A Novel Method for the Synthesis of 4-Isoquinolinols

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1-Substituted 1,2-dihydroisoquinolines, derived from isoquinoline and organolithium reagents, readily undergo autoxidation to lead to 4-isoquinolinols in moderate yields.

Isoquinoline alkaloids are widely found in nature and many efforts have been made to construct various isoquinoline skeletons [1]. However, there are few methods available for preparing 4-isoquinolinol derivatives. Only successful methods involve the isomerization of isoquinoline N-oxides by treatment with p-toluenesulfonyl chloride [2] or acetic anhydride [3], and by irradiation with light [4]. In this paper, we wish to report a new simple and apparently general synthesis of 4-isoquinolinol derivatives from isoquinoline based on the air-sensitive property of 1-substituted 1,2-dihydroisoquinolines.

We have recently reported that 1,2-dihydro-1-perfluorohexylisoquinoline (**2b**), obtained by the boron trifluoride-assisted addition of perfluorohexyllithium to isoquinoline, readily underwent autoxidation to give considerable amounts of a hydroxylated 1-perfluorohexylisoquinoline along with the expected 1-perfluorohexylisoquinoline (**4b**) [5]. This unusual product was quantitatively acetylated on treatment with acetic anhydride in pyridine and was tentatively assumed to have a 3-hydroxylated structure. In order to confirm its structure, we attempted to prepare 1-perfluorohexyl-4-isoquinolinol (**3b**) from **4b** according to

Scheme 1
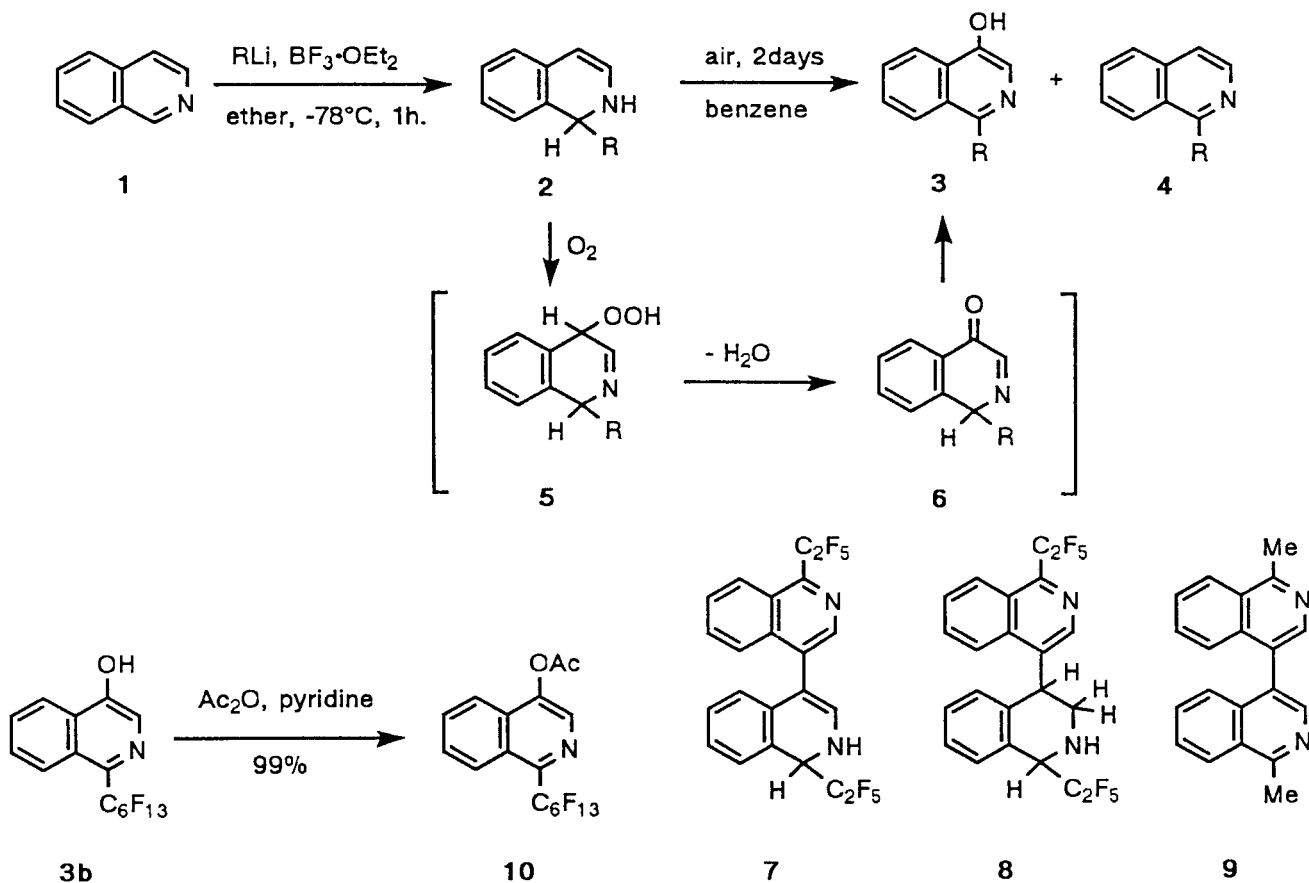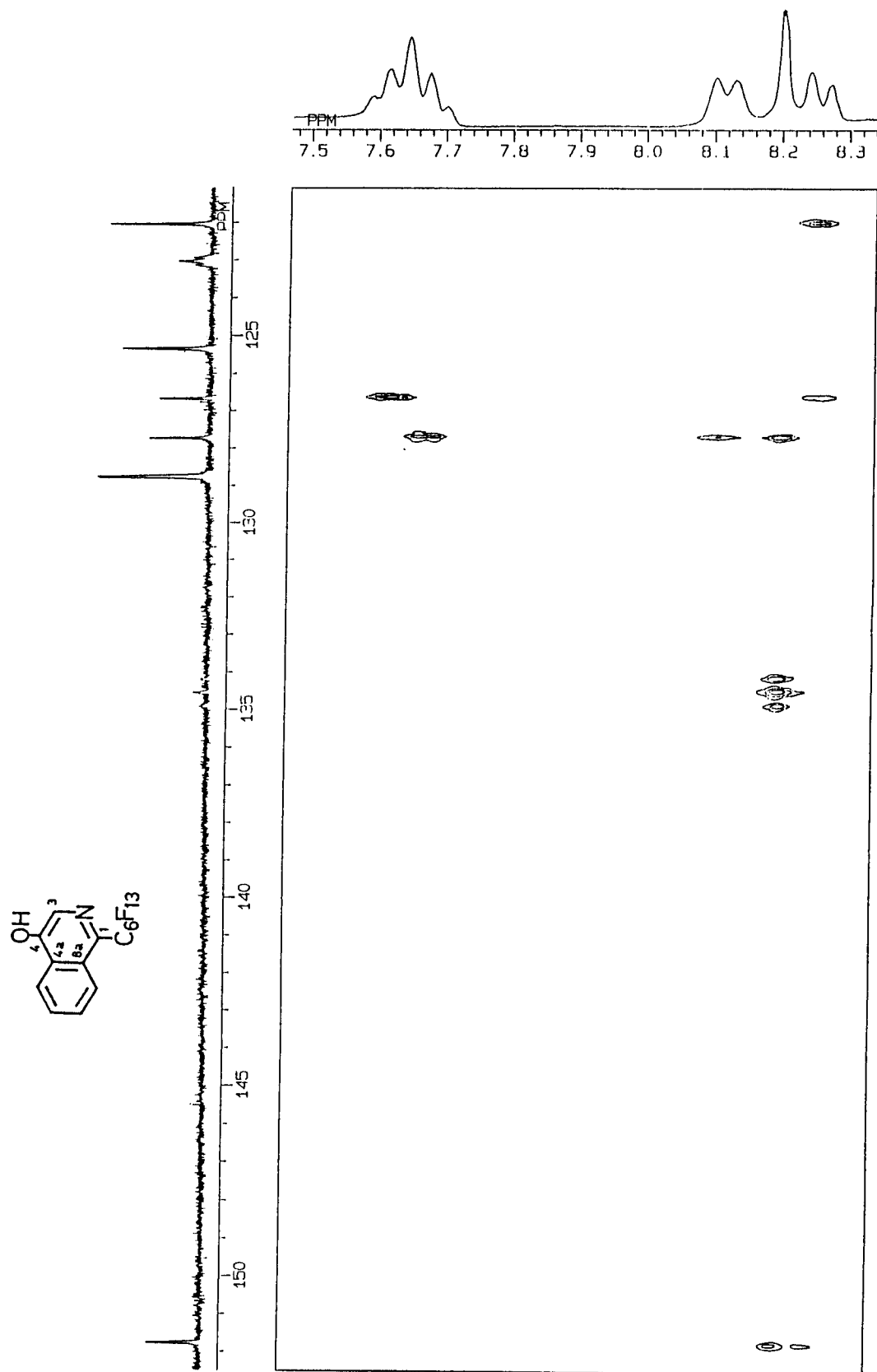
Figure 1.   Long-range CH COSY spectra of **3b** (J = 9 Hz).
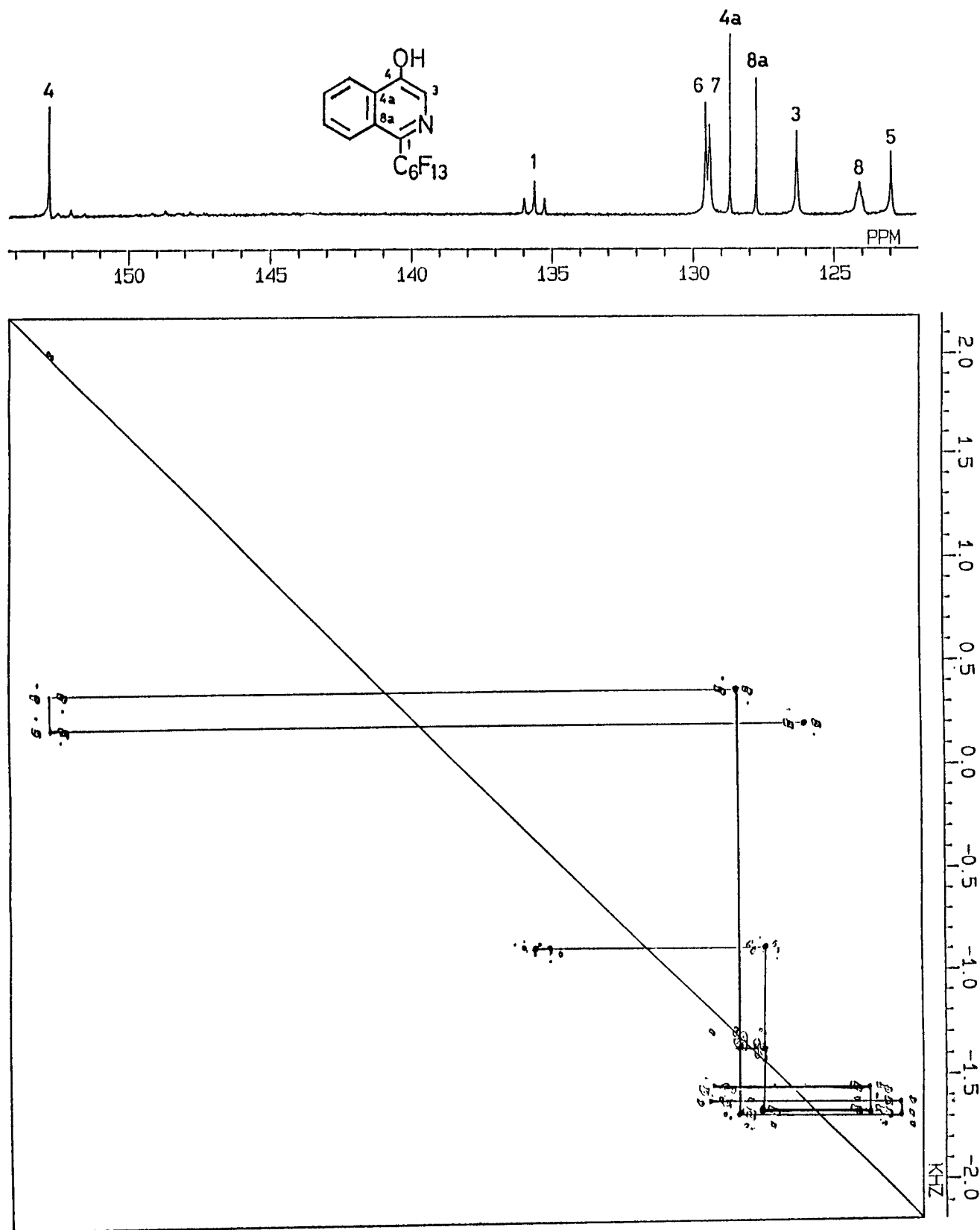
Figure 2. 2D INADEQUATE spectra of **3b**.

a similar route based on the isomerization of isoquinoline N-oxide [4,6]. Attempted oxidation of **4b** by trifluoroacetic acid/30% hydrogen peroxide gave, however, none of perfluorohexylisoquinoline N-oxide and the starting **4b** was recovered under the similar conditions used for 2-trifluoromethylquinoline N-oxide [7]. Although 1-trifluoromethyl-4-isoquinolinol is a known compound [4], the spectroscopic data are not given. We decided to determine the structure of the hydroxylated compound by means of 2D nmr techniques. Long-range CH COSY spectra (J = 9 Hz) of the perfluorohexylisoquinolinol in DMSO-d_6 are shown in Figure 1. Absorption due to isolated hydrogen on the pyridine nucleus is found at 8.20 ppm. Signals due to carbons bearing a perfluorohexyl group and a hydroxyl group are found at 134.8 and 152.0 ppm, respectively. From CH COSY spectra of the compound, fused carbon signals are identified at 127.9 and 128.8 ppm. There is an obvious correlation between the carbon bearing the perfluorohexyl group and the isolated hydrogen. This has thrown a doubt on our tentative assignment of the 3-hydroxy structure. In Figure 2, 2D INADEQUATE spectra of the compound in DMSO-d_6 are shown. In this spectra, the hydroxyl-bearing carbon shows two correlations with the fused carbon and a hydrogen-attached carbon which does not show any other correlations. Thus, the 4-hydroxy structure depicted in Figures is fully confirmed.

On exposure to air in ether, 1-perfluorohexyl-1,2-dihydroisoquinoline (**2b**) gave 1-perfluorohexylisoquinoline (**4b**) and its 4-hydroxy derivative **3b** in variable ratios (**4b:3b** = 50:15 ~ 36:43). Oxidation of **2b** with potassium permanganate led exclusively to **4b** in a 79% yield. Similarly, the autoxidation of 1-perfluoroalkyl-1,2-dihydroisoquinolines **2a-d** in benzene afforded 4-hydroxy derivatives **3a-d** in moderate isolated yields (Scheme 1, Table 1). With 1-alkyl- and 1-phenyl-1,2-dihydroisoquinolines **2e-g** [8], the yields of 4-hydroxy derivatives were rather low. In the case of **2d**, the dimerization products **7** and **8** were obtained as by-product in 14% and 7% yields, respectively. A mixture of such dimerization products was also obtainable from the reaction of 1-methyl derivative **2e**. The gc-ms analysis of the mixture revealed the presence of 2,2'-dimethyl-4,4'-biisoquinoline **9**, together with its hydro derivatives [9]. Only **9** was obtained by gpc in rather impure form.

Autoxidation of indoles, especially for 3-alkylindoles, is well known to be initiated by hydroperoxylation at C-3 electrophilic carbon [10]. As the partial structure of 1,2-dihydroisoquinoline is related to that of indole, this unusual autoxidation of 1,2-dihydroisoquinoline to 4-isoquinolinol may be similarly thought to proceed *via* hydroperoxylation at C-4 followed by loss of water (Scheme 1). Although formation of dehydration compound **4** is inevitable, the present method opens a new simple route to various 4-hydroxylated isoquinolines, which are otherwise less easily acces-

Table 1
Autoxidation of 1,2-Dihydroisoquinolines

2-4	R	Yields/% [a]		
		3	4	dimer
a	n-C$_8$F$_{17}$	66	10	trace
b	n-C$_6$F$_{13}$	78	13	trace
c	n-C$_4$F$_9$	60	14	trace
d	C$_2$F$_5$	30	32	21 [b]
e	Me	49	30	8 [c]
f	n-Bu	44	17	trace
g	Ph	40	17	trace

[a] Based on **1**. [b] **7**, 14%; **8**, 7%. [c] Calculated as **9**.

sible.

EXPERIMENTAL

Melting points were measured with a Yanagimoto micro-melting point apparatus and are uncorrected. All nmr spectra were observed with a GSX-270 spectrometer by using tetramethylsilane as an internal standard for ¹H and ¹³C, and fluorotrichloromethane for ¹⁹F. Mass spectra were measured with a Hitachi M80LCAPI spectrometer under the following ionizing conditions: EI (20 eV) and CI (70 eV, methane as CI gas). The ir spectra were recorded on a Hitachi 270-30 spectrophotometer. Column chromatography was carried out using Wakogel C-200. Preparative gpc was performed using JAI LC-08 with JAI-1H (20 mm ID x 60 cm) and JAI-2H (20 mm ID x 60 cm) columns. Diethyl ether was distilled from sodium benzophenone ketyl and stored over sodium wire. Isoquinoline and perfluoroalkyl iodides were purified by simple distillation. Methyllithium, butyllithium, and phenyllithium were titrated prior to use. Other commercially available materials were used without further purification.

General Procedure for the Reaction of Isoquinoline with Perfluoroalkyllithiums.

Under an inert atmosphere, an ethereal solution of methyllithium/lithium bromide (1.15 moles/1, 2.1 ml, 2.4 mmoles) was added with stirring to an ethereal solution (20 ml) of isoquinoline (**1**, 0.258 g, 2.0 mmoles), perfluoroalkyl iodide (2.4 mmoles), and boron trifluoride etherate (0.31 ml, 2.4 mmoles) at −78° over 10 minutes. After being stirred at this temperature for 1 hour the mixture was quenched with saturated aqueous ammonium chloride (20 ml). The organic phase was separated and the aqueous phase was extracted twice with ether (20 ml x 2). The combined organic phase was washed with brine (30 ml), dried over sodium sulfate, and evaporated to give crude 1-perfluoroalkyl-1,2-dihydroisoquinoline (**2**). The crude **2** was dissolved in benzene (20 ml) and stirred for 2 days at ambient temperature. After the solvent was removed, the residue was chromatographed on silica gel (hexane/dichloromethane = 1/1 ~ dichloromethane/methanol = 19/1). 1-Perfluoroalkyl-4-isoquinolinol **3** was obtained in the more polar fractions.

1-Perfluorooctyl-4-isoquinolinol (3a).

This compound was obtained as colorless rods (chloroform), mp 148-156°; ir: 3092, 1588, 1370, 1300-1100 cm⁻¹; ¹H nmr

(acetone-d$_6$): δ 7.79 (m, 2H, 6- and 7-H), 8.21 (s, 1H, 4-H), 8.25 (m, 1H, 8-H), 8.35 (m, 1H, 5-H), 10.28 (br, 1H, OH); ^{19}F nmr (acetone-d$_6$): δ −80.58 (tt, 3F, J = 10, 2 Hz), −103.85 (tm, 2F, J = 14 Hz), −119.40 (m, 2F), −119.84 (m, 2F), −121.27 (m, 4F), −122.22 (m, 2F), −125.66 (m, 2F); ms: (EI, 20 eV) (m/e) 563 (M$^+$), 543, 194, 147.

Anal. Calcd. for C$_{17}$H$_6$F$_{17}$NO: C, 36.25; H, 1.07; N, 2.49. Found: C, 35.95; H, 1.08; N, 2.50.

1-Perfluorohexyl-4-isoquinolinol (3b).

This compound was obtained as colorless rods (chloroform), mp 158-160°; ir: 3088, 1586, 1364, 1300-1100 cm^{-1}; ^{1}H nmr (acetone-d$_6$): δ 7.80 (m, 2H), 8.22 (s, 1H), 8.27 (m, 1H), 8.36 (m, 1H), 10.27 (br, 1H); ^{13}C nmr (DMSO-d$_6$): δ 105-125 (6C), 122.18, 123.20, 125.53, 126.89, 127.91, 128.75, 128.85, 134.80 (t, J = 24 Hz), 152.00; ^{19}F nmr (acetone-d$_6$): δ −80.64 (tt, 3F, J = 10, 2 Hz), −103.85 (tm, 2F, J = 14 Hz), −119.45 (m, 2F), −120.05 (m, 2F), −122.26 (m, 2F), −125.61 (m, 2F); ms (CI, methane): (m/e) 464 (M$^+$ + 1), 444, 194.

Anal. Calcd. for C$_{15}$H$_6$F$_{13}$NO: C, 38.90; H, 1.31; N, 3.02. Found: C, 38.56; H, 1.42; N, 3.14.

1-Perfluorobutyl-4-isoquinolinol (3c).

This compound was obtained as colorless rods (chloroform), mp 148-150°; ir: 3124, 1586, 1352, 1300-1100 cm^{-1}; ^{1}H nmr (acetone-d$_6$): δ 7.80 (m, 2H), 8.21 (s, 1H), 8.26 (m, 1H), 8.35 (m, 1H), 10.25 (br, 1H); ^{19}F nmr (acetone-d$_6$): δ −80.88 (tt, 3F, J = 10, 2 Hz), −103.85 (tm, 2F, J = 13 Hz), −120.21 (m, 2F), −124.01 (m, 2F); ms: (EI, 20 eV) (m/e) 363 (M$^+$), 343, 194, 147.

Anal. Calcd. for C$_{13}$H$_6$F$_9$NO: C, 42.99; H, 1.67; N, 3.86. Found: C, 42.65; H, 1.65; N, 3.98.

1-Perfluoroethyl-4-isoquinolinol (3d).

This compound was obtained as colorless rods (chloroform-acetone), mp 152-154°; ir: 3028, 1584, 1354, 1300-1100 cm^{-1}; ^{1}H nmr (acetone-d$_6$): δ 7.79 (m, 2H), 8.14 (s, 1H), 8.26 (m, 1H), 8.34 (m, 1H), 10.23 (br, 1H); ^{19}F nmr (acetone-d$_6$): δ −80.40 (t, 3F, J = 2 Hz), −105.10 (s, 2F); ms (EI, 20 eV): (m/e) 264 (M$^+$ + 1), 263 (M$^+$), 243, 194.

Anal. Calcd. for C$_{11}$H$_6$F$_5$NO: C, 50.20; H, 2.30; N, 5.32. Found: C, 49.95; H, 2.30; N, 5.20.

1-Perfluorooctylisoquinoline (4a).

This compound was obtained as colorless rods (hexane-chloroform), mp 121-125°; ir: 1620, 1588, 1372, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 7.75 (m, 2H, 6- and 7-H), 7.87 (d, 1H, 4-H, J = 5.5 Hz), 7.94 (dd, 1H, 8-H, J = 7.3, 1.8 Hz), 8.38 (d, 1H, 5-H, J = 7.9 Hz), 8.67 (d, 1H, 3-H, J = 5.5 Hz); ^{19}F nmr (deuteriochloroform): δ −81.28 (tt, 3F, J = 10, 2 Hz), −106.71 (tm, 2F, J = 14 Hz), −120.62 (m, 2F), −121.29 (m, 2F), −122.26 (m, 4F), −123.19 (m, 2F), −126.60 (m, 2F); ms: (EI, 20 eV) (m/e) 547 (M$^+$), 178, 128.

Anal. Calcd. for C$_{17}$H$_6$F$_{17}$N: C, 37.31; H, 1.11; N, 2.56. Found: C, 36.98; H, 1.21; N, 2.71.

1-Perfluorohexylisoquinoline (4b).

This compound was obtained as colorless rods (hexane-chloroform), mp 38-40°; ir: 1624, 1584, 1366, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 7.70 (m, 2H), 7.82 (d, 1H, J = 5.5 Hz), 7.89 (dd, 1H, J = 7.3, 1.5 Hz), 8.36 (d, 1H, J = 8.9 Hz), 8.65 (d, 1H, J = 5.5 Hz); ^{19}F nmr (deuteriochloroform): δ −81.34 (tt, 3F, J = 10, 2 Hz), −106.48 (tm, 2F, J = 14 Hz), −120.49 (m, 2F),

−121.35 (m, 2F), −123.08 (m, 2F), −126.50 (m, 2F); ms: (CI, methane) (m/e) 448 (M$^+$ + 1), 428, 178.

Anal. Calcd. for C$_{15}$H$_6$F$_{13}$N: C, 40.29; H, 1.35; N, 3.13. Found: C, 39.94; H, 1.45; N, 3.31.

1-Perfluorobutylisoquinoline (4c).

This compound was obtained as colorless oil; ir: 1626, 1588, 1356, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 7.73 (m, 2H), 7.85 (d, 1H, J = 5.5 Hz), 7.92 (dd, 1H, J = 7.6, 1.5 Hz), 8.36 (d, 1H, J = 9.2 Hz), 8.66 (d, 1H, J = 5.5 Hz); ^{13}C nmr (deuteriochloroform) δ 105-125 (4C), 124.57, 124.93 (tt, J = 7, 3 Hz), 127.72 (t, J = 1 Hz), 128.82, 125.03, 130.62, 137.33, 140.96, 146.12 (t, J = 24 Hz); ^{19}F nmr (deuteriochloroform): δ −81.41 (tt, 3F, J = 10, 3 Hz), −106.70 (tm, 2F, J = 13 Hz), −121.47 (m, 2F), −125.49 (m, 2F); ms: (EI, 20 eV) (m/e) 347 (M$^+$), 178, 128.

Anal. Calcd. for C$_{13}$H$_6$F$_9$N: C, 44.97; H, 1.74; N, 4.03. Found: C, 44.94; H, 1.69; N, 3.73.

1-Perfluoroethylisoquinoline (4d).

This compound was obtained as colorless needles (hexane-chloroform), mp 41-42°; ir: 1626, 1588, 1334, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 7.70 (m, 2H), 7.79 (d, 1H, J = 5.5 Hz), 7.87 (dd, 1H, J = 7.6, 1.5 Hz), 8.37 (d, 1H, J = 8.2 Hz), 8.58 (d, 1H, J = 5.8 Hz); ^{13}C nmr (deuteriochloroform): δ 105-125 (2C), 124.37, 124.70 (t, J = 6 Hz), 125.79, 127.68, 128.72 (t, J = 1 Hz), 130.64, 137.19, 140.67, 146.27 (t, J = 26 Hz); ^{19}F nmr (deuteriochloroform): δ −81.56 (t, 3F, J = 2 Hz), −107.92 (m, 2F); ms: (CI, methane) (m/e) 248 (M$^+$ + 1), 228.

Anal. Calcd. for C$_{11}$H$_6$F$_5$N: C, 53.45; H, 2.45; N, 5.67. Found: C, 53.28; H, 2.53. N, 5.49.

1,1'-Bis(perfluoroethyl)-1,2-dihydro-4,4'-biisoquinoline (7).

This compound was obtained as pale yellow rods (chloroform), mp 179-180°; ir: 3064, 1622, 1394, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 6.03 (tm, 1H, J = 7.0 Hz), 7.14 (s, 1H), 7.25 (s, 1H), 7.41 (dt, 1H, J = 7.6, 0.9 Hz), 7.58 (m, 2H), 7.66 (dm, 1H, J = 7.9 Hz), 7.78 (m, 2H), 8.27 (dm, 1H, J = 7.6 Hz), 7.78 (m, 2H), 8.27 (dm, 1H, J = 7.6 Hz), 8.46 (dm, 1H, J = 8.5 Hz); ^{13}C nmr (deuteriochloroform): δ 60.88 (dd, J = 31, 28 Hz), 91.87, 105-125 (4C), 121.19, 121.73, 121.90, 123.37, 125.63, (t, J = 6 Hz), 125.81 (t, J = 6 Hz), 128.32, 130.00, 130.37, 132.36, 132.49, 136.95, 137.05, 138.93, 139.32 (t, J = 27 Hz), 144.34; ^{19}F nmr (deuteriochloroform): δ −80.84 (m, 3F), −81.14 (m, 3F), −104.63 (dd, 2F, J = 11, 1 Hz), −111.25 (ddd, 1F, J = 278, 9, 4 Hz), −117.44 (dd, 1F, J = 280, 4 Hz); ms: (CI, methane) (m/e) 493 (M$^+$ − 1), 473.

Anal. Calcd. for C$_{22}$H$_{12}$F$_{10}$N$_2$: C, 53.45; H, 2.45; N, 5.67. Found: C, 53.23; H, 2.07; N, 5.68.

1,1'-Bis(perfluoroethyl)-1,2,3,4-tetrahydro-4,4'-biisoquinoline (8).

This compound was obtained as colorless needles (chloroform), mp 127-128°; ir: 3356, 2920, 1330, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.29 (br, 1H, NH), 3.00 (dd, 1H, 3-H, J = 15.3, 2.7 Hz), 3.16 (m, 1H, 3-H), 4.88 (d, 1H, J = 11.3 Hz), 5.07 (m, 1H), 7.23 (m, 1H), 7.35 (m, 3H), 7.75 (m, 2H), 8.28 (d, 1H, J = 8.2 Hz), 8.46 (dd, 1H, J = 8.5, 1.5 Hz), 9.02 (d, 1H, J = 5.2 Hz); ^{13}C nmr (deuteriochloroform) δ 38.26, 51.87, 57.99 (t, J = 24 Hz), 105-125 (4C), 122.95, 125.38, 125.59 (t, J = 6 Hz), 126.87, 127.39, 128.25, 128.45, 128.49, 129.18 (t, J = 3 Hz), 130.77, 134.90, 136.00, 137.52, 139.57, 146.13 (t, J = 26 Hz); ^{19}F nmr (deuteriochloroform): δ −79.06 (t, 3F, J = 2 Hz), −81.43 (m, 3F), −107.41 (m, 2F), −116.25 (ddd, 1F, J = 270, 7, 2 Hz), −124.15 (dd, 1F, J =

270, 17 Hz); ms: (CI, methane) (m/e) 497 (M$^+$ + 1), 477, 377.

Anal. Calcd. for C$_{22}$H$_{14}$F$_{10}$N$_2$: C, 53.24; H, 2.84; N, 5.64. Found: C, 53.18; H, 2.83; N, 5.75.

General Procedure for the Reaction of Isoquinoline with Organolithiums.

Under an inert atmosphere, an ethereal solution of organolithium (2.4 mmoles) was added with stirring to an ethereal solution (20 ml) of isoquinoline (1; 0.258 g, 2.0 mmoles) and boron trifluoride etherate (0.31 ml, 2.4 mmoles) at −78° over 10 minutes. After being stirred at this temperature for 1 hour the mixture was quenched with saturated aqueous ammonium chloride (20 ml). The organic phase was separated and the aqueous phase was extracted twice with ether (20 ml x 2). The combined organic phase was washed with brine (30 ml), dried over sodium sulfate, and evaporated to give crude 1-alkyl-1,2-dihydroisoquinoline (2). The crude 2 was dissolved in benzene (20 ml) and stirred for 2 days at the ambient temperature. After the solvent was removed, the residue was chromatographed on silica gel (hexane/dichloromethane = 1/1 ~ dichloromethane/methanol = 19/1). 1-Alkyl-4-isoquinolinol 3 was obtained in the more polar fractions.

1-Methyl-4-isoquinolinol (3e).

This compound was obtained as colorless rods (chloroform), mp 199-201° subl; ir: 2560, 1586, 1398, 1360 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 2.74 (s, 3H, Me), 7.67 (m, 2H, 6- and 7-H), 7.90 (s, 1H, 3-H), 8.07 (d, 1H, J = 8.0 Hz), 8.12 (d, 1H, J = 8.2 Hz), 10.21 (br, 1H, OH); ^{13}C nmr (DMSO-d$_6$): δ 21.03, 121.18, 125.04, 125.28, 126.83, 127.09, 127.26, 128.35, 146.61, 147.84; ms: (CI, methane) (m/e) 160 (M$^+$ + 1).

Anal. Calcd. for C$_{10}$H$_9$NO: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.09; H, 5.63; N, 8.62.

1-Butyl-4-isoquinolinol (3f).

This compound was obtained as colorless rods (hexane-chloroform), mp 99-101°; ir: 3016, 2960, 2588, 1586 cm^{-1}; ^{1}H nmr (acetone-d$_6$): δ 0.86 (t, 3H, 4′-H, J = 7.3 Hz), 1.37 (dt, 2H, J = 7.6, 7.3 Hz), 1.71 (m, 2H), 3.18 (t, 2H, 1′-H, J = 7.6 Hz), 7.63 (m, 2H, 6-and 7-H), 8.08 (s, 1H, 3-H), 8.12 (dm, 1H, J = 8.5 Hz), 8.24 (dm, 1H, J = 8.2 Hz); ^{13}C nmr (acetone-d$_6$): δ 14.70, 23.82, 33.29, 35.00, 123.28, 125.91, 126.47, 128.65, 128.74, 129.95, 130.16, 149.30, 153.86; ms: (EI, 20 eV) (m/e) 201 (M$^+$), 159.

Anal. Calcd. for C$_{13}$H$_{15}$NO: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.25; H, 7.66; N, 6.63.

1-Phenyl-4-isoquinolinol (3g).

This compound was obtained as colorless rods (acetone), mp 245-249° (lit 248-251° [11]); ir: 2664, 1584, 1386 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 7.46-7.64 (m, 6H), 7.74 (m, 1H), 7.95 (d, 1H, J = 8.2 Hz), 8.16 (s, 1H), 8.22 (d, 1H, J = 8.2 Hz), 10.54 (br, 1H); ^{13}C nmr (DMSO-d$_6$): δ 121.53; 126.13, 126.29, 126.52, 127.67, 127.71, 127.86, 128.19, 128.87, 129.78, 139.57, 147.73, 150.51; ms: (CI, methane) (m/e) 222 (M$^+$ + 1).

Anal. Calcd. for C$_{15}$H$_{11}$NO: C, 81.43; H, 5.01; N, 6.33. Found: C, 81.43; H, 5.04; N, 6.04.

1,1′-Dimethyl-4,4′-biisoquinoline (9).

This compound was obtained as pale yellow oil; ir: 3068, 1626, 1566, 1396 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.08 (s, 6H), 7.40 (dm, 2H, J = 7.9 Hz), 7.52 (tm, 2H, J = 6.9 Hz), 7.62 (tm, 2H, J = 6.9 Hz), 8.23 (dm, 2H, J = 7.9 Hz), 8.40 (s, 2H); ^{13}C nmr (deuterio-

chloroform): δ 22.50, 125.69, 125.85, 126.91, 126.99, 127.14, 130.22, 135.62, 142.74, 159.02; ms: (CI, methane) (m/e) 285 (M$^+$ + 1), 269.

1-Perfluorohexylisoquinoline (4b). Oxidation of 2b with Potassium Permanganate.

To an acetone solution (50 ml) of crude 2b, prepared from isoquinoline (0.646 g, 5 mmoles) and perfluorohexyl iodide (2.676 g, 6 mmoles) in a similar manner as described above, was added an acetone solution (100 ml) of potassium permanganate (0.79 g, 5 mmoles) with stirring at room temperature. After the mixture is stirred for 1 hour, 2-propanol (5 ml) was added. Manganese dioxide was removed by filtration and the filtrate was concentrated *in vacuo* to give a brown oil, which was purified by column chromatography on silica gel (hexane-dichloromethane) to afford 1.769 g (79%) of 4b.

4-Acetoxy-1-perfluorohexylisoquinoline (10).

Acetic anhydride (0.153 g, 1.5 mmoles) was added to a pyridine solution (5 ml) of 3b (0.230 g, 0.5 mmole) at room temperature. The mixture was stirred for 17 hours, then water (10 ml) and ether (10 ml) were added to the mixture. The organic phase is separated and the aqueous phase was extracted with ether (10 ml x 2). The combined organic phase was evaporated to give a pale yellow oil. The oil was chromatographed on silica gel (dichloromethane) to give 0.251 g, (99%) of 10, colorless rods (chloroform), mp 42-43°; ir: 1778, 1372, 1300-1100 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.51 (s, 3H, Me), 7.76 (m, 2H, 6- and 7-H), 8.00 (dd, 1H, 3-H, J = 7.6, 1.2 Hz), 8.39 (dd, 1H, 5-H, J = 8.2, 1.5 Hz), 8.57 (s, 1H, 8-H); ^{13}C nmr (deuteriochloroform): δ 20.79, 105-125 (6C), 121.25, 125.07 (tt, J = 7, 2 Hz), 127.58, 129.17, 130.93, 130.96, 134.09, 143.43, (t, J = 24 Hz), 144.68, 168.31; ^{19}F nmr (deuteriochloroform): δ −81.29 (tt, 3F, J = 10, 2 Hz), −106.13 (tm, 2F, J = 14 Hz), −120.45 (m, 2F), −121.39 (m, 2F), −123.11 (m, 2F), −126.05 (m, 2F); ms: (EI, 20 eV) (m/e) 505 (M$^+$), 463, 194.

Anal. Calcd. for C$_{17}$H$_8$F$_{13}$NO$_2$: C, 40.41; H, 1.60; N, 2.77. Found: C, 40.46; H, 1.66; N, 2.72.

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