A NEW SYNTHESIS OF 7,12-DIHYDRO-12-PHENYL-5H-6,12-METHANODIBENZ[c,f]-AZOCINES VIA N-BENZYL-1,2,3,4-TETRAHYDRO-4-PHENYLISOQUINOLIN-4-OLS

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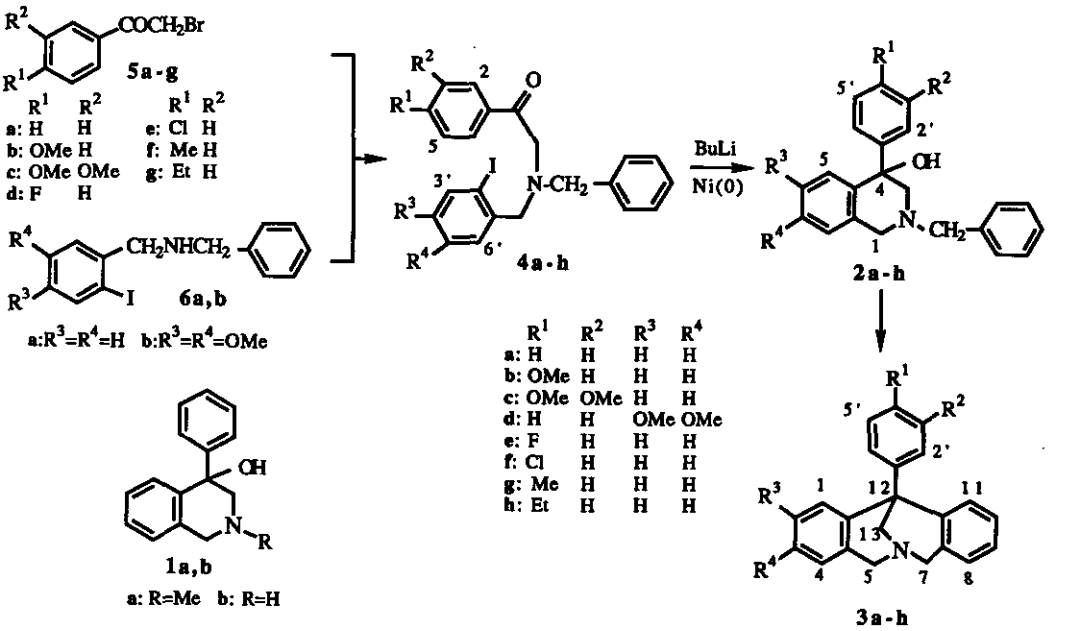
Abstracts- 7,12-Dihydro-12-phenyl-5H-6,12-methanodibenz[c,f]azocine derivatives were prepared from N-benzyl-1,2,3,4-tetrahydro-4-phenylisoquinolin-4-ols by an intramolecular Friedel-Crafts reaction.

We have recently reported the convenient synthesis of 1,2,3,4-tetrahydro-N-methyl-4-phenylisoquinolin-4-ol(PI-OH)(**1a**) and its derivatives by an intramolecular Barbier reaction with BuLi[1,2] and by an insertion reaction with zerovalent nickel[1,3] of phenacylamine derivatives. The isoquinolin-4-ol(**1a**) was also found to have a strong and selective noradrenaline potentiating activity.[4,5] In order to study the structure-activity relationships of PI-OH analogues, the synthesis of a secondary amine(**1b**) was attempted by debenzylation of an N-benzylisoquinolin-4-ol(**2a**) with $AlCl_3$ according to the method reported by Murakami.[6] The structure of the product was found to be not **1b** but 7,12-dihydro-12-phenyl-5H-6,12-methanodibenz[c,f]azocine(**3a**). This result indicates that the intramolecular Friedel-Crafts reaction in the treatment of **2a** with $AlCl_3$ predominates over the N-debenzylation reaction because of the reactive hydroxy group at a double benzylic position. Although the preparation of dibenz[c,f]azocines(**3**) via N,N-dibenzylaminoacetaldehyde dialkyl acetals was reported by Takayama,[7] the reaction of isoquinolin-4-ols(**2**) with acids should offer a new method for the preparation of **3**.



Scheme 1

This paper describes a new synthesis of dibenz[c,f]azocine derivatives(3) via N-benzyltetrahydroisoquinolin-4-ols(2) by an intramolecular Friedel-Crafts reaction.

The key intermediates(2a-h) were prepared by both methods using an intramolecular Barbier reaction with BuLi[1,2] and using an insertion reaction with zerovalent nickel[1,3] from N-benzyl-N-(2-iodobenzyl)phenacylamines(4a-h), which were obtained from the corresponding phenacyl bromides(5a-g) and N-benzyl-2-iodobenzylamines(6a,b) in good yields(Scheme 1 and Table III). The reaction of phenacylamines(4a-h) with BuLi gave higher yields of isoquinolin-4-ols(2a-h) than those with zerovalent nickel(Table I). These results are consistent with those of the reaction of N-methylphenacylamine derivatives with BuLi and zerovalent nickel reported in the previous papers.[1,3]

Isoquinolin-4-ol(2a) was treated with $AlCl_3$ in benzene at room temperature to give a cyclization product(3a) in 83% yield. Reaction of other isoquinolin-4-ols(2e-h) with $AlCl_3$ also gave good yields of the dibenz[c,f]azocines(3e-h)(Table II). The debenzylation products of 2a and 2e-h were not isolated in these reactions. The reaction of a methoxy derivative of isoquinolin-4-ol(2a) with $AlCl_3$ was predicted to give a cleaved product of the methyl ether. In fact, the reaction of 2d with $AlCl_3$ gave only a poor yield of 3d

Table I. Yields and Physical Data for Isoquinolin-4-ols(2c-h)[a]

No	Yield(%)		mp(°C)	Formula	Elemental Analysis Calcd (Found)		
	BuLi	Ni(0)			C	H	N
2c	74	37	181-182	$C_{24}H_{25}NO_3 \cdot HCl$	69.98	6.36	3.40
					(69.74	6.56	3.36)
2d	71	51	182-184	$C_{24}H_{25}NO_3 \cdot HCl$	69.98	6.36	3.40
					(70.14	6.39	3.39)
2e	80	31	205-209	$C_{22}H_{20}NOF \cdot HCl$	71.44	5.72	3.89
					(71.20	5.39	3.97)
2f	73	15	215-219	$C_{22}H_{20}NOCl \cdot HCl$	68.40	5.48	3.63
					(68.36	5.42	3.58)
2g	77	32	201-203	$C_{23}H_{23}NO \cdot HCl$	75.50	6.61	3.83
					(75.14	6.67	3.72)
2h	86	33	195-198	$C_{24}H_{25}NO \cdot HCl \cdot 1/4H_2O$	74.98	6.95	3.64
					(75.20	6.84	3.53)

a. Ref. 1 for 2a,b.

Table II. Yields and Physical Data for Dibenz[c,f]azocines(3a-h)

No	Yield (%)			mp(°C)	Formula	Elemental Analysis Calcd (Found)		
	$AlCl_3$	85%H_2SO_4	CF_3SO_3H			C	H	N
3a	83	78	----	140-145	$C_{22}H_{19}N$	88.85	6.44	4.71
						(89.06	6.45	4.63)
3b	----	21	57	165-166.5	$C_{23}H_{21}NO \cdot HCl \cdot 3/2H_2O$	70.67	6.45	3.58
						(70.84	6.32	3.31)
3c	----	96	----	170-175	$C_{24}H_{23}NO_2 \cdot HCl \cdot 1/3H_2O$	72.08	6.22	3.50
						(71.98	6.10	3.46)
3d	4	43	----	212-214	$C_{24}H_{23}NO_2 \cdot HCl \cdot 1/3H_2O$	72.08	6.22	3.50
						(71.96	5.83	3.60)
3e	80	----	----	199-205	$C_{22}H_{18}NF \cdot HCl$	75.10	5.44	3.98
						(74.86	5.16	3.97)
3f	82	----	----	131-132	$C_{22}H_{18}NCl$	79.63	5.47	4.22
						(79.71	5.46	4.16)
3g	47	----	----	190-191.5	$C_{23}H_{21}N \cdot HCl$	79.41	6.37	4.03
						(79.08	6.38	4.05)
3h	57	----	----	167-169	$C_{24}H_{23}N \cdot HCl \cdot 1/3H_2O$	77.71	6.79	3.78
						(77.87	6.70	3.60)

with ambiguous products. Thus, the isoquinolin-4-ol(**2a**) was tried to treat with 85% H_2SO_4[8] to give a desired product(**3a**) in 78% yield. The treatment of the methoxy compounds (**2b-d**) in the same way as **2a** afforded methoxyazocines(**3b-c**). As the yield of **3b** from **2b** was low, **2b** was cyclized with CF_3SO_3H and the azocine(**3b**) was obtained in 57% yield.

The structures of the dibenz[c,f]azocines(**3a-h**) were confirmd by their physical properties (Table II) and ^{1}H-nmr spectra(Table IV). In the ^{1}H-nmr spectra of **3a-c** and **3e-h**, the methylene protons at C-5 and C-7 showed same chemical shifts but the protons of C-5 in **3d** were in higher field than those of C-7, which were assigned by determination of its 2D-NOESY spectrum.

EXPERIMENTAL

All melting points are given as uncorrected values. Ir spectra were taken with a Perkin-Elmer 1720 infrared fourier transform spectrophotometer and are given in cm^{-1}. High-resolution mass spectra were recorded on a JEOL JMS-D 300 spectrometer. ^{1}H- And ^{13}C-nmr spectra were recorded on a JEOL JNM-FX 200 spectrometer in $CDCl_3$ with tetramethylsilane as a standard and are given in δ values.

4-Methylphenacyl Bromide(**5f**) A solution of benzyltrimethylammonium tribromide[9](5.13 g, 13.2 mmol) in CH_2Cl_2-MeOH(5:2) (50 ml) was added to a solution of 4'-methylacetophenone (1.60 g, 11.94 mmol) in CH_2Cl_2-MeOH(5:2) (20 ml) and was stirred for 2 h at room temperature. The mixture was evaporated in vacuo and H_2O(50 ml) was added to the residue. The mixture was extracted with ether(50 ml x 3). The extract was washed with H_2O, dried over $MgSO_4$ and evaporated to give **5f** as colorless crystals(2.49 g, 98%), mp 41-44°C. ^{1}H-Nmr:7.86 (2H,d,J=8 Hz, H-2 and H-6), 7.26(2H,d,J=8 Hz,H-3 and H-5), 4.42(2H,s,CH_2) 2.40 (3H,s,CH_3). Ir(KBr):1694 (C=O). Ms(m/z)(M^+):Calcd for C_9H_9OBr:211.9838. Found:211.9861.

Phenacyl bromide(**5g**) was prepared in the same way as **5f**. Phenacyl bromides(**5a,b** and **5e**) were commercially available, and **5c**[3] and **5d**[1] have been reported by us.

4-Ethylphenacyl Bromide(**5g**) A colorless oil(99%). ^{1}H-Nmr: 7.90(2H,d,J=8.5 Hz,H-2 and H-6), 7.30(2H,d,J=8.5 Hz,H-3 and H-5), 4.43(2H,s,CH_2Br), 2.71(2H,q,J=7.5 Hz,CH_2CH_3), 1.26 (3H,t,J=7.5 Hz,CH_2CH_3). Ir(KBr): 1678(C=O). Ms(m/z)(M^+): Calcd for $C_{10}H_{11}OBr$: 225.9992.

Found:225.9982.

N-Benzyl-2-iodo-4,5-dimethoxybenzylamine(**6b**) 2-Iodo-4,5-dimethoxybenzaldehyde(5.85 g, 20.0 mmol) and 6.5N HCl-MeOH(6 ml, 39 mmol) were added to a solution of benzylamine(12.9 g, 120 mmol) in absolute MeOH(25 ml) and $NaBH_3CN$(0.88 g, 13.5 mmol) was added. The mixture was stirred for 48 h at room temperature. The precipitates formed were filtered and the filtrate was acidified with conc. HCl and evaporated. H_2O(100 ml) was added to the residue and the mixture was washed with ether, basified with powdered KOH and extracted with $CHCl_3$. The extract was dried over $MgSO_4$ and evaporated to give a crude product. This was purified by flash chromatography on SiO_2 with $CHCl_3$-MeOH(10:1) to give **6a** as a pale yellow oil(5.32 g, 69%), which was converted to the hydrochloride as colorless needles (from MeOH), mp 176-177.5 °C. ^{1}H-Nmr(free base):7.22(1H,s,H-3), 6.94(1H,s,H-6), 3.85 and 3.86(each 3H,s, 2xOCH_3), 3.77 and 3.81(each 2H,s,2xCH_2),1.74(1H, br s,NH). Anal.Calcd for $C_{16}H_{18}NI \cdot HCl$:C,45.79;H,4.56; N,3.34. Found:C,45.64;H,4.58;N, 3.28.

The benzylamine(**6a**) was reported in our previous paper.[1]

General Procedure for Preparation of N-Benzyl-N-(2-iodobenzyl)phenacylamines This is exemplified by the preparation of **4c**. A solution of the benzylamine(**6a**)(1.640 g, 5.11 mmol) in dioxane(15 ml) was added to a solution of phenacyl bromide(**5c**)(686 mg, 2.64 mmol) in dioxane(15 ml). The mixture was stirred for 5 h at room temperature. The colorless precipitates(866 mg) of the hydrobromide of **6a** formed were filtered and the filtrate was evaporated to give a crude oil(1.513 g). This was purified by flash chromatography on SiO_2 with $CHCl_3$-benzene(2:1) to give **4c** as an oil(1.204 g, 91%). The spectral data for **4c** thus obtained are shown in Table III.

Other N-benzylphenacylamines(**4d-h**) were prepared in the same way as **4c**(Table III).

General Procedure for Reaction of N-Benzyl-N-(2-iodobenzyl)phenacylamines with BuLi This is exemplified by the reaction of **4c** with BuLi. BuLi(1.6 M sol. in hexane, 0.41 ml, 0.65 mmol) was added to a solution of the phenacylamine(**4c**)(252 mg, 0.50 mmol) in dry THF (4 ml) by a syringe at -78°C under N_2 and the mixture was stirred for 10 min at -78°C. H_2O(20 ml) was added and the mixture was extracted with ether(20 ml x 3). The extract was dried over $MgSO_4$ and evaporated to give an oil(195 mg). This was subjected to preparative tlc on SiO_2 with $CHCl_3$. The fraction of Rf 0.04-0.24 gave **2c** as a pale brown oil(141 mg,

Table III. Yields and Ms, Ir and ^{1}H-Nmr Spectral Data for Phenacylamines(**4c-h**)[a]

No	Yield (%)	Formula	Ms(m/z)(M^+) Calcd(Found)	Ir(KBr) (cm^{-1})	^{1}H-Nmr($CDCl_3$) δ
4c	91	$C_{24}H_{24}NO_3I$	501.0800 (501.0793)	1683	7.85 and 7.82(each 1H,dd,J=8 and 2 Hz,H-3' and 6),6.93(1H,ddd,J=8, 8 and 2 Hz,H-4'), 6.79(1H,d,J=8 Hz,H-5),3.91 and 3.86(each 2H, s,2xCH_2),3.92(3H,s,OCH_3),3.89(5H,s,CH_2 and OCH_3)
4d	80	$C_{24}H_{24}NO_3I$	501.0800 (501.0790)	1691	7.79(2H,d,J=7 Hz,H-2 and 6),7.38(2H,dd,J=7 and 7 Hz,H-3 and 5),7.34-7.21(5H,m,C_6H_5), 7.17(1H,s,H-3'),7.03(1H,s,H-6'),3.90,3.82, and 3.80(each 2H,s,3xCH_2),3.83 and 3.75(each 3H,s,OCH_3)
4e	83	$C_{22}H_{19}NOFI$	459.0494 (459.0453)	1687	7.82(1H,m,H-3'),7.80(2H,dd,J=9 and 5.5 Hz,H-2 and 6),7.47(1H,dd,J=7.5 and 2 Hz,H-6'), 7.37-7.23(5H,m,C_6H_5),7.02(2H,dd,J=9 and 9 Hz,H-3 and 5),6.93(1H,ddd,J=8, 7 and 2 Hz, H-4'),3.88, 3.85 and 3.84(each 2H,s,3xCH_2)
4f	77	$C_{22}H_{19}NOClI$	474.0121[b] (474.0081)	1690	7.81(1H,d,J=8 Hz,H-3'),7.70(2H,d,J=8 Hz,H-2 and 6),7.45(1H,d,J=7 Hz,H-6'),7.35-7.23(5H, m,C_6H_5),7.27(2H,d,J=8 Hz,H-3 and 5),6.93(1H, ddd,J=8, 7 and 1 Hz,H-4'),3.87 and 3.83(4H and 2H,s,3xCH_2)
4g	75	$C_{23}H_{22}NOI$	453.0592 (453.0598)	1688	7.81(1H,dd,J=8 and 1 Hz,H-3'),7.71(2H,d,J= 8 Hz,H-2 and 6),7.55(1H,dd,J=8 and 1.5 Hz, H-6'),7.18(2H,d,J=8 Hz,H-3 and 5),6.93(1H, ddd,J=8, 7 and 1.5 Hz,H-4'),3.93,3.91,3,88 (each 2H,s,3xCH_2),2.38(3H,s,CH_3)
4h	85	$C_{24}H_{24}NOI$	469.0902 (469.0875)	1689	7.81(1H,dd,J=8 and 1 Hz,H-3'),7.74(2H,J=8 Hz,H-2 and 6),7.53(1H,dd,J=7.5 and 2 Hz,H-6'),7.20(2H,d,J=8 Hz,H-3 and 5),6.93(1H,ddd, J=8, 7.5 and 2 Hz,H-4'),3.92,3.91 and 3.88 (each 2H,s,3xCH_2),2.67(2H,q,J=7.5 Hz, CH_2CH_3),1.23(3H,t,J=7.5 Hz,CH_2CH_3)

a. Ref. 1 for **4a,b**. b. M-1.

74%). This was converted to the hydrochloride as colorless cubes(from EtOH-acetone), mp 181-182°C(decomp.). The physical and spectral data for **2c** are shown in Tables I and IV. Reactions of other phenacylamines(**4d-h**) with BuLi were carried out in the same way as **4c**. The physical and spectral data for the products(**2d-h**) are summerized in Tables I and IV.

General Procedure for Reaction of N-Benzyl-N-(2-iodobenzyl)phenacylamines with Zerovalent Nickel This is exemplified by the reaction of **4c** with zerovalent nickel.[1,3] Ph_3P(2.503 g, 9.12 mmol), $NiCl_2$(580 mg, 4.47 mmol), and Zn(297 mg, 4.54 mmol) were placed in a two-necked flask. The flask was evacuated and filled with N_2. Dry oxygen-free DMF(35 ml) was added through a syringe. The mixture was stirred at 60°C for 5 min. A solution of **4c**(1.072 g, 2.14 mmol) in dry oxygen-free DMF(5 ml) was added and the mixture was stirred for 10 h at 60°C. Then, the mixture was acidified with 2% HCl and washed with ether. The aqueous layer was basified with 25% NH_4OH and extracted with $CHCl_3$(50 ml x 4). The extract was dried over $MgSO_4$ and evaporated to give a crude product(850 mg). This was subjected to preparative tlc on Al_2O_3 with benzene-$CHCl_3$(5:1) to give the isoquinolin-4-ol(**2c**) as a pale yellow oil(298 mg, 37%). This was identical with **2c** prepared with BuLi as described above by comparison of their ^{1}H-nmr spectra.

Reactions of other phenacylamines(**4d-h**) with zerovalent nickel were carried out in the same way as **4c**.

General Procedure for Reaction of N-Benzyl-1,2,3,4-tetrahydro-4-phenylisoquinolin-4-ols with $AlCl_3$ This is exemplified by the reaction of **2a**. $AlCl_3$(129 mg, 0.97 mmol) was added to a solution of **2a**(76 mg, 0.24 mmol) in benzene(2 ml). The mixture was stirred for 30 min at room temperature. H_2O(30 ml) was added and the mixture was basified with powdered Na_2CO_3. The mixture was extracted with benzene(30 ml x 3). The extract was washed with brine, dried over $MgSO_4$ and evaporated *in vacuo* to give a crude product(80 mg). This was subjected to preparative tlc on SiO_2 with benzene-EtOH(10:1) to give 3a as colorless needles(59 mg, 83%), mp 140-145°C(from MeOH)(lit.,[7] mp 138-139°C). ^{13}C-Nmr: 144.30(s,C- 1'), 143.13(s,C-11a and 12a), 135.57(s,C-4a and 7a), 129.26(d,C-1 and 11), 126.20(d, C-4'), 61.00(t,C-13), 57.70(t,C-5 and 7), 44.76(s,C-12). The physical and ^{1}H-nmr spectral data are shown in Tables II and IV.

Reactions of other isoquinolin-4-ols(**2d-h**) were carried out in the same way as **2a**. The physical and spectral data for the products(**3d-h**) are summarized in Tables II and IV.

Table IV. ^{1}H-Nmr Spectral Data for Isoquinolin-4-ols(**2c-h**)[a] and Azocines(**3a-h**)

2c	6.85(1H,d,J=2 Hz,H-2'), 6.80(1H,d,J=8.5 Hz,H-5'), 3.94 and 3.56(each 1H,d,J=15 Hz, CH_2-1), 3.88 and 3.85(each 3H,s,2XOCH_3), 3.94 and 3.56(each 1H,d,J=13 Hz,NCH_2Ph), 3.03 and 2.79(each 1H,d,J=12 Hz,CH_2-3)
2d	7.34(5H,s,NCH_2Ph), 6.52(1H,s,H-8), 6.42(1H,s,H-5), 3.85 and 3.47(each 1H,d,J=15 Hz,CH_2-1), 3.83 and 3.62(each 3H,s,2XOCH_3), 3.78 and 3.68(each 1H,d,J=13 Hz, NCH_2Ph), 3.02 and 2.73(each 1H,d,J=12 Hz,CH_2-3)
2e	7.39(2H,dd,J=9 and 5.5 Hz,H-2' and 6'), 6.99(2H,dd,J=9 and 9 Hz,H-3' and 5'), 3.93 and 3.56(each 1H,d,J=15 Hz,CH_2-1), 3.73(2H,s,NCH_2Ph), 2.99 and 2.74(each 1H,d,J= 12 Hz,CH_2-3)
2f	6.92(1H,dd,J=7.5 and 1.5 Hz,H-5), 3.93 and 3.56(each 1H,d,J=15 Hz,CH_2-1), 3.73 (2H,s,NCH_2Ph), 2.98 and 2.73(each 1H,d,J=12 Hz,CH_2-3)
2g	3.94 and 3.54(each 1H,d,J=15 Hz,CH_2-1), 3.73(2H,s,NCH_2Ph),3.02 and 2.76(each 1H,d, J=12 Hz,CH_2-3), 2.34(3H,s,CH_3)
2h	7.34 and 7.16(each 2H,d,J=8 Hz,H-2' and 6', and H-3' and 5'), 6.97(1H,dd,J=7 and 2 Hz,H-5), 3.95 and 3.56(each 1H,d,J=15 Hz,CH_2-1), 3.74(2H,s,NCH_2Ph),3.03 and 2.77 (each 1H,d,J=12 Hz,CH_2-3), 2.65(2H,q,J=7.5 Hz,CH_2CH_3), 1.25(3H,t,J=7.5 Hz,CH_2CH_3)
3a	4.72 and 3.96(each 2H,d,J=17.5 Hz,CH_2-5 and 7), 3.34(2H,s,CH_2-13)
3b	7.32(2H,d,J=9 Hz,H-2' and 6'), 6.87(2H,d,J=9 Hz,H-3' and 5'), 4.71 and 3.95(each 2H,d,J=17 Hz,CH_2-5 and 7), 3.82(3H,s,OCH_3), 3.31(2H,s,CH_2-13)
3c	6.91(1H,d,J=2 Hz,H-2'), 6.84(1H,d,J=8.5 Hz,H-5'), 4.72 and 3.96(each 2H,d,J=18 Hz, CH_2-5 and 7), 3.92 and 3.90(each 3H,s,2XOCH_3), 3.34(2H,s,CH_2-13)
3d	7.46-7.28(5H,m,C_6H_5-12), 7.12-7.03(4H,m,H-8, 9, 10 and 11), 6.76(1H,s,H-1), 6.51 (1H,s,H-4), 4.79 and 4.07(each 1H,d,J=17 Hz,CH_2-7), 4.70 and 3.92(each 1H,d,J=16.5 Hz,CH_2-5), 3.81(3H,s,OCH_3-3), 3.71(3H,s,OCH_3-2), 3.35(2H,s,CH_2-13)
3e	7.38(2H,dd,J=9 and 5.5 Hz,H-2' and 6'), 4.71 and 3.96(each 2H,d,J=17.5 Hz,CH_2-5 and 7), 3.30(2H,s,CH_2-13)
3f	7.37 and 7.28(each 2H,d,J=9 Hz,H-2' and 6', and H-3'and 5'), 4.70 and 3.94(each 2H,d,J=18 Hz,CH_2-5 and 7), 3.30(2H,s,CH_2-13)
3g	7.30 and 7.14(each 2H,d,J=8 Hz,H-2' and 6', and H-3' and 5'), 4.70 and 3.99(each 2H,d,J=17.5 Hz,CH_2-5 and 7), 3.30(2H,s,CH_2-13), 2.67(3H,s,CH_3)
3h	7.32 and 7.16(each 2H,d,J=8 Hz,H-2' and 6', and H-3' and 5'), 4.69 and 3.94(each 2H,d,J=18 Hz,CH_2-5 and 7), 3.31(2H,s,CH_2-13), 2.67(2H,q,J=7.5 Hz,CH_2CH_3), 1.27 (3H,t,J=7.5 Hz,CH_2CH_3)

a. Ref. 1 for **2a,b**.

General Procedure for Reaction of N-Benzyl-1,2,3,4-tetrahydro-4-phenylisoquinolin-4-ols with 85% H_2SO_4 This is exemplified by the reaction of **2a**. The hydrochloride(52.9 mg, 0.15 mmol) of **2a** was suspended in 85% H_2SO_4(1 ml) and was stirred for 30 min under ice-cooling. The reaction mixture was poured into ice-water(30 ml) and basified with powdered Na_2CO_3. The mixture was extracted with $CHCl_3$(50 ml x 3). The extract was washed with H_2O, dried over $MgSO_4$, and evaporated to give a crude product(63 mg). This was purified by preparative tlc on SiO_2 with benzene-EtOH(10:1) to give colorless crystals(34.8 mg, 78%), mp 139-142°C. This was identical with a sample of **3a** prepared with $AlCl_3$ as described above by comparison of their ^{1}H-nmr spectra and by a mixed melting point test.

Reaction of other N-benzylisoquinolin-4-ols(**2b-d**) with 85% H_2SO_4 was carried out in the same way as **2a**. The physical and ^{1}H-nmr spectral data for the products(**3b-d**) are shown in Tables II and IV.

Reaction of N-Benzyl-1,2,3,4-tetrahydro-4-(4-methoxyphenyl)isoquinolin-4-ol(**2b**) with CF_3SO_3H The free base(86.1 mg, 0.26 mmol) of **2b** was dissolved in CF_3SO_3H(3 ml) under ice-cooling. The solution was stirred at room temperature overnight. The reaction mixture was poured into ice-water(20 ml) and basified with 25% NH_4OH. The mixture was extracted with $CHCl_3$(20 ml x 4). The extract was dried over $MgSO_4$ and evaporated to give an oil (82.7 mg). This was subjected to preparative tlc on SiO_2 with benzene-EtOH(10:1) to give **3b** as a pale yellow oil(45.7 mg, 57%). Ms(m/z)(M^+):Calcd for $C_{23}H_{21}NO$:327.1622. Found:327.1622. This oily product was converted to the hydrochloride as colorless needles (from MeOH), mp 165-166.5°C. This was identical with the hydrochloride of **3b** prepared with 85% H_2SO_4 by comparison of the ^{1}H-nmr spectra of their free bases.

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