.14	-	0.19	-0.01	-0.01	-0.01	-0.01	0.02	0	-0.01	

[a] Chemical Shifts δ_H(ppm); solvent deuteriochloroform-TMS. [b] $\Delta\delta_3 = \delta_{H8}-\delta_{H3}$. [c] $\Delta\delta_5 = \delta_{H8}-\delta_{H5}$. [d] $\Delta\delta_7 = \delta_{H8}-\delta_{H7}$.

the NOEs between the methyl group at 3-C with 2'-H and 4-H, and the methyl group at 1-N with 7-H respectively, the stereochemical correlation of these protons could be assigned. Further, on the basis of the ^{1}H-^{13}C COSY spectrum of **3** [9], we could assign the corresponding chemical shifts of the carbons, as summarized in Table 2. It is clear that the 8'-C and 10'-C were affected (the shift to higher field) by the hydroxy group at 9'-C [11], consistent with that obtained from ^{1}H nmr data.

Introduction of a fluorine-containing substituent into a molecule is known to modify greatly the physicochemical properties and the biological activities [12]. As one of the practical approaches for this purpose, we examined the reaction of **3** with hexafluoropropene trimer **4**. The isomers involved in **4** were confirmed by ^{19}F and ^{13}C nmr spectra. Among the three possible isomers, *i.e.*, perfluoro-3-ethyl-2,4-dimethyl-2-pentene (**4a**), perfluoro-3-(1-methylethyl)-4-methyl-2-pentene (**4b**), perfluoro-2,4-dimethyl-3-heptene (**4c**) [13], the trimer used in this work contained **4a** and **4b**, as a 2:1 tautomeric mixture based on ^{19}F nmr spectrum [14]. The reaction of **3** with **4** in the presence of triethylamine in DMF at 60-65° for 2 hours afforded **5** in 80% yield as colorless crystals after the usual workup and recrystallization from ethanol (Scheme 1). The assignment of ^{19}F nmr spectal data of thus obtained **5** is shown in Figure 3.

The peaks A ~ F and C' of **4** (shown in Scheme 1 as a tautomeric mixture) disappeared and instead, a new peak (B'') at δ 205.2 appeared, indicating that the isomer **4b** reacted selectively with **3** to yield **5**. As the result of reaction of **4b** with the hydroxy group of **3**, the peak (C') at δ 121.0 on **4b** disappeared, and a new peak, B'' appeared. This reaction pattern, *i.e.* addition-elimination sequence is chemically similar to that of phenol [14], indicating that the hydroxy group of **3** is reactive enough against perfluoroalkenes. The ^{1}H and ^{13}C nmr spectral data are also compatible with the given structure (Table 1 and 2).

The reaction of **3** with 4-{perfluoro(2-isopropyl-1,3-dimethyl-1-butenyl)oxy}benzoyl chloride **6** in acetone containing sodium hydroxide at 40-50° for 1 hour gave the ester **7** as colorless crystals in 91% yield. The ^{19}F nmr spectrum of **7** shown in Figure 4 is very similar to that of **5** (Figure 3). On the base of the above ^{19}F nmr spectrum, the chemical structure of **7** was confirmed as shown in Scheme 1 as well as other spectral and analytical data.

The 9'-substituents effects on the ^{1}H chemical shifts (δ) of these spiroindolinonaphthoxazine derivatives are summarized as $\Delta\delta$ values in Table 1 and schematically shown in Figure 2.

Perfluoroalkenylation, **5**, and 4-perfluoroalkenoxybenzoylation, **7**, of 9'-hydroxyl group in **3** reduced clearly the $\Delta\delta$ values for the naphthoxazine ring protons. This may be attributed mainly to the difference of the electron

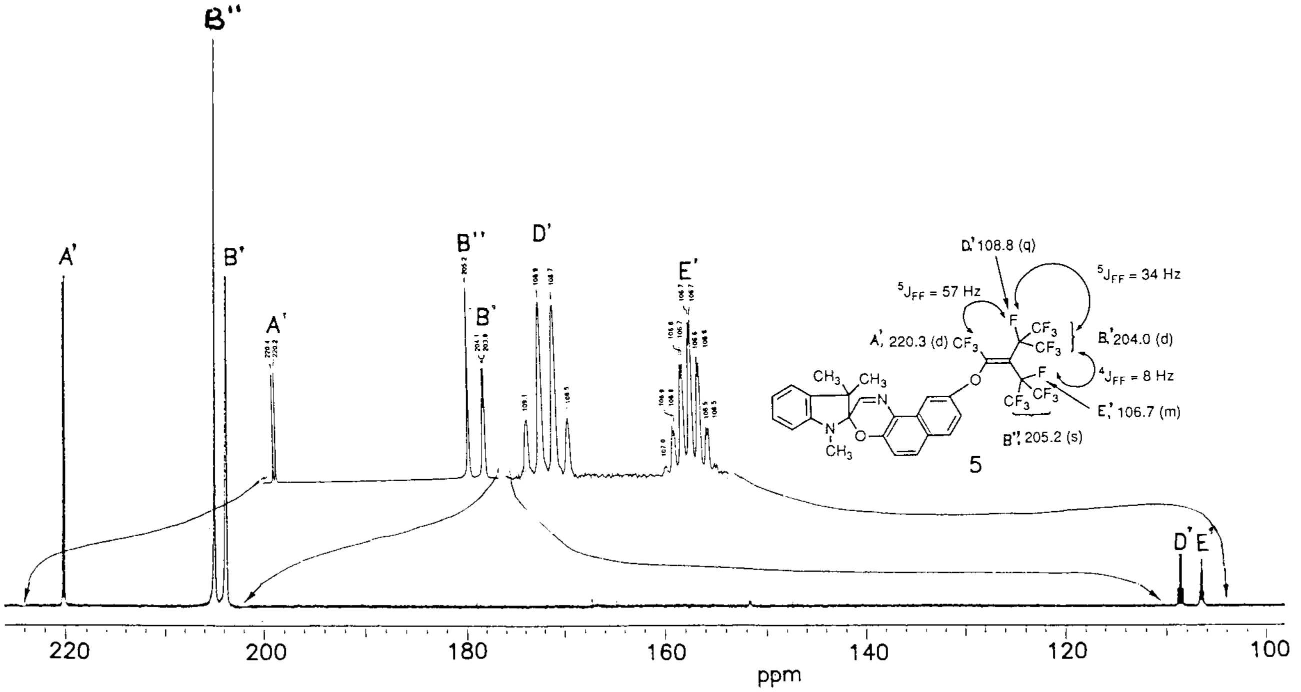


Figure 3. ^{19}F-nmr spectrum of **5** in deuteriochloroform (trifluroacetic acid as an external standard).

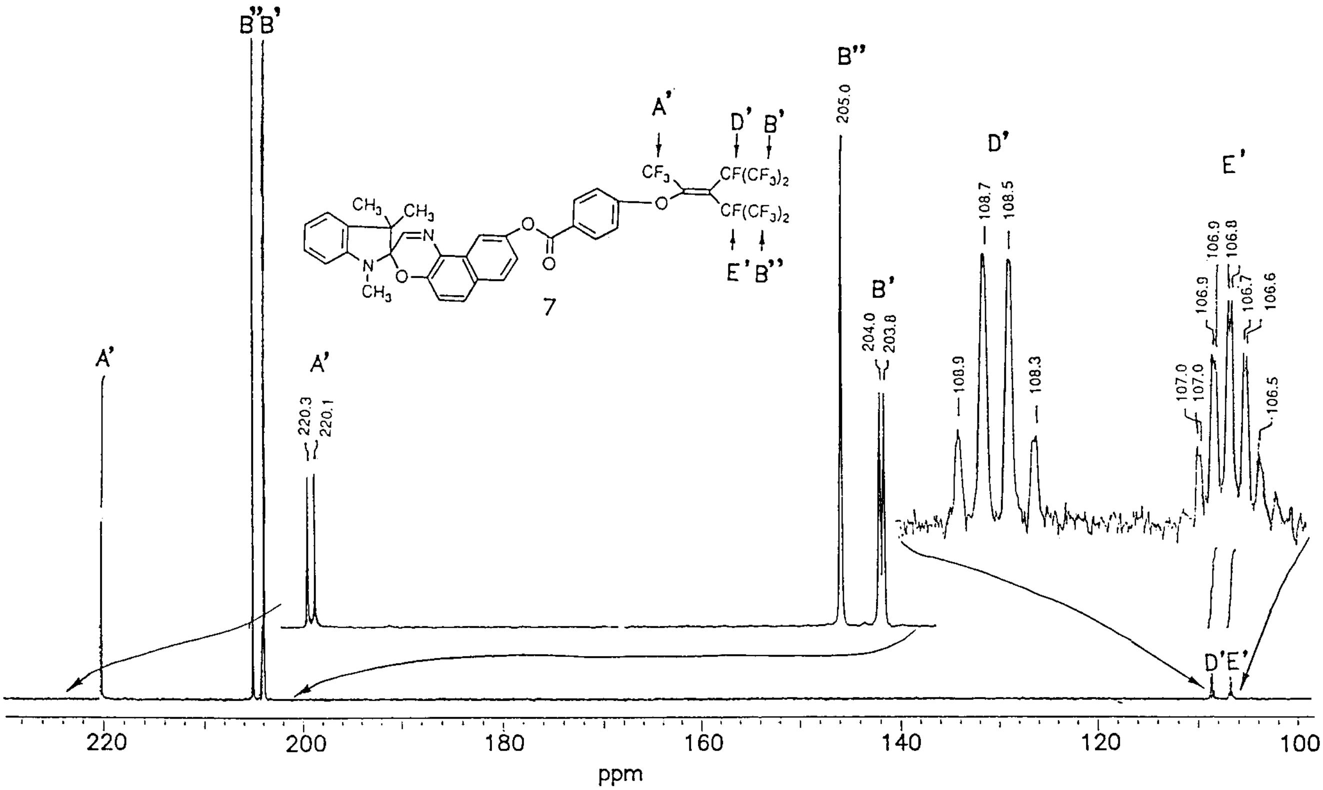


Figure 4. ^{19}F-nmr spectrum of **7** in deuteriochloroform (trifluroacetic acid as an external standard).

donating properties among the substituents [10]. The most influenced proton is 10′-H and then 8′-H. Other protons such as 5′-H, 6′-H, 7′-H and 2′-H were also shifted. These differences may play an important role to control their photochromic behaviors, in particular, in polymer matrices [15].

EXPERIMENTAL

Melting points were determined on a Perkin-Elmer DSC-2C apparatus. Infrared spectra were recorded on a Nicolet 719 FTIR spectrometer as potassium bromide pellets. The ^{1}H- and ^{13}C nmr spectra were recorded on a Varian VXR-300 spectrometer, using tetramethylsilane as internal standard. For ^{19}F nmr spectra, trifluoroacetic acid was used as external standard. The nmr multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet. Microanalysis were performed by a Heraus CHN-O-RAPID element analyser. Compounds **3** and **4** were prepared according to literature procedures [3] and [8], respectively. Pure high grade 4-[perfluoro(2-isopropyl-1,3-dimethyl-1-butenyl)]oxybenzoyl chloride (**6**) (bp 98.5-99.5°/2 mm Hg) was obtained from Neos Co., Ltd. [16].

1,3,3-Trimethyl-9′-hydroxyspiro[indoline-2,3′(3*H*)naphtho[2,1-*b*]-[1,4]oxazine] (**3**).

A solution of 1-nitroso-2,7-dihydroxynaphthalene (**2**) (20.0 g, 106 mmoles) dissolved in 200 ml of ethanol was heated at about 80°. To this solution was added dropwise 100 ml of an ethanol solution containing triethylamine (13.0 g, 220 mmoles) and 1,2,3,3-tetramethylindolenium iodide (**1**) (35 g, 87 mmoles) over a period of 30 minutes, and the mixture was refluxed for 2 hours. The reaction mixture was distilled under reduced pressure until the excess ethanol was reduced to about one-fourth. Upon cooling, there were precipitated crude crystals which were recrystallized from ethanol to afford 15.0 g (50%) of **3** as colorless crystals, mp 224-226°; ^{1}H nmr (deuteriochloroform): δ 7.71 (s, 2′-H), 6.84 (d, 5′-H), 7.58 (d, 6′-H), 7.65 (d, 7′-H), 7.02 (d, 8′-H), 7.88 (s, 10′-H), 7.08 (d, 4-H), 6.89 (t, 5-H), 7.22 (t, 6-H), 6.57 (d, 7-H), 2.77 (s, 8-H), 1.37 (s, 9-H), 1.35 (s, 10-H); ir (potassium bromide): 3325, 3280, 3230, 3216, 3144, 3105, 3051, 2968, 2928, 2904, 2870, 2816, 1913, 1902, 1885, 1843, 1771, 1631, 1608, 1590, 1525, 1511, 1486, 1451, 1426, 1385, 1361, 1302, 1246, 1217, 1198, 1168, 1136, 1119, 1084, 1069, 1034, 1021, 969, 927, 896, 885, 831, 799, 745 cm^{-1}.

Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.43; H, 5.85; N, 8.01.

1,3,3-Trimethyl-9′-[perfluoro(2-isopropyl-1,3-dimethyl-1-butenyl)-oxy]spiro[indoline-2,3′(3*H*)naphtho[2,1-*b*][1,4]oxazine] (**5**).

To a DMF solution (50 ml) of **3** (5.00 g, 14.5 mmoles) and **4** (7.85 g, 17.4 mmoles) was added triethylamine (1.5 g, 15 mmoles). The solution was warmed to 60-65°, and stirred for 2 hours. The resulting reaction mixture was then poured into water. The brown precipitate was collected by filtration. It was then dissolved into acetone and decolorized using activated charcoal powder. The acetone solution was evaporated under reduced pressure to afford white crystals. It was purified further by recrystallization from ethanol to yield **5** 9.0 g (80%), mp 154-156°; ^{1}H nmr (deuteriochloroform): δ 7.75 (s, 2′-H), 7.01 (d, 5′-H), 7.65 (d, 6′-H), 7.76 (d, 7′-H), 6.99 (d, 8′-H), 8.06 (s, 10′-H), 7.10 (d, 4-H), 6.91 (t, 5-H), 7.23 (t, 6-H), 6.59 (d, 7-H), 2.75 (s, 8-H), 1.37 (s, 9-H), 1.36 (s, 10-H); ir (potassium bromide): 3097, 3089, 3068, 3058, 3020, 2999, 2983, 2972, 2945, 2931, 2901, 2890, 2873, 2819, 1626, 1609, 1576, 1513, 1487, 1470, 1445, 1387, 1360, 1291, 1242, 1195, 1128, 1083, 1032, 1016, 979, 905, 880, 866, 850, 835, 795, 744, 734, 704 cm^{-1}.

Anal. Calcd. for $C_{31}H_{19}N_2O_2F_{17}$: C, 48.08; H, 2.47; N, 3.62. Found: C, 48.17; H, 2.52; N, 3.66.

1,3,3-Trimethyl-9′-{4-[perfluoro(2-isopropyl-1,3-dimethyl-1-butenyl)oxy]benzoyl}spiro[indoline-2,3′(3*H*)naphtho[2,1-*b*][1,4]oxazine] (**7**).

A solution of **3** (3.4 g, 10 mmoles) and sodium hydroxide (0.4 g, 10 mmoles) in acetone (100 ml) was heated at 40-50° with stirring. To this solution was added **6** (6.90 g, 10.1 mmoles) dissolved in acetone (10 ml), and stirred for a further 1 hour. The solution was then cooled and the resulting white crystalline precipitate was collected by filtration. After one recrystallization from ethanol, further purification was carried out by dissolving the above crystals in chloroform (100 ml) to remove any insoluble substances such as sodium chloride. The solvent was then removed to afford pure **7** as a colorless crystal 8.1 g (91%), mp 191-193°; ^{1}H nmr (deuteriochloroform): δ 7.72 (s, 2′-H), 7.02 (d, 5′-H), 7.69 (d, 6′-H), 7.81 (d, 7′-H), 7.26 (d, 8′-H), 8.37 (s, 10′-H), 7.10 (d, 4-H), 6.91 (t, 5-H), 7.23 (t, 6-H), 6.59 (d, 7-H), 2.77 (s, 8-H), 1.37 (s, 9-H), 1.36 (s, 10-H), 7.08, 8.32 (d, phenyl protons); ir (potassium bromide): 3104, 3071, 3035, 3019, 2961, 2933, 2902, 2881, 2870, 2808, 1745, 1630, 1600, 1512, 1503, 1486, 1468, 1445, 1420, 1386, 1359, 1291, 1248, 1186, 1134, 1121, 1087, 1065, 1032, 1012, 979, 884, 853, 826, 797, 750, 741, 703 cm^{-1}.

Anal. Calcd. for $C_{38}H_{23}N_2O_4F_{17}$: C, 51.02; H, 2.59; N, 3.13. Found: C, 51.07; H, 2.62; N, 3.02.

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