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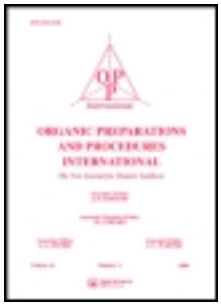

Organic Preparations and Procedures International: The New Journal for Organic Synthesis

Publication details, including instructions for authors and subscription information:
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SYNTHESIS OF NITRONES FROM 3,4-DIHYDROISOQUINOLINE DERIVATIVES BY OXIDATION WITH m-CHLOROPEROXYBENZOIC ACID

Bao-Xiang Zhao [a] , Yang Yu [a] & Shoji Eguchi [a]

[a] Institute of Applied Organic Chemistry, Department of Molecular Design and Engineering Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464-01, JAPAN

Published online: 09 Feb 2009.

To cite this article: Bao-Xiang Zhao , Yang Yu & Shoji Eguchi (1997) SYNTHESIS OF NITRONES FROM 3,4-DIHYDROISOQUINOLINE DERIVATIVES BY OXIDATION WITH m-CHLOROPEROXYBENZOIC ACID, Organic Preparations and Procedures International: The New Journal for Organic Synthesis, 29:2, 185-194, DOI: 10.1080/00304949709355182

To link to this article: http://dx.doi.org/10.1080/00304949709355182

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ORGANIC PREPARATIONS AND PROCEDURES INT., 29 (2), 185-194 (1997)

SYNTHESIS OF NITRONES FROM 3,4-DIHYDROISOQUINOLINE DERIVATIVES BY OXIDATION WITH *m*-CHLOROPEROXYBENZOIC ACID

Bao-Xiang Zhao, Yang Yu and Shoji Eguchi*

Institute of Applied Organic Chemistry, Department of Molecular Design and Engineering
Graduate School of Engineering, Nagoya University
Furo-cho, Chikusa-ku, Nagoya 464-01, JAPAN

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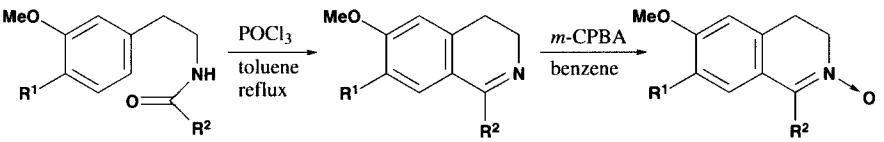
Nitrones are versatile and widely used intermediates in organic synthesis[1] and excellent spin trapping reagents.[2] Particularly, nitrones are useful in 1,3-dipolar cycloaddition reaction leading to various nitrogen-containing biologically active compounds, *e.g.*, antibiotics,[3] alkaloids,[4] and lactams.[5] Methods for the preparation of nitrones involve oxidation of imines.[6] However, only a few of nitrones prepared by the oxidation of 3,4-dihydroisoquinoline derivatives have been described. Although a study on the kinetics and mechanism of peracid oxidation of 3,4-dihydroisoquinoline and 3,4-dihydro-1-methyl-isoquinoline was reported,[7] heretofore an efficient synthesis of this type of nitrones seems not to have been described. We thus become interested in the synthesis of nitrones derived from 3,4-dihydroisoquinoline derivatives and their application for synthesis of bioactive compounds. The present paper reports our results.



1 2 3

a) R^1 = MeO, R^2 = H b) R^1 = MeO, R^2 = Me c) R^1 = MeO, R^2 = Et
d) R^1 = MeO, R^2 = $PhCH_2$ e) R^1 = MeO, R^2 = Ph f) R^1 = MeO, R^2 = *p*-$NO_2C_6H_4$
g) R^1 = MeO, R^2 = *p*-$MeOC_6H_4$ h) R^1 = H, R^2 = Me i) R^1 = H, R^2 = Ph
j) R^1 = H, R^2 = $PhCH_2$ k) R^1 = MeO, R^2 = PhCO l) R^1 = H, R^2 = PhCO

3,4-Dihydroisoquinoline derivatives **2a-j** were synthesized in 60-85% yields from **1** based on the Bischler-Napieralski synthesis (Scheme 1). In the case of compound **2d**, we found that the additional product (**2k**) was formed in 18% yield; the IR spectrum showed a characteristic absorption at 1672 cm^{-1} due to the carbonyl stretching frequency. The ^{13}C NMR spectrum showed a low field signal at δ 194 ppm in consistent with the presence of carbonyl and the ^1H NMR spectrum ($CDCl_3$, 200

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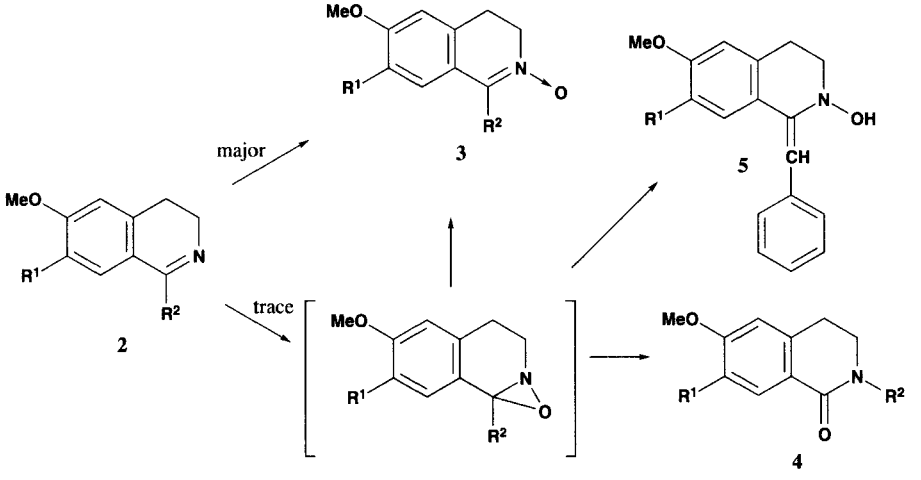
MHz) had peaks of δ 2.82 (t, 2H, J = 7.8 Hz), 3.79 (s, 3H), 3.93 (t, 2H, J = 7.8 Hz), 3.94 (s, 3H), 6.76 (s, 1H), 6.96 (s 1H), 7.45-7.65 (m, 3H), 8.03-8.06 (m, 2H). Indeed, we found that 6-methoxy-1-benzyl-3,4-dihydroisoquinoline (**2j**) was easily air-oxidized being completely converted after one day at RT to (**2l**). Such facile air oxidation of benzilic carbon is often observed in the similar imine system.[8]

Treatment of 3,4-dihydroisoquinoline derivatives 2a-i with *m*-CPBA gave the corresponding nitrones **3a-i**, in a single step in good yields (Table 1). It is known that oxidation of imines with peracid may lead to oxaziridines as the main product,[9,10] whether the oxaziridines or the nitrones are formed being dependent on the structure of imines and the reaction conditions. In our studies, we examined the influence of the amount of *m*-CPBA and pH on the yields and found that the reaction conditions shown in Table 1 gave the best results. C-1 Aryl substituted 3,4-dihydroisoquinolines were converted cleanly and efficiently to nitrones. In the case of C-1 alkyl substituted 3,4-dihydroisoquinoline derivatives (**2c**, **2h**), trace amounts of the rearranged product (**4a**, **4b**) were isolated. The structure shown (**4**) was supported by spectral data. The IR spectrum of **4a**, for example, showed absorption at 1678 cm^{-1} due to the lactam carbonyl. The ^{13}C NMR spectrum showed a signal at δ 202.6 ppm which is characteristic of the carbonyl C. When C-1 is benzyl (**2d**), a different trace product was separated, which had the spectrum consistent with the structure (**5**). On the basis of these facts, we believe that the nitrones result mainly from the direct oxidation of imines rather than from the oxaziridines; the minor additional products isolated, are presumably formed by the rearrangement of the oxaziridines. For comparison, 6,7-dimethoxy-3,4-dihydroisoquinoline N-oxide (**3a**) was also synthesized from 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline following the method described in literature;[11] however, the yield of (**3a**) was only 37% compared with 57% by the present method.

Nitrones exhibit two characteristic bands resulting from N-O and C=N bond stretching vibrations. The IR spectra of the present nitrones show stretching frequencies of C=N at 1593-1608 cm^{-1} and of N-O at 1215-1238 cm^{-1}. Comparison of the proton chemical shifts of C-3 and C-4 of **2** and



4a R^1 = MeO, R^2 = Et **4b** R^1 = H, R^2 = Me **5** R^1 = MeO

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3, revealed some useful features. The proton signals at C-3 and C-4 of the nitrones appeared at a field lower than those of corresponding imines apparently due to deshielding influence of nitrone oxygen. The magnitude of this deshielding influence is about 0.35-0.49 ppm (see Table 2). The MS (EI) of these nitrones showed the M^+ peak and the M-16 peak which results from the loss of oxygen. This is a peak of some diagnostic value.

In summary, 3,4-dihydroisoquinoline derivatives can be converted efficiently to corresponding nitrones by oxidation with *m*-CPBA in aprotic solvents. This one-step method has practical importance for synthesizing new nitrogen heterocycllic compounds *via* the nitrones.

TABLE 1. Oxidation of 3,4-Dihydroisoquinoline Derivatives **2** to Nitrones **3**[a]

entry	imines	time (hrs) 10°C	time (hrs) rt	nitrones	yield (%)[b]	mp. (°C)
1	**2a**	1	2	**3a**	57	181-184
2	**2b**	1.5	2	**3b**	75	195-198
3	**2c**	2	2	**3c**	70	112-115
4	**2d**	2	2	**3d**	50	177-180
5	**2e**	1	2	**3e**	96	66-69
6[c]	**2f**	1	1	**3f**	80	232-234
7	**2g**	1	2	**3g**	71	204-205
8	**2h**	2	2	**3h**	70	oil
9	**2i**	0.5	1	**3i**	92	135-137

a) Initial concentration of imine is 0.1 M and the molar ratio of imine with *m*-CPBA is 1:1.05 in benzene. b) Isolated yield. c) Solvent is chloroform.

EXPERIMENTAL SECTION

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The IR spectra of liquids were measured as films on sodium chloride plates and those of solids as KBr pellets on a JASCO FT/IR 5300 Spectrometer. ^1H and ^{13}C NMR spectra were obtained on a Varian GEMINI 200 spectrometer at 200 and at 50 MHz, respectively. Chemical shifts are recorded in part per million (ppm) for samples in $CDCl_3$ solution with Me_4Si as internal standard. Coupling constants *J* are reported in Hz. Elemental analyses were carried out on a Perkin-Elmer 2400S elemental analyzer. Mass spectra (EI) were obtained using a JEOL JMS-AX505 HA mass spectrometer at 70 eV. The TLC was performed on Merck Kieselgel $60F_{254}$ and/or on Merck Aluminiumoxid F_{254}.

Synthesis of 3,4-Dihydroisoquinoline Derivatives 2. General Procedure[12].- To a round-bottom flask equipped with a magnetic stirrer, under a nitrogen atmosphere was added β-arylethylamide **1** (5.0 mmol) in dry toluene (20 mL). The mixture was heated until the amide dissolved, then phosphorus oxychloride (2.0 mL, 21.5 mmol) was added to the warm solution. The solution was stirred under reflux for 1-3 hrs, followed by cooling to room temperature, then toluene and phosphorus oxychloride were removed under reduced pressure. The solid or glassy residue was dissolved in water

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and/or ethanol, triturated with aqueous 10% sodium hydroxide solution (15 mL) and then extracted with methylene chloride or ether (6 mL x 4), the combined extracts were washed with water (6 mL). After drying the extracts over sodium sulfate, the solvent was evaporated under reduced pressure to give solid or oily residue. The product was purified by recrystallization or column chromatography to give **2** with 60-85% yields.

TABLE 2. ^{1}H and ^{13}C NMR Spectral Data of Compounds **2** and **3**

Cmpd	^{1}H NMR	^{13}C NMR
2a	2.68 (t, 2H, *J* = 7.4), 3.73 (td, 2H, *J* = 7.4 and 2.2), 3.91 (s, 3H), 3.93 (s, 3H), 6.68 (s, 1H), 6.82 (s, 1H), 8.24 (t, 1H).	24.8, 47.5, 56.2, 56.3, 110.6, 110.7, 121.9, 130.2, 148.2, 151.6, 160.1.
3a	3.12 (t, 2H, *J* = 7.8), 3.89 (s, 3H), 3.92 (s, 3H), 4.08 (t, 2H, *J* = 7.8), 6.63 (s, 1H), 6.74 (s, 1H), 7.68 (s, 1H).	27.7, 56.3, 56.4, 57.9, 108.8, 111.0, 121.4, 123.7, 134.3, 148.9, 150.4.
2b	2.37 (s, 3H), 2.64 (t, 2H, *J* = 7.4), 3.63 (t, 2H, *J* = 7.4), 3.92 (s, 3H), 3.92 (s, 3H), 6.70 (s, 1H), 7.00 (s, 1H).	23.5, 25.8, 47.1, 56.1, 56.4, 109.3, 110.6, 122.8, 131.5, 147.9, 151.3, 164.3.
3b	2.46 (t, 3H, *J* = 1.4), 3.05 (t, 2H, *J* = 7.4), 3.92 (s, 6H), 4.11 (td, 2H, *J* = 7.4 and 1.4), 6.73 (s, 1H), 6.83 (s, 1H).	13.2, 27.5, 56.2, 56.4, 57.8, 108.3, 110.9, 123.1, 124.9, 142.3, 148.5, 149.9.
2c	1.23 (t, 3H, *J* = 7.4), 2.62 (t, 2H, *J* = 7.4), 2.73 (qt, 2H, *J* = 7.4 and 1.4), 3.65 (tt, 2H, *J* = 7.4 and 1.4), 3.90 (s, 3H), 3.92 (s, 3H), 6.70 (s, 1H), 7.02 (s, 1H).	11.3, 25.9, 29.0, 47.1, 56.1, 56.4, 109.0, 110.6, 122.3, 131.9, 147.8, 151.1, 167.9.
3c	1.26 (t, 3H, *J* = 7.4), 3.00 (q, 2H, *J* = 7.4), 3.05 (t, 2H, *J* = 7.6), 3.92 (s, 6H), 4.11 (t, 2H, *J* = 7.6), 6.73 (s, 1H), 6.85 (s, 1H).	9.9, 20.0, 27.6, 56.2, 56.4, 58.1, 108.0, 111.0, 122.2, 125.3, 146.7, 148.6, 149.8.
2d	2.65 (t, 2H, *J* = 7.6), 3.72 (s, 3H), 3.74 (t, 2H, *J* = 7.6), 3.88 (s, 3H), 4.05 (s, 2H), 6.66 (s, 1H), 6.95 (s, 1H), 7.18-7.34 (m, 5H).	25.5, 25.7, 47.5, 56.2, 56.3, 110.0, 110.8, 119.7, 128.9 (2C), 130.9 (2C), 131.5, 134.3, 136.0, 148.1, 152.2, 164.9.
3d	3.09 (t, 2H, *J* = 7.6), 3.75 (s, 3H), 3.89 (s, 3H), 4.22 (t, 2H, *J* = 7.6), 4.37 (s, 2H), 6.71 (s, 1H), 6.83 (s, 1H), 7.19-7.34 (m, 5H)	27.8, 32.5, 56.7, 58.6 (2C), 108.9, 110.0, 122.7, 125.5, 127.1, 129.0 (2C), 129.3 (2C), 137.5, 144.6, 148.6, 150.0.
2e	2.74 (t, 2H, *J* = 7.6), 3.73 (s, 3H), 3.82 (t, 2H, *J* = 7.6), 3.96 (s, 3H), 6.79 (s, 1H), 6.81 (s, 1H), 7.41-7.47 (m, 3H), 7.59 (m, 2H).	26.1, 47.8, 56.2, 56.3, 110.5, 111.8, 121.9, 128.5 (2C), 129.1 (2C), 129.6, 132.9, 139.6, 147.5, 151.3, 167.2.
3e	3.18 (t, 2H, *J* = 7.6), 3.64 (s, 3H), 3.93 (s, 3H), 4.29 (t, 2H, *J* = 7.6), 6.39 (s, 1H), 6.78 (s, 1H), 7.41-7.61 (m, 5H).	27.7, 56.2, 56.3, 59.6, 110.5, 110.9, 123.6, 125.9, 128.7 (2C), 129.8, 130.5 (2C), 131.4, 143.1, 148.2, 150.0.
2f	2.77 (t, 2H, *J* = 7.6), 3.74 (s, 3H), 3.87 (t, 2H, *J* = 7.6), 3.97 (s, 3H), 6.65 (s, 1H), 6.82 (s, 1H), 7.80 (d, 2H, *J* = 9.0), 8.31 (d, 2H, *J* = 9.0).	25.9, 48.1, 56.3 (2C), 110.8, 111.0, 121.1, 123.9 (2C), 130.1 (2C), 133.0, 145.8, 147.8, 148.8, 151.9, 165.6.

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TABLE 2. Continued

Cmpd	^{1}H NMR	^{13}C NMR
3f	3.21 (t, 2H, *J* = 7.6), 3.66 (s, 3H), 3.95 (s, 3H), 4.32 (t, 2H, *J* = 7.6), 6.29 (s, 1H), 6.82 (s, 1H), 7.84 (d, 2H, *J* = 9.0), 8.36 (d, 2H, *J* = 9.0).	27.8, 56.5 (2C), 60.0, 110.2, 111.2, 122.5, 124.0 (2C), 126.3, 132.2 (2C), 138.2, 141.5, 148.6 (2C), 150.7.
2g	2.72 (t, 2H, *J* = 7.4), 3.75 (s, 3H), 3.78 (t, 2H, *J* = 7.4), 3.87 (s, 3H), 3.96 (s, 3H), 6.79 (s, 1H), 6.85 (s, 1H), 6.96 (d, 2H, *J* = 9.0), 7.58 (d, 2H, *J* = 9.0).	26.1, 47.7, 55.5, 56.2, 56.3, 110.5, 111.9, 113.8 (2C), 122.0, 130.6 (2C), 132.1, 133.1, 147.4, 151.2, 161.0, 166.5.
3g	3.15 (t, 2H, *J* = 7.6), 3.67 (s, 3H), 3.88 (s, 3H), 3.93 (s, 3H), 4.26 (t, 2H, *J* = 7.6), 6.46 (s, 1H), 6.77 (s, 1H), 7.01 (d, 2H, *J* = 9.0), 7.59 (d, 2H, *J* = 9.0).	27.7, 55.5, 56.2 (2C), 59.6, 110.7, 111.1, 113.9 (2C), 123.4, 123.8, 126.2, 132.3 (2C), 142.6, 148.1, 149.9, 160.6.
2h	2.34 (s, 3H), 2.68 (t, 2H, *J* = 7.6), 3.63 (t, 2H, *J* = 7.6), 3.83 (s, 3H), 6.71 (s, 1H), 6.80 (d, 1H, *J* = 8.0), 7.44 (d, 1H, *J* = 8.0).	23.2, 26.6, 46.8, 55.3, 112.0, 112.1, 112.9, 127.4, 139.9, 161.5, 164.2.
3h	2.46 (s, 3H), 3.10 (t, 2H, *J* = 7.2), 3.84 (s, 3H), 4.12 (t, 2H, *J* = 7.2), 6.75 (d, 1H, *J* = 2.4), 6.83 (dd, 1H, *J* = 8.6 and 2.4), 7.29 (d, 1H, *J* = 8.6).	13.1, 28.1, 55.6, 57.4, 112.7, 113.7, 123.2, 126.5, 133.8, 143.4, 160.7.
2i	2.78 (t, 2H, *J* = 7.2), 3.83 (t, 2H, *J* = 7.2), 3.85 (s, 3H), 6.76 (m, 2H), 7.22 (d, 1H, *J* = 8.4), 7.45-7.55 (m, 5H).	27.0, 47.7, 55.5, 111.8, 113.2, 122.7, 128.5 (2C), 129.1 (2C), 129.6, 130.2, 139.7, 141.5, 161.7, 167.3.
3i	3.22 (t, 2H, *J* = 7.4), 3.83 (s, 3H), 4.30 (tt, 2H, *J* = 7.4 and 2.6), 6.68 (dd, 1H, *J* = 8.6 and 2.6), 6.83 (d, 2H, *J* = 8.6), 7.45-7.55 (m, 5H).	28.3, 55.6, 59.2, 112.4, 113.6, 123.9, 128.7 (2C), 129.2, 129.7, 130.5 (2C), 131.5, 134.6, 143.51, 160.6.
2j	2.69 (t, 2H, *J* = 7.0), 3.73 (t, 2H, *J* = 7.0), 3.78 (s, 3H), 4.04 (s, 2H), 6.65-6.71 (m, 2H), 7.16-7.32 (m, 5H), 7.37-7.41 (m, 1H).	26.8, 43.2, 47.2, 55.4, 112.1, 113.2, 122.7, 126.7, 128.0, 128.9 (2C), 129.0 (2C), 138.6, 140.7, 161.4, 166.0.
2k	2.82 (t, 2H, *J* = 7.8, 3.79 (s, 3H), 3.93 (t, 2H, *J* = 7.8), 3.94 (s, 3H), 6.76 (s, 1H), 6.96 (s, 1H), 7.45-7.65 (m, 3H), 8.03-8.06 (m, 2H).	25.4, 47.4, 56.2 (2C), 110.0, 110.8, 119.6, 128.8 (2C), 130.8 (2C), 131.5, 134.2, 135.9, 148.0, 152.1, 164.8, 194.5.
2l	2.86 (t, 2H, *J* = 7.0), 3.84 (s, 3H), 3.94 (t, 2H, *J* = 7.0), 6.77 (m, 2H), 7.32 (d, 1H, *J* = 8.2), 7.43-7.65 (m, 3H), 8.02 (d, 2H, *J* = 8.2).	26.3, 47.3, 55.6, 112.4, 113.8, 120.5, 128.9 (3C), 130.7 (2C), 134.2, 135.9, 139.9, 162.4, 165.3, 194.6.

Synthesis of 3,4-Dihydroisoquinoline N-Oxides (3). General Procedure.- To a two-necked round-bottom flask equipped with a magnetic stirrer, under an Argon atmosphere was added the compound **2** (0.5 mmol) in dry benzene or chloroform (5.0 mL). The purified *m*-CPBA (0.53 mmol) was added at 10°, after stirring the mixture for 1-2 hrs at this temperature, the reaction was continued for 1-2 hrs at room temperature. The solvent was evaporated under reduced pressure and the residue was subjected to preparative TLC to give the nitrones 3 in 50-96% yields (see Table 1).

6,7-Dimethoxy-3,4-dihydroisoquinoline (2a), 66% yield, a colorless oil. R_f = 0.40 (silica gel, CH_2Cl_2/MeOH, 20:1). IR (neat): 1630, 1607, 1574, 1516, 1464, 1350, 1323, 1265, 1238, 1121, 1028,

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987, 860, 815 cm^{-1}. MS, m/z (%), 192 (11), 191 (M^+, 100), 176 (14).

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.13; H, 6.63; N, 7.10

6,7-Dimethoxy-1-methyl-3,4-dihydroisoquinoline (2b), 72% yield, white solid from CH_2Cl_2, mp. 100-101°, lit.[12a] 102-104°(from cyclohexane). R_f = 0.35 (silica gel, CH_2Cl_2/MeOH, 4:1). IR (KBr): 1604, 1572, 1514, 1451, 1375, 1352, 1331, 1288, 1275, 1215, 1159, 1063, 961, 872, 810 cm^{-1}. MS, m/z (%), 206 (12), 205 (M^+, 100), 190 (65).

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.22; H, 7.36; N, 6.82

6,7-Dimethoxy-1-ethyl-3,4-dihydroisoquinoline (2c), 61% yield, a colorless oil. R_f = 0.25 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (neat): 1626, 1605, 1572, 1514, 1464, 1367, 1321, 1273, 1208, 1148, 1072, 1020, 949, 862, 808 cm^{-1}. MS, m/z (%), 220 (7.48), 219 (M^+, 55), 218 (100), 204 (40), 202 (12), 189 (11), 188 (33).

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.27; H, 7.78; N, 6.35

6,7-Dimethoxy-1-benzyl-3,4-dihydroisoquinoline (2d), 65% yield, colorless needles from hexane, mp. 84-86°, lit.[13] 84-87°. R_f = 0.74 (silica gel, CH_2Cl_2/MeOH, 15:1). IR (KBr): 1605, 1572, 1516, 1466, 1358, 1323, 1271, 1215, 1148, 1045, 858, 810 cm^{-1}. MS, m/z (%), 281 (M^+, 41), 280 (100), 250 (32).

Anal. Calcd. for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.76; H, 6.78; N, 5.00

6,7-Dimethoxy-1-phenyl-3,4-dihydroisoquinoline (2e), 81% yield, colorless needles from aq. EtOH, mp. 120-122°, lit.[14] 122-123°. R_f = 0.42 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:10:1). IR (KBr): 1607, 1562, 1514, 1462, 1356, 1279, 1209, 1115, 1026, 947, 868, 806 cm^{-1}. MS, m/z (%), 268 (10), 267 (M^+, 63), 266 (100).

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.49; H, 6.33; N, 5.20

6,7-Dimethoxy-1-(*p*-nitrophenyl)-3,4-dihydroisoquinoline (2f), 80% yield, yellowish needles from aq. EtOH, mp. 158-160°, lit.[15] 150-152°. R_f = 0.59 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1603, 1564, 1520, 1468, 1352, 1279, 1215, 1123, 1026, 949, 862 cm^{-1}. MS, m/z (%), 313 (17), 312 (M^+, 92), 311 (100), 297 (8), 281 (6), 266 (8), 265 (32).

Anal. Calcd. for $C_{17}H_{16}N_2O_4$: C, 65.36; H, 5.17; N, 8.97. Found: C, 65.47; H, 5.28; N, 8.90

6,7-Dimethoxy-1-(*p*-methoxyphenyl)-3,4-dihydroisoquinoline (2g), 83% yield, colorless needles from CH_2Cl_2, mp. 120-121°, lit.[15] 118-119°. R_f = 0.37 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1604, 1561, 1512, 1464, 1406, 1356, 1258, 1213, 1171, 1119, 1030, 941, 896, 838, 808 cm^{-1}. MS, m/z (%), 298 (10), 297 (M^+, 58), 296 (100), 282 (12), 280 (10), 266 (15).

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.93; H, 6.38; N, 4.72

6-Methoxy-1-methyl-3,4-dihydroisoquinoline (2h), 70% yield, a colorless oil. R_f = 0.24 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (neat): 1607, 1570, 1501, 1433, 1372, 1312, 1281, 1254, 1148, 1073, 1026, 895, 816 cm^{-1}. MS, m/z (%), 175 (M^+, 100), 174 (84).

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.30; H, 7.63; N, 7.85

6-Methoxy-1-phenyl-3,4-dihydroisoquinoline (2i), 74% yield, a pale yellowish oil. R_f = 0.38 (silica gel, CH_2Cl_2/EtOAc/MeOH, 8:2:1). IR (neat): 1607, 1562, 1496, 1446, 1433, 1346, 1307, 1283, 1254,

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1120, 1036, 943, 821 cm^{-1}. MS, m/z (%), 237 (M^+, 42), 236 (100), 206 (14), 165 (11). This oil was crystallized as oxalate.

Anal. Calcd. for $C_{16}H_{15}NO(CO_2H)_2$: C, 66.05; H, 5.25; N, 4.28. Found: C, 66.22; H, 5.24; N, 4.18

6-Methoxy-1-benzyl-3,4-dihydroisoquinoline (2j), 60% yield, a pale yellowish oil. R_f = 0.33 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (neat): 1604, 1570, 1521, 1456, 1350, 1324, 1268, 1214, 1148, 1045, 860, 810 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.18; H, 6.95; N, 5.61

6,7-Dimethoxy-1-benzoyl-3,4-dihydroisoquinoline (2k), 18% yield, a pale yellowish oil . R_f = 0.33 (silica gel, CH_2Cl_2/MeOH, 15:1). IR (neat): 1672, 1602, 1566, 1514, 1450, 1362, 1319, 1202, 1144, 904, 798 cm^{-1}.

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.16; H, 5.85; N, 4.82

6-Methoxy-1-benzoyl-3,4-dihydroisoquinoline (2l), 100% yield based (**2j**), a white solid from CH_2Cl_2, mp. 88-90°. R_f = 0.72 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1670, 1610, 1566, 1495, 1448, 1427, 1322, 1283, 1256, 1233, 1144, 1069, 1022, 901, 835, 814 cm^{-1}. MS, m/z (%), 265 (M^+, 28), 237 (100).

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.92; H, 5.84; N, 5.28

6,7-Dimethoxy-3,4-dihydroisoquinoline N-Oxide (3a), a yellowish solid, mp. 181-184° from CH_2Cl_2/EtOAc/MeOH, lit.[16] 188-189° (from CH_2Cl_2/light petroleum ether). R_f = 0.20 (silica gel, CH_2Cl_2/EtOAc/MeOH, 10:5:1). IR (KBr): 1599, 1518, 1466, 1371, 1282, 1230, 1165, 1126, 1017, 986, 872, 789 cm^{-1}. MS, m/z (%), 208 (9), 207 (M^+, 100), 192 (30), 191 (13).

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.73; H, 6.46; N, 6.63

6,7-Dimethoxy-1-methyl-3,4-dihydroisoquinoline N-Oxide (3b), a pale yellowish solid from CH_2Cl_2/MeOH, mp. 195-198°. R_f = 0.55 (silica gel, CH_2Cl_2/MeOH, 4:1). IR (KBr): 1593, 1522, 1449, 1364, 1285, 1219, 1154, 1057, 895, 794 cm^{-1}. MS, m/z (%), 222 (13), 221 (M^+, 100), 206 (14), 205 (14), 204 (10), 161 (7), 160 (7), 133 (12).

Anal. Calcd. for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.20; H, 6.99; N, 6.10

6,7-Dimethoxy-1-ethyl-3,4-dihydroisoquinoline N-Oxide (3c), a pale yellowish solid from CH_2Cl_2/MeOH, mp. 112-115°. R_f = 0.36 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1605, 1593, 1518, 1464, 1329, 1285, 1219, 1202, 1149, 1073, 1014, 901, 853, 800 cm^{-1}. MS, m/z (%), 236 (14), 235 (M^+, 100), 234 (31), 220 (14), 219 (15), 218 (69), 204 (16), 202 (11).

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.35; H, 7.29; N, 5.96. Found: C, 66.47; H, 7.34; N, 5.77

6,7-Dimethoxy-1-benzyl-3,4-dihydroisoquinoline N-Oxide (3d), a faintly yellowish solid from CH_2Cl_2/MeOH, mp. 177-180°. R_f = 0.25 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1607, 1520, 1456, 1381, 1275, 1219, 1140, 1049, 1028, 956, 891, 841 cm^{-1}. MS, m/z (%), 297 (M^+, 10), 281 (29), 280 (100), 266 (7), 265 (9), 264 (17), 250 (25).

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.98; H, 6.43; N, 4.47

6,7-Dimethoxy-1-phenyl-3,4-dihydroisoquinoline N-Oxide (3e), a pale yellowish solid from CH_2Cl_2/MeOH, mp. 66-69°. R_f = 0.31 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:10:1). IR (KBr): 1610,

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1591, 1512, 1460, 1381, 1285, 1221, 1202, 1126, 1022, 868, 794 cm^{-1}. MS, m/z (%), 284 (16), 283 (M^+, 100), 282 (73), 267 (14), 266 (27), 252 (11), 250 (14), 236 (4).

Anal. Calcd. for $C_{17}H_{17}NO_3$: C, 72.05; H, 6.05; N, 4.95. Found: C, 72.28; H, 6.13; N, 4.74

6,7-Dimethoxy-1-(*p*-nitrophenyl)-3,4-dihydroisoquinoline N-Oxide (3f), a yellow solid from CH_2Cl_2/MeOH, mp. 232-234°. R_f = 0.35 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1603, 1514, 1446, 1346, 1284, 1206, 1130, 1022, 858 cm^{-1}. MS, m/z (%), 329 (16), 328 (M^+, 100), 327 (33), 312 (42), 311 (5), 297 (13), 265 (24).

Anal. Calcd. for $C_{17}H_{16}N_2O_5$: C, 62.18; H, 4.91; N, 8.54. Found: C, 62.11; H, 4,81; N, 8.50

6,7-Dimethoxy-1-(*p*-methoxyphenyl)-3,4-dihydroisoquinoline N-Oxide (3g), a pale yellowish solid from CH_2Cl_2/MeOH, mp. 204-205°. R_f = 0.39 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1606, 1514, 1466, 1412, 1379, 1287, 1171, 1128, 1024, 920, 872, 829, 797 cm^{-1}. MS, m/z (%), 314 (18), 313 (M^+, 100), 312 (61), 297 (23), 296 (45), 282 (16).

Anal. Calcd. for $C_{18}H_{19}NO_4$: C, 68.98; H, 6.12; N, 4.47. Found: C, 69.22; H, 6.12; N, 4.23

6-Methoxy-1-methyl-3,4-dihydroisoquinoline N-Oxide (3h), a pale yellowish oil, R_f = 0.27 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (neat): 1608, 1504, 1435, 1383, 1312, 1258, 1207, 1184, 1132, 1088, 1045, 1022, 845 cm^{-1}. MS, m/z (%), 191 (M^+, 100), 175 (28), 174 (32), 163 (16).

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7,32. Found: C, 69.17; H, 6.70; N, 7.05

6-Methoxy-1-phenyl-3,4-dihydroisoquinoline N-Oxide (3i), a pale yellowish solid from CH_2Cl_2/MeOH, mp. 135-137°. R_f = 0.42 (silica gel, CH_2Cl_2/EtOAc/MeOH, 8:2:1). IR (KBr): 1605, 1501, 1468, 1439, 1368, 1265, 1213, 1169, 1107, 1032, 960, 862, 827, 766 cm^{-1}. MS, m/z (%), 253 (M^+, 87), 252 (97), 237 (36), 236 (100), 165 (11).

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.03; H, 5.90; N, 5.40

6,7-Dimethoxy-2-ethyl-3,4-dihydro-1(2H)isoquinolinone (4a), 15% yield, a pale yellowish solid from CH_2Cl_2, mp. 114-117°. R_f = 0.73 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1678, 1604, 1570, 1520, 1360, 1294, 1271, 1182, 1136 cm^{-1}. ^1H NMR, δ 1.20 (t, 3H, *J* = 7.4), 2.95 (q, 2H, *J* = 7.4), 3.36 (t, 2H, *J* = 7.2), 3.90 (s, 3H), 3.92 (s, 3H), 4.54 (t, 2H, *J* = 7.2), 6.76 (s, 1H), 7.27 (s, 1H). ^{13}C NMR, δ 8.5, 30.3, 34.0, 56.2, 59.9 (2C), 113.0, 115.0, 129.8, 132.5, 147.6, 152.0, 202.6. MS, m/z (%), 235 (M^+, 5), 234 (35), 233 (37), 222 (67), 216 (100).

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.35; H, 7.29; N, 5.96. Found: C, 66.31; H, 7.23; N, 6.12

6-Methoxy-2-methyl-3,4-dihydro-1(2H)isoquinolinone (4b), 14% yield, a pale yellowish solid from CH_2Cl_2, mp. 113-114°. R_f = 0.72 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (KBr): 1672, 1599, 1564, 1423, 1356, 1319, 1290, 1236, 1194, 1128, 1022, 955, 824 cm^{-1}. ^1H NMR, δ 2.57 (s, 3H), 3.44 (t, 2H, *J* = 7.0), 3.83 (s, 3H), 4.53 (t, 2H, *J* = 7.0), 6.82 (dd, 2H, *J* = 2.6 and 8.6), 7.80 (d, 1H, *J* = 8.6); ^{13}C NMR, δ 29.0, 30.9, 55.6, 59.6, 112.4, 118.1, 129.9, 133.6, 141.4, 162.7, 199.7; MS, m/z (%), 191 (M^+, 8), 190 (64), 173 (100).

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.20; H, 6.80; N, 7.39

6,7-Dimethoxy-1-benzylidene-2-hydroxy-1,2,3,4-tetrahydroisoquinoline (5), 25% yield, a colorless oil. R_f = 0.28 (silica gel, CH_2Cl_2/EtOAc/MeOH, 20:2:1). IR (neat): 1605, 1516, 1452, 1373, 1281,

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1215, 1130, 1024, 952, 864, 797 cm^{-1}. ^1H NMR, δ 3.10 (t, 2H, J = 7.6), 3.80 (s, 3H), 3.92 (s, 3H), 4.13 (q, 2H, J = 7.6), 6.16 (s, 1H), 6.74 (s, 1H), 6.98 (s, 1H), 7.30-7.51 (m, 5H), 7.96 (m, 1H). ^{13}C NMR, δ 27.5, 56.3 (2C), 58.5, 70.9, 108.5, 111.1, 120.8, 126.0, 126.2 (2C), 128.3, 129.0 (2C), 133.2, 140.8, 148.7, 150.8.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.52; H, 6.19; N, 4.74

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(Received April 23, 1996; in revised form September 17, 1996)

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