A Convenient Synthesis of 3-Aryl-3,4-dihydroisoquinolinium Salts

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A convenient synthesis of the title compounds proceeding *via* direct Bischler-Napieralski cyclization reaction of the appropriate *N,N*-dialkylformamides obtained from the adequate imines is described. The reported procedure implies synthetically useful yields and mild reaction conditions.

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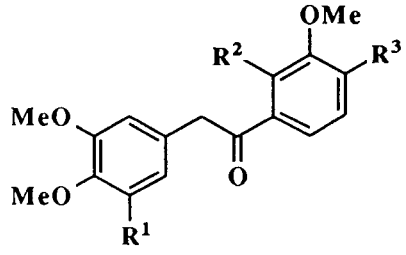
In connection with our investigations in the field of 3-arylisoquinoline derivatives, we required a convenient procedure for the synthesis of *N*-alkyl-3-aryl-3,4-dihydroisoquinolinium salts. Although the already mentioned synthetic objective, often involves treatment of the adequate deoxybenzoin under Leuckart amination conditions [1], nevertheless this procedure is not always compatible with functionalities elsewhere in the substrate [2], and in most cases affords stilbene, pyrimidine, isoflavone and pyridine derivatives as by-products, during the formation of the expected formamide derivatives [3]. Even more, in our hands, the Leuckart reaction with appropriate phenolic deoxybenzoines always failed to yield the anticipated formamide, affording exclusively the already mentioned compounds in significant yields [4].

Besides, in connection with our continuous interest in the synthesis of isoquinoline derivatives, experiments carried out by our research group have proved that the already mentioned amination conditions are not compatible with the presence of labile protective groups in the starting deoxybenzoin derivative [5], probably due to the reaction condtions.

We wish now to report further investigations that we have done on the preparation of formamide derivatives of the required type **2** by an alternative route which implies condensation reaction of the deoxybenzoin **1** with an adequate *N*-alkylamine followed by reduction of the obtained imine and subsequent formylation, and the results obtained when the latter compounds were applied to the direct synthesis of the corresponding 3-aryl-3,4-dihydroisoquinolium salts, avoiding the final *N*-alkylation reaction, thus reducing the total number of steps. This new approach is



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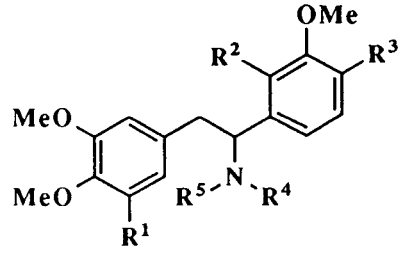
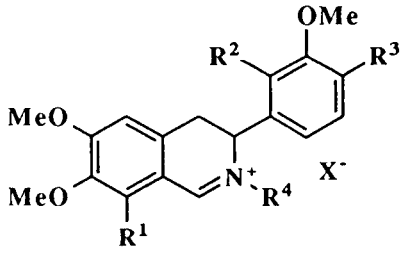


2

1	R^1	R^2	R^3
a	H	H	OMe
b	H	OMe	H
c	OMe	H	OMe

2	R^1	R^2	R^3	R^4	R^5
a	H	H	OMe	Pr	H
b	H	H	OMe	Me	H
c	H	H	OMe	Pr	CHO
d	H	H	OMe	Me	CHO
e	H	H	OMe	H	CHO
f	H	OMe	H	H	CHO
g	OMe	H	OMe	H	CHO



3

3	R^1	R^2	R^3	R^4	X
a	H	H	OMe	Pr	Cl
b	H	H	OMe	Me	Cl
c	H	H	OMe	H	Cl
d	H	OMe	H	H	Cl
e	OMe	H	OMe	H	Cl
f	H	H	OMe	Me	I
g	H	OMe	H	Me	I
h	OMe	H	OMe	Me	I

Table 1. Compounds 2 and 3 Prepared.

Sub-strate	Reaction Time (h)	Prod-uct	Yield[a] (%)	Mp (°C) (Solvent)	Formula or Lit. mp (°C)	Calcd. (Found) (%) C	H	N	X
1a	4.5	**2a**	75	146-147 (Ethyl acetate)	$C_{21}H_{29}NO_4$	70.21 (70.35)	8.14 (8.13)	3.90 (3.91)	
1a	4.5	**2b**	92	syrup	$C_{19}H_{25}NO_4$	68.86 (68.75)	7.60 (7.61)	4.23 (4.22)	
1b	3	**2f**	80	116-118 (Ethanol)	$C_{19}H_{22}NO_5$	66.26 (66.34)	6.44 (6.45)	4.67 (4.67)	
2a	9	**2c**	62	110-111 (Ethyl acetate)	$C_{22}H_{29}NO_5$	68.20 (68.33)	7.54 (7.53)	3.61 (3.60)	
2b	7	**2d**	75	151-152 (Ethyl acetate)	$C_{20}H_{25}NO_5$	66.84 (66.90)	7.01 (7.01)	3.90 (3.91)	
2c	0.3	**3a**	91	syrup	$C_{22}H_{28}ClNO_4$	65.10 (65.18)	6.95 (6.96)	3.45 (3.45)	8.75 (8.74)
2d	0.3	**3b**	95	syrup	$C_{20}H_{24}ClNO_4$	63.57 (63.48)	6.40 (6.41)	3.71 (3.71)	9.38 (9.40)
2e	3	**3c**	81	240-242 (Acetone)	240-242 [11]				
2f	0.5	**3d**	90	180-182 (Acetone/Methanol)	$C_{19}H_{22}ClNO_4$	62.72 (62.67)	6.10 (6.10)	3.85 (3.85)	9.74 (9.71)
2g	0.5	**3e**	90	--[b]	$C_{20}H_{24}ClNO_5$	63.57 (63.51)	5.87 (5.88)	3.71 (3.71)	9.38 (9.37)
3c	50	**3f**	90	203-205 (Methanol)	204-205 [12]				
3d	144	**3g**	86	115[c] (Methanol)	$C_{20}H_{24}INO_4$	51.15 (51.09)	5.15 (5.15)	2.98 (2.98)	27.02 (26.91)
3e	40	**3h**	88	205[c] (Acetonitrile)	$C_{21}H_{26}INO_5$	50.51 (50.63)	5.25 (5.24)	2.81 (2.82)	25.41 (25.52)

[a] Yield of pure isolated product.
[b] Hygroscopic compound; decomposes by standing.
[c] Decomposes on heating. The given temperatures are oven temperatures, not true melting points.

Table 2. Spectral Data of New Compounds **2** and **3**.

Product	IR(KBr) ν(cm-1)	PMR[a] δ,J (Hz)	CMR[b] δ
2a		0.88(t,J=7.3,3H,C<u>H</u>$_3$CH$_2$); CH$_3$C<u>H</u>$_2$); 2.71(m,2H,CH$_2$N); 3.44(m, 1H,C<u>H</u>$_2$CH); 3.63(s,3H,CH$_3$O); 3.78(s, 3H,CH$_3$O); 3.85(s,3H,CH$_3$O); 3.94(m, 1H,C<u>H</u>$_2$CH); 3.98(s,3H,CH$_3$O); 4.08(m, 1H,CH$_2$C<u>H</u>); 6.55-6.70(m,5H,Harom); 7.45(s,1H,Harom)	1.98(m,2H, 11.24(<u>C</u>H$_3$CH$_2$);19.38(CH$_3$<u>C</u>H$_2$); 40.14(<u>C</u>H$_2$CH); 47.49(CH$_2$N); 55.51, 55.55,55.64,56.45(CH$_3$O); 65.33 (CH$_2$<u>C</u>H); 110.25,110.60,110.71, 112.31,121.43,121.93(HCarom); 125.86, 128.14(C<u>C</u>arom); 147.54,148.31,149.37, 149.72(CH$_3$O<u>C</u>arom)
2b		1.81(br s,1H,NH); 2.23(s,3H,CH$_3$N); 2.81(dd,J$_{AX}$=8.0,J$_{AB}$=13.5,1H,C<u>H</u>$_2$CH); 2.89(dd,J$_{BX}$=5.8,J$_{AB}$=13.5,1H,C<u>H</u>$_2$CH); 3.63(dd,J$_{AX}$=8.0,J$_{BX}$=5.8,1H,CH$_2$C<u>H</u>); 3.81(s,3H,CH$_3$O); 3.85(s,3H,CH$_3$O); 3.87 (s,3H,CH$_3$O); 3.88(s,3H,CH$_3$O); 6.60(dd, Jmeta=1.6,1H,Harom); 6.69(dd, Jortho=8.1, 1H,Harom); 6.76-6.87(m,4H,Harom)	34.38(CH$_3$N); 44.61(<u>C</u>H$_2$CH);55.66, 55.75,55.76,55.80(CH$_3$O); 66.61 (CH$_2$<u>C</u>H);109.82,110.70,111.03,112.37, 119.64,121.17(HCarom); 131.12,135.46 (C<u>C</u>arom); 147.45,146.96,148.58,148.95 (CH$_3$O<u>C</u>arom)
2c	1670 (C=O)	0.68,0.71(2t,J=7.3,J=7.2,3H,C<u>H</u>$_3$CH$_2$); 1.05,1.42(2m,2H,CH$_3$C<u>H</u>$_2$); 2.83-3.34 (m,4H,CH$_2$N and C<u>H</u>$_2$CH); 3.83-3.90 (6s,12H,CH$_3$O); 4.59(dd,J$_{AX}$=6.6,J$_{BX}$= 8.4,0.65H,CH$_2$C<u>H</u>); 5.59(dd,J$_{AX}$=8.0, J$_{BX}$=8.2,0.35H,CH$_2$C<u>H</u>); 6.60-6.97(m, 6H,Harom); 8.00(s,0.65H,CHO); 8.08(s, 0.35H,CHO); (mixture of rotamers, ratio 1.9:1)	11.16,11.58(<u>C</u>H$_3$CH$_2$); 21.35,23.63 (CH$_3$<u>C</u>H$_2$); 36.68,38.25(<u>C</u>H$_2$CH);43.89, 47.48(CH$_2$N); 55.84-56.86(CH$_3$O); 63.46(CH$_2$<u>C</u>H);110.59-121.29(HCarom); 129.91-131.96(C<u>C</u>arom); 147.55-149.09 (CH$_3$O<u>C</u>arom); 162.51,163.36(C=O)[c]
2d	1675 (C=O)	2.65,2.66(2s,1H,CH$_3$N); 3.15(dd,J$_{AX}$= 10.1,J$_{AB}$=15.0,0.65H,C<u>H</u>$_2$CH); 3.16(dd, J$_{AX}$=10.3,J$_{AB}$=14.8,0.35H,C<u>H</u>$_2$CH);3.24 (dd,J$_{BX}$=6.5,J$_{AB}$=15.0,0.65H,C<u>H</u>$_2$CH); 3.25(dd,J$_{BX}$=4.7,J$_{AB}$=14.8,0.35H,C<u>H</u>$_2$CH); 3.84-3.90(6s,12H,CH$_3$O);4.68(dd,J$_{AX}$= 10.1,J$_{BX}$=6.5,0.65H,CH$_2$C<u>H</u>); 5.99(dd, J$_{AX}$=10.3,J$_{BX}$=4.7,0.35H,CH$_2$C<u>H</u>); 6.62-6.98(m,6H,Harom); 7.89(s,0.65H,CHO); 7.97(s,0.35H,CHO); (mixture of rotamers, ratio 1.9:1)	25.85,29.83(CH$_3$N); 34.96,36.16 (<u>C</u>H$_2$CH); 53.50-55.87(CH$_3$O); 62.92 (CH$_2$<u>C</u>H); 110.56-121.03(HCarom); 129.71-130.91(C<u>C</u>arom); 147.99-149.18 (CH$_3$O<u>C</u>arom); 162.50,162.75(C=O)[c]
2f	3300,3100 (NH) 1690,1660 (C=O)	3.04(m,2H,C<u>H</u>$_2$CH); 3.72-3.88(8s,12H, CH$_3$O); 4.88(m,0.25H,CH$_2$C<u>H</u>); 5.51(m, 0.75H,CH$_2$C<u>H</u>); 6.40-7.06(m,7H,Harom and NH); 7.87(d,J=12.8,0.25H,CHO); 8.11(br s,0.75H,CHO); (mixture of rotamers, ratio 3:1)	41.68,42.92(<u>C</u>H$_2$CH); 50.18,54.29 (CH$_2$<u>C</u>H); 55.63-60.71(CH$_3$O); 111.00-124.14(HCarom);129.61-134.50(CCarom); 146.00-152.63 (CH$_3$O<u>C</u>arom); 160.18, 164.00(C=O)[c]

Tabla 2. Continued.

3a	1645 (C=N$^+$)[d]	1.01(t,J=7.3,3H,C<u>H</u>$_3$CH$_2$); 1.93(m,2H, CH$_3$C<u>H</u>$_2$); 3.39(dd,JAX=3.4,JAB=17.3, 1H,H-4); 3.76(s,3H,CH$_3$O); 3.78(s,3H, CH$_3$O); 3.82(dd,JBX=7.9,JAB=17.3,1H, H-4); 3.92(s,3H,CH$_3$O); 3.93(s,3H, CH$_3$O); 5.38(dd,JAX=3.4,JBX=7.9,1H, H-3); 6.66-6.78(m,3H,Harom); 7.28(s,1H, H-5); 8.04(s,1H,H-8); 10.66(s,1H,H-1)	10.62(<u>C</u>H$_3$CH$_2$);22.01(CH$_3$<u>C</u>H$_2$);34.25 (C-4);55.72,56.05,56.46,56.53(CH$_3$O); 59.47(CH$_2$N),60.80(C-3);109.39,110.86 111.23,116.15(HCarom);117.23(C<u>C</u>arom); 118.46(HCarom);126.62,129.61(C<u>C</u>arom); 148.64,149.42,149.68,157.42 (CH$_3$O<u>C</u>arom); 165.93(C-1)
3b	1655 (C=N$^+$)[d]	3.19(dd,JAX=3.8,JAB=17.3,1H,H-4);3.81 (s,3H,CH$_3$O); 3.84(s,3H,CH$_3$O); 3.87(s, 3H,CH$_3$O); 3.94(s,6H,CH$_3$O and CH$_3$N); 4.03(dd,J$_B$BX=8.3,JAB=17.3,1H,H-4);5.35 (dd,JAX=3.8,JBX=8.3,1H,H-3); 6.65-6.80 (m,3H,Harom); 7.30(s,1H,H-5); 7.77(s,1H, H-8); 10.49(s,1H,H-1)	33.84(C-4); 45.57(CH3N); 55.83,56.06, 56.47,56.56,62.82(CH$_3$O and C-3); 109.74,110.76,111.42, 115.72(HCarom); 117.11(C<u>C</u>arom);118.68(HCarom;126.93, 129.90(C<u>C</u>arom); 148.61,149.56,149.92, 157.31(CH$_3$O<u>C</u>arom); 166.15(C-1)
3d	1630 (C=N$^+$)	3.4(m,2H,C-4); 3.9(s,3H,CH$_3$O); 4.0(s,9H, CH$_3$O); 5.6(m,1H,C-3); 6.7-7.1(m,5H, Harom); 7.7(br s,1H,N$^+$H); 9.5(br s,1H, C-1)[e]	[f]
3g	1650 (C=N$^+$)	3.26(dd,JAX=4.2,JAB=16.2,1H,H-4); 3.79(s,3H,CH$_3$N); 3.90(dd,JBX=7.9, JAB=16.2,1H,H-4); 3.92(s,3H,CH$_3$O); 3.98 (s,3H,CH$_3$O); 3.99(s,3H,CH$_3$O); 4.00(s,3H, CH$_3$O); 5.52(dd,JAX=4.2,JBX=8.5,1H, CH$_2$C<u>H</u>); 6.62(dd,Jmeta=1.8,Jortho=7.5,1H, H-4'); 6.69(s,1H,H-5); 6.95(dd,Jmeta=1.8, Jortho=8.4,1H,H-6'); 6.99(d,J=7.5,1H, H-5'); 7.90(s,1H,H-8); 10.5(s,1H,H-1)	32.87(C-4); 46.08(CH$_3$N); 55.92,56.72, 56.90,57.97,61.34(CH$_3$O and C-3); 111.10,113.81,115.89,117.03,118.07 (HCarom); 124.78, 127.37,130.55 (C<u>C</u>arom); 146.24, 148.83,152.98, 157.74(CH$_3$O<u>C</u>arom); 165.59(C-1)
3h	1640 (C=N$^+$)	3.29(dd,JAX=4.9,JAB=17.2,1H,H-4 eq); 3.80(s,3H,CH$_3$N); 3.85(s,6H,CH$_3$O); 3.87 (s,3H,CH$_3$O); 3.97(s,3H,CH$_3$O); 3.98(dd, JBX=8.1,JAB=17.2,1H,H-4 ax); 4.24(s,3H, CH$_3$O); 5.48(dd,JAX=4.9,JBX=8.1,1H,H-3); 6.60(s,1H,H-5); 6.73(dd,Jmeta=1.8,Jortho= 8.3,1H,H-6'); 6.79(d,Jortho=8.3,1H,H-5'); 6.97(d,Jmeta=1.8,1H,H-2'); 9.30(s,1H,H-1)	34.39(C-4); 46.97(CH$_3$N); 55.86,56.42, 56.91,61.13, 62.49,62.67 (CH$_3$O and C-3); 107.28,110.41 (HCarom); 111.08 (C<u>C</u>arom); 111.32, 118.79(HCarom); 126.88,133.17 (C<u>C</u>arom); 139.56, 149.50,149.79, 155.52,160.47 (CH$_3$O<u>C</u>arom);163.11(C-1)

[a] Assignements made using "double resonance decoupling experiments"
[b] Assignements were made with the aid of DEPT experiments
[c] The reported spectra are superpositions of two rotamers
[d] Film
[e] Recorded on a Perkin-Elmer R-12 (60MHz)
[f] Spectrum could not be recorded due to lack of sufficient material

particularly useful in the synthesis of isoquinolone derivatives [6] and tetracyclic alkaloids such as protoberberines [7] and benzophenanthridines [8]. Moreover, imines [9] and iminium salts [10] are known to be very interesting reagents for the formation of carbon-carbon bonds α to a nitrogen atom, upon reaction with carbanion equivalents.

Formation of amines **2a** and **2b** was carried out by direct reaction of ketone **1a** with propyl- and methylamine respectively followed by reduction of the so-obtained crude imine. The adequate treatment of compounds **2a** and **2b** with freshly prepared dry chloral afforded the corresponding formamides **2c** and **2d** in good yields. One-pot preparation of *N*-alkyl-3-aryl-3,4-dihydroisoquinolinium salts was carreid out *via* classical Bischler-Napieralski (BN) cyclization reaction conditions. The overall yield obtained following this sequence, for the synthesis of the 6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-2-methyl-3,4-dihydroisoquinolinium chloride, **3b** starting from deoxybenzoin **1a**, was 65%.

Together with the development of this strategy for isoquinolinium ring construction and in order to adequately evaluate the obtained results, we carried out the classical procedure which implies reductive amination reaction, followed by BN cyclization conditions and quaternization of the so-obtained dihydroisoquinoline derivatives. This *modus operandi* afforded the *N*-methyl salt **3f** starting from **1a**, with only an overall yield of 45%, the same procedure applied to salts **3g** and **3h** implied overall yields of 36% and 49% respectively.

To sum up, we may propose from our results that, the reported method appears to be more efficient for the synthesis of *N*-alkylated dihydroisoquinolinium salts. In fact, the relatively high conversion and regioselectivity, the tolerance towards functionalities combined with the mild conditions and the simplicity of the operations should make it potentially very useful in the synthesis of *N*-alkyl-3-aryl-3,4-dihydroisoquinolinium salts. Synthetic data for the obtained compounds are given in Table 1.

On the other hand, in accordance with the behaviour of similar compounds [13], we suggest that the obtained formamide derivatives should present two amide bond rotamers. In fact, compounds **2c**, **2d** and **2f** are obtained as mixtures of rotamers, as can be deduced from the signals of the pmr and cmr spectra. See Table 2 for spectroscopic data.

EXPERIMENTAL

Melting points were determined on either Electrothermal 1A 6304 or Büchi apparatus and are uncorrected. The ir spectra were measured in a Perkin-Elmer 1430 spectrophotometer and only noteworthy absorptions are given. The pmr spectra were recorded, except when otherwise stated, at 250.13 MHz and cmr spectra at 62.83 MHz on a Bruker ACE-250 spectrometer interfaced with an ASPECT-3000 computer, operating in the Fourier transform mode, at ambient temperature. Chemical shifts are reported in parts per million (ppm) downfield (δ) from internal tetramethylsilane; the solvent was deuteriochloroform. Combustion analyses were performed with a Perkin-Elmer model 240B apparatus. The reactions were performed under an atmosphere of dry, deoxygenated argon, unless otherwise indicated. All glassware was dried at 150° overnight, assembled hot, and allowed to cool in a stream of dry argon. All transfers of liquid solutions and solvents were performed by syringe techniques or *via* canula [14]. All solvents were freshly distilled from the appropriate drying agent before use [15]. Chloral was carefully prepared from commercial hydrate of chloral (Merck) [16]. All reactions were monitored by ir spectroscopy or by thin-layer chromatography (tlc) carried out on 0.2 mm silica gel 60 GF-254 (Merck) plates using uv light and Dragendorff's reagent [17] as the developing agents. The flash column chromatography [18] was performed on Merck Kieselgel 60 (0.040-0.063 nm, 230-400 mesh).

1,2-Bis(3,4-dimethoxyphenyl)-*N*-methylethylamine (**2b**).

Typical Procedure.

To a solution of titanium tetrachloride (1.10 ml, 0.01 mole) in dry chloroform (32.5 ml) at 0°, a solution of ketone **1a** [19] (3.20 g, 0.01 mole), and methylamine (0.95 g, 0.03 mole) in dry chloroform (105 ml) was added and then the mixture was refluxed. When the reaction was completed, the precipitates were removed by filtration, and the filtrate was evaporated to dryness *in vacuo*, to afford a syrup. Analysis by means of ir spectroscopy of this crude material showed the presence of the imine bond (band at 1640 cm^{-1}). This residue, without further purification was dissolved in dry methanol, and then treated with sodium borohydride at room temperature (portions of 40 mg every 30 minutes) until the reaction was completed, then diluted with a large amount of water and extracted with chloroform (4 x 50 ml). The combined extracts were dried over sodium sulfate and evaporated to dryness in a rotatory evaporator, yielding ethylamine **2b** as an oily product.

N-Formyl-1,2-bis(3,4-dimethoxyphenyl)-*N*-methylethylamine (**2d**).

Typical Procedure.

To a solution of the amine **2b** (3.31 g, 0.01 mole) in dry chloroform (36 ml), freshly prepared chloral (4.10 ml, 0.04 mole) was added portionwise and the whole was refluxed for 8 hours. Water was added and the reaction mixture was extracted with chloroform (4 x 50 ml), dried (sodium sulfate) and then concentrated under reduced pressure. Flash column chromatography of the crude was run with chloroform/ethyl acetate 1:9, affording compound **2d** as the major product.

6,7-Dimethoxy-3-(3,4-dimethoxyphenyl)-2-methyl-3,4-dihydroisoquinolinium Chloride (**3b**).

Typical Procedure.

To a solution of the *N*-methylformamide **2d** (3.60 g, 0.02 mole) in dry acetonitrile (15 ml), phosphorus oxychloride (0.60 ml) was added *via* canula and the reaction mixture was refluxed for 20 minutes. The solvent was evaporated in a rotatory evaporator and the residue was submitted to purification by flash column chromatography, first with dichloromethane/ethyl acetate 8:2 followed by chloroform/methanol 9:1 affording the expected isoquinolinium chloride **3b**.

N-Formyl-1-(2,3-dimethoxyphenyl)-2-(3,4-dimethoxyphenyl)ethylamine (**2f**).

Typical Procedure.

A mixture of ketone **1b** [20] (12.64 g, 0.04 mole), ammonium formate (22.22 g, 0.40 mole), 98% formic acid (4 ml, 0.10 mole) and formamide (4 ml, 0.10 mole) was heated at 185-190° for 3 hours. After cooling to room temperature the reaction mixture was poured into ice-water and an abundant brown gum was produced. After filtration the obtained crude material, chromatographically pure, was crystallized from ethanol to yield compound **2f** as a white solid.

6,7-Dimethoxy-3-(2,3-dimethoxyphenyl)-3,4-dihydroisoquinolinium Chloride (**3d**).

Typical Procedure.

To a magnetically stirred solution of the ethylformamide **2f** (34.50 g, 0.10 mole) in dry dichloromethane, anhidrous phosphorus pentachloride (166.60 g, 0.80 mole) was added. The addition was carried out in portions under argon atmosphere at 0°. After 1 hour the cooling bath was removed and the stirring was continued until the reaction was completed (tlc monitored using dichloromethane/ethyl acetate 6:4 as eluent). In order to destroy the excess of phosphorus pentachloride, water was added slowly. After the extraction with dichloromethane and drying (sodium sulfate), the solvent was removed under reduced pressure and a yellow solid was obtained, which consisted in nearly pure isoquinoline **3d**.

6,7-Dimethoxy-3-(2,3-dimethoxyphenyl)-2-methyl-3,4-dihydroisoquinolinium Iodide (**3g**).

Typical Procedure.

The isoquinoline derivative **3d** (3.65 g, 0.01 mole) was dissolved in a mixture of methanol-ethyl ether 2:1 (135 ml). Methyl iodide (28 ml, 0.45 mole) was added and the reaction mixture was refluxed for the required period of time (tlc, chloroform/methanol 9.5:0.5). The solvent was evaporated under vacuum and the residue was washed with ethyl ether to eliminate the excess of methyl iodide. Water was added and the crude was extracted with chloroform, the organic layer was dried (sodium sulfate) and then evaporated under reduced pressure. The so-obtained residue was chromatographed affording a pure material which decomposed by standing. We have improved the preparation of methiodide **3g** by following the procedure recently described by Fodor and co-workers [21].

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