A Facile Synthesis of 1-Substituted 3-Alkoxy-1*H*-isoindoles Based on the Reaction of 2-(Dialkoxymethyl)phenyllithiums with Nitriles, Followed by Acid-Catalyzed Cyclization

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A two-step synthesis of 1-substituted 3-alkoxy-1*H*-isoindoles **4** has been developed. Thus, the reaction of 2-(dialkoxymethyl)phenyllithium compounds, which are easily generated *in situ* by Br/Li exchange between 1-bromo-2-(dialkoxymethyl)benzenes **1** and BuLi in THF at −78°, with nitriles afforded [2-(dialkoxymethyl)phenyl]methanimines **2**, which were treated with a catalytic amount of $TsOH \cdot H_2O$ in refluxing $CHCl_3$ to give the desired products in reasonable yields. Similarly, 3-aryl-1-ethoxy-1-methyl-1*H*-isoindoles **7** have been prepared starting from 1-bromo-2-(1,1-diethoxyethyl)benzenes **5**.

Introduction. – 3-Alkoxy-1*H*-isoindole derivatives have received much attention, because some of them have been shown to be useful precursors for the construction of structurally complex and biologically important molecules, such as 2,3,4,6-tetrahydropyrimido[2,1-*a*]isoindoles [1], phthalazines [2], and pyrido[2,1-*a*]isoindoles [3]. To date, 3-alkoxy-1*H*-isoindoles have been commonly prepared by treating 2,3-dihydro-1*H*-isoindol-1-ones with F_3CSO_3Me [3] or $R_3O^+BF_4^-$ [4], while an elegant preparation by the Pd-catalyzed reaction of 2-alkynylbenzonitriles with aryl iodides has also been reported [5]. In the course of our studies on the development of new methods for the preparation of benzo-fused heterocycles [6], in which reactions of 2-(1,1-dialkoxyalkyl)phenyllithium compounds [7] with various electrophiles are utilized, it was anticipated that 3-alkoxy-1*H*-isoindoles could be prepared *via* the reaction of 2-(dialkoxymethyl)phenyllithiums with nitriles, followed by acid-catalyzed cyclization of the resulting [2-(dialkoxymethyl)phenyl]methanimines. We herein report the results of our investigation, which offer a new and facile two-step approach toward the preparation of 1-substituted 3-alkoxy-1*H*-isoindoles **4** from 1-bromo-2-(dialkoxymethyl)benzenes **1**.

Results and Discussion. – Our two-step synthesis of **4** from **1** was conducted according to the procedure outlined in *Scheme 1*. Compounds **1** were easily prepared from the respective 2-bromobenzaldehydes as described in [1], and were subjected to Br/Li exchange with BuLi in THF at −78° to generate 2-(dialkoxymethyl)phenyllithium derivatives as described in [6]. These Li compounds were then allowed to react with nitriles to afford, after aqueous workup, the corresponding imines **2** in generally good yields (*cf. Table*). Not only aromatic nitriles but also an aliphatic nitrile, *i.e.*, 2,2-

Scheme 1

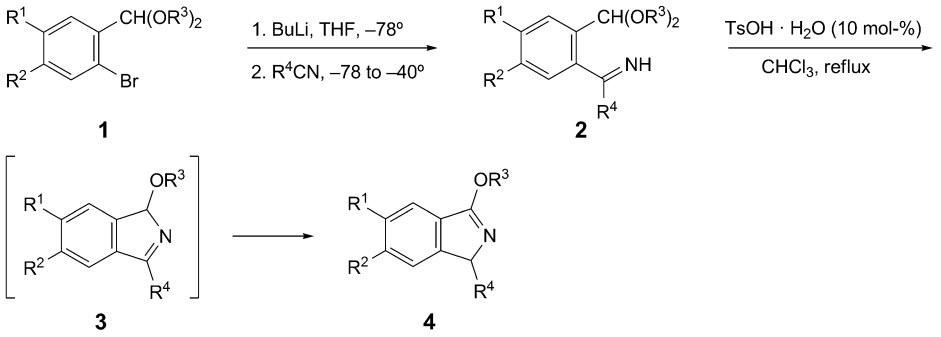


Table. *Preparation of 1-Substituted 3-Alkoxy-1*H*-isoindoles* **4**

Entry	**1**	R^4	**2**	Yield [%][a])	**4**	Yield [%][a])
1	**1a** ($R^1 = R^2 = H$, $R^3 = Et$)	Ph	**2a**	95	**4a** [12a]	65
2	**1a**	3-Cl–C_6H_4	**2b**	87	**4b**	76
3	**1a**	4-Cl–C_6H_4	**2c**	81	**4c** [2]	80
4	**1a**	4-MeO–C_6H_4	**2d**	66	**4d** [13]	70
5	**1a**	^{t}Bu	**2e**	36	**4e**	63
6	**1b** ($R^1 = R^2 = H$, $R^3 = Me$)	Ph	**2f**	81	**4f** [12]	43
7	**1b**	3-Cl–C_6H_4	**2g**	82	**4g**	52
8	**1c** ($R^1 = Cl$, $R^2 = H$, $R^3 = Et$)	Ph	**2h**	69	**4h**	64
9	**1c**	3-Cl–C_6H_4	**2i**	72	**4i**	66
10	**1d** ($R^1 = MeO$, $R^2 = H$, $R^3 = Et$)	Ph	**2j**	68	**4j**	57
11	**1d**	3-Cl–C_6H_4	**2k**	68	**4k**	69
12	**1e** ($R^1 = R^2 = MeO$, $R^3 = Et$)	Ph	**2l**	68	**4l**	65
13	**1e**	3-Cl–C_6H_4	**2m**	65	**4m**	57
14	**1e**	4-Cl–C_6H_4	**2n**	60	**4n**	63

[a]) Yields of the isolated products.

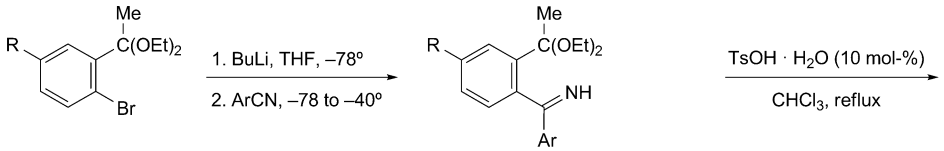
dimethylpropanenitrile, was used in this reaction; however, the yield of the product was rather lower than those from aromatic nitriles (*Entry 5*). Unfortunately, the reaction of 2-(diethoxymethyl)phenyllithium with propanenitrile gave only a trace amount of the expected imine. The failure is assumed to be attributable to the abstraction of the α-H-atom of propanenitrile by the Li compound. Since the imines **2** were somewhat unstable during separation by column chromatography on usual acidic SiO_2, their isolation was achieved by using neutral SiO_2.

Subsequently, [2-(dialkoxymethyl)phenyl]methanimines **2** were converted to the desired 3-alkoxy-1*H*-isoindole derivatives **4**. After preliminary some experiments, $CHCl_3$ proved to be a solvent superior to others, such as CH_2Cl_2 and toluene. When these imines **2** were treated with a catalytic amount of $TsOH \cdot H_2O$ (10 mol-%) in refluxing $CHCl_3$, cyclization by substitution of one of the alkoxy groups by the imino N-atom, giving the strained 3-substituted 1-alkoxy-1*H*-isoindole intermediate **3**, pro-

ceeded gradually, and a quick double-bond migration took place to give rise to the less strained 1-substituted 3-alkoxy-1*H*-isoindoles **4**. No spots corresponding to the intermediates **3** could be observed by TLC during the reaction. The yields of **4** are also compiled in the *Table*, which indicate that generally fair yields were obtained. The products carrying electron-donating group(s) on the 1*H*-isoindole benzene ring or an electron-withdrawing group on the 1-aryl ring were formed more smoothly than the others, though there was no significant difference in the yields of the products. It should be noted that the yields of 3-MeO derivatives **4f** and **4g** (*Entries 6* and *7*) were rather lower than those of the corresponding 3-EtO derivatives **4a** and **4b**, respectively (*Entries 1* and *2*). This may be attributable to the difference of lability between 3-MeO and 3-EtO derivatives toward the acidic reaction conditions. Therefore, (±)-camphor-10-sulfonic acid (CSA) could be used in this cyclization. Although the reactions appeared to proceed more cleanly than those with $TsOH \cdot H_2O$, extended reaction times were required, and no significant improvement of the yields of the products was observed.

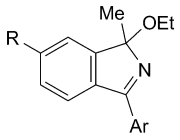
To probe the preparation of 1-alkoxy-1*H*-isoindole derivatives **7**, 1-bromo-2-(1,1-diethoxyethyl)benzenes **5** were prepared and subjected to the same reaction sequence as for the preparation of **4** from **1**. As outlined in *Scheme 2*, successive treatment of **5** with BuLi and nitriles afforded the corresponding imine precursors **6**. When compounds **6** were subjected to the treatment with a catalytic amount of $TsOH \cdot H_2O$ in refluxing $CHCl_3$, the desired cyclization products **7** were obtained. However, the yields of **7** were much lower than those of **4**. This may be ascribed to the lability of **7** toward the reaction conditions due to the strained 3-substituted 1-alkoxy-1*H*-isoindole structure compared to the 1-substituted 3-alkoxy-1*H*-isoindole structure of **4**.

Scheme 2



5a R = H
5b R = MeO

6a R = H, Ar = 4-Cl–C_6H_4 (75%)
6b R = MeO, Ar = Ph (59%)
6c R = MeO, Ar = 3-Cl–C_6H_4 (75%)



7a R = H, Ar = 4-Cl–C_6H_4 (32%)
7b R = MeO, Ar = Ph (45%)
7c R = MeO, Ar = 3-Cl–C_6H_4 (45%)

Conclusions. – It has been demonstrated that the reaction of 2-(dialkoxymethyl)-phenyllithium compounds with nitriles, followed by acid-catalyzed cyclization of the resulting [2-(dialkoxymethyl)phenyl]methanimines, provides a reliable two-step meth-

od for the preparation of 1-substituted 3-alkoxy-1*H*-isoindoles from 1-bromo-2-(dialkoxymethyl)benzenes. The presented protocol has advantages over previous methods in that starting materials are readily available and that the operations with inexpensive reagents are very simple. We are currently evaluating further utilizations of 2-(dialkoxymethyl)phenyllithiums for the preparation of other heterocyclic systems.

Experimental Part

General. All org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E* or *Kanto Silica Gel 60 N*. M.p.: *Laboratory Devices MEL-TEMP II* melting-point apparatus; uncorrected. IR Spectra: *PerkinElmer Spectrum65* FT-IR spectrophotometer; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker Biospin AVANCE II 600* FT NMR spectrometer or *JEOL ECP500* FT NMR spectrometer (at 600 and 500 MHz, resp., for ^1H, and at 150 and 125 MHz, resp., for ^{13}C), in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-MS (DART, pos.): *Thermo Scientific Exactive* spectrometer; in *m*/*z*.

1-(2-Bromo-5-methoxyphenyl)ethanone [8], *1-bromo-2-(dimethoxymethyl)benzene* (**1b**) [9], and *1-bromo-4-chloro-2-(diethoxymethyl)benzene* (**1c**) [6a] were prepared according to the appropriate reported procedures. BuLi was supplied by *Asia Lithium Corporation*. All other chemicals used were commercially available.

1-Bromo-4-methoxy-2-(diethoxymethyl)benzene (**1d**) [10] was prepared from 2-bromo-5-methoxybenzaldehyde and $HC(OEt)_3$ as described in [9] for **1b**. Yield: 82%. Pale-yellow liquid. R_f (CH_2Cl_2/hexane 2:3) 0.43. IR (neat): 1060. ^1H-NMR (500 MHz): 1.25 (*t*, *J* = 6.9, 6 H); 3.56–3.62 (*m*, 2 H); 3.66–3.72 (*m*, 2 H); 3.80 (*s*, 3 H); 5.60 (*s*, 1 H); 6.75 (*dd*, *J* = 8.4, 3.1, 1 H); 7.21 (*d*, *J* = 3.1, 1 H); 7.42 (*d*, *J* = 8.4, 1 H).

1-Bromo-2-(diethoxymethyl)-4,5-dimethoxybenzene (**1e**) [11] was prepared from 2-bromo-4,5-dimethoxybenzaldehyde and $HC(OEt)_3$ as described in [9] for **1b**. Yield: 96%.Colorless liquid. R_f (CH_2Cl_2/hexane 1:3) 0.39. IR (neat): 1603, 1163, 1060. ^1H-NMR (500 MHz):1.25 (*t*, *J* = 6.9, 6 H); 3.54–3.60 (*m*, 2 H); 3.69–3.73 (*m*, 2 H); 3.87 (*s*, 3 H); 3.89 (*s*, 3 H); 5.59 (*s*, 1 H); 6.99 (*s*, 1 H); 7.16 (*s*, 1 H).

1-Bromo-2-(1,1-diethoxyethyl)benzene (**5a**) was prepared from 1-(2-bromophenyl)ethanone and $HC(OEt)_3$ as described in [9] for **1b**. Yield: 85%. Colorless liquid. R_f (CH_2Cl_2/hexane 1:5) 0.40. IR (neat): 1165, 1057. ^1H-NMR (500 MHz): 1.25 (*t*, *J* = 6.9, 6 H); 1.70 (*s*, 3 H); 3.33–3.39 (*m*, 2 H); 3.47–3.53 (*m*, 2 H); 7.11 (*td*, *J* = 7.6, 1.5, 1 H); 7.30 (*td*, *J* = 7.6, 1.5, 1 H); 7.59 (*dd*, *J* = 7.6, 1.5, 1 H); 7.85 (*dd*, *J* = 7.6, 1.5, 1 H). Anal. calc. for $C_{12}H_{17}BrO_2$ (273.17): C 52.76, H 6.27; found: C 52.73, H 6.37.

1-Bromo-2-(1,1-diethoxyethyl)-4-methoxybenzene (**5b**) was prepared from 1-(2-bromo-5-methoxyphenyl)ethanone [8] and $HC(OEt)_3$ as described in [9] for **1b**. Yield: 79%. Colorless liquid. R_f (CH_2Cl_2/hexane 1:3) 0.26. IR (neat): 1164, 1055. ^1H-NMR (500 MHz): 1.25 (*t*, *J* = 7.6, 6 H); 1.69 (*s*, 3 H); 3.33–3.39 (*m*, 2 H); 3.46–3.52 (*m*, 2 H); 3.80 (*s*, 3 H); 6.68 (*dd*, *J* = 8.4, 3.1, 1 H); 7.45 (*d*, *J* = 3.1, 1 H); 7.47 (*d*, *J* = 8.4, 1 H). Anal. calc. for $C_{13}H_{19}BrO_3$ (303.19): C 51.50, H 6.32; found: C 51.49, H 6.35.

1-(3-Chlorophenyl)-1-[2-(diethoxymethyl)phenyl]methanimine (**2b**): *Representative Procedure.* To a stirred soln. of *1-bromo-2-(diethoxymethyl)benzene* (**1a**; 0.52 g, 2.0 mmol) in THF (4 ml) at $-78°$ was added BuLi (1.6M in hexane, 2.0 mmol). After 15 min, a soln. of 3-Cl–C_6H_4CN (0.28 g, 2.0 mmol) in THF (2 ml) was added, and the temp. was gradually raised to $-40°$. Stirring was continued for 1 h before H_2O (15 ml) was added. The mixture was warmed to r.t. and extracted with AcOEt (3 × 10 ml). The combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by CC (neutral SiO_2) to give **2b** (0.56 g, 87%). Pale-yellow oil. R_f (AcOEt/hexane 1:10) 0.18. IR (neat): 3261, 1610, 1061. ^1H-NMR (500 MHz): 1.12 (*t*, *J* = 7.6, 6 H); 3.33–3.39 (*m*, 2 H); 3.52 (*m*, 2 H); 5.24 (br. *s*, 1 H); 7.18 (*d*, *J* = 7.6, 1 H); 7.32 (*t*, *J* = 7.6, 1 H); 7.39 (*d*, *J* = 7.6, 6.9, 1 H); 7.43 (*d*, *J* = 7.6, 1 H); 7.48 (*t*, *J* = 7.6, 1 H); 7.54 (*d*, *J* = 6.9, 1 H); 7.736 (*s*, 1 H); 7.743 (*d*, *J* = 7.6, 1 H); 9.80 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{20}ClNO_2$ (317.81): C 68.03, H 6.34, N 4.41; found: C 67.85, H 6.40, N 4.20.

1-[2-(Diethoxymethyl)phenyl]-1-phenylmethanimine (**2a**). Pale-yellow oil. R_f (AcOEt/hexane 1:3) 0.36. IR (neat): 3260, 1607, 1062. ^1H-NMR (500 MHz): 1.11 (*t*, *J* = 6.9, 6 H); 3.31–3.37 (*m*, 2 H); 3.52–3.58 (*m*, 2 H); 5.25 (br. *s*, 1 H); 7.21 (*d*, *J* = 6.9, 1 H); 7.36–7.40 (*m*, 3 H); 7.44–7.48 (*m*, 2 H); 7.64–7.72

(br., 2 H); 7.75 (*d*, *J* = 7.6, 1 H); 9.67 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{21}NO_2$ (283.36): C 76.29, H 7.47, N 4.94; found: C 76.21, H 7.54, N 4.91.

1-(4-Chlorophenyl)-1-[2-(diethoxymethyl)phenyl]methanimine (**2c**). Yellow oil. R_f (AcOEt/hexane 1:5) 0.31. IR (neat): 3263, 1609, 1062. ^{1}H-NMR (500 MHz): 1.12 (*t*, *J* = 6.9, 6 H); 3.32–3.38 (*m*, 2 H); 3.52–3.58 (*m*, 2 H); 5.22 (br. *s*, 1 H); 7.17 (*d*, *J* = 7.6, 1 H); 7.35 (*d*, *J* = 8.4, 2 H); 7.38 (*ddd*, *J* = 7.6, 6.9, 1.5, 1 H); 7.47 (*td*, *J* = 7.6, 1.5, 1 H); 7.65 (br., 2 H); 7.74 (*d*, *J* = 6.9, 1 H); 9.69 (br., 1 H). Anal. calc. for $C_{18}H_{20}ClNO_2$ (317.81): C 68.03, H 6.34, N 4.41; found: C 67.90, H 6.18, N 4.28.

1-[2-(Diethoxymethyl)phenyl]-1-(4-methoxyphenyl)methanimine (**2d**). Yellow oil. R_f (AcOEt/hexane 1:2) 0.34. IR (neat): 3262, 1604, 1254, 1061. ^{1}H-NMR (600 MHz): 1.12 (*t*, *J* = 7.1, 6 H); 3.33–3.38 (*m*, 2 H); 3.52–3.57 (*m*, 2 H); 3.84 (*s*, 3 H); 5.27 (*s*, 1 H); 6.89 (*d*, *J* = 8.9, 2 H); 7.20 (*d*, *J* = 7.4, 1 H); 7.36 (*td*, *J* = 7.4, 1.1, 1 H); 7.45 (*td*, *J* = 7.4, 1.1, 1 H); 7.64 (br. *d*, *J* = 8.9, 2 H); 7.74 (*d*, *J* = 7.4, 1 H); 9.42 (br., 1 H). Anal. calc. for $C_{19}H_{23}NO_3$ (313.39): C 72.82, H 7.40, N 4.47; found: C 72.71, H 7.41, N 4.36.

1-[2-(Diethoxymethyl)phenyl]-1-(1,1-dimethylethyl)methanimine (**2e**). Yellow oil. R_f (AcOEt/hexane 1:3) 0.40. IR (neat): 3260, 1615, 1064. ^{1}H-NMR (600 MHz): 1.23 (*t*, *J* = 7.0, 6 H); 1.26 (*s*, 9 H); 3.44–3.49 (*m*, 2 H); 3.63–3.68 (*m*, 2 H); 5.21 (*s*, 1 H); 7.12 (*dd*, *J* = 7.6, 1.1, 1 H); 7.29 (*td*, *J* = 7.6, 1.1, 1 H); 7.37 (*td*, *J* = 7.6, 1.1, 1 H); 7.70 (*dd*, *J* = 7.6, 1.1, 1 H); 9.42 (br., 1 H). Anal. calc. for $C_{16}H_{25}NO_2$ (263.38): C 72.96, H 9.57, N 5.32; found: C 72.90, H 9.60, N 5.27.

1-[2-(Dimethoxymethyl)phenyl]-1-phenylmethanimine (**2f**). Yellow oil. R_f (AcOEt/hexane 1:1) 0.43. IR (neat): 3260, 1607, 1088. ^{1}H-NMR (500 MHz): 3.22 (*s*, 6 H); 5.15 (*s*, 1 H); 7.24 (*d*, *J* = 8.4, 1 H); 7.38–7.41 (*m*, 3 H); 7.44–7.49 (*m*, 2 H); 7.66 (*d*, *J* = 7.6, 2 H); 7.70 (*d*, *J* = 7.6, 1 H); 9.52 (br., 1 H). Anal. calc. for $C_{16}H_{17}NO_2$ (255.31): C 75.27, H 6.71, N 5.49; found: C 75.15, H 6.73, N 5.44.

1-(3-Chlorophenyl)-1-[2-(dimethoxymethyl)phenyl]methanimine (**2g**). Yellow oil. R_f (AcOEt/hexane 1:2) 0.37. IR (neat): 3258, 1610, 1087. ^{1}H-NMR (500 MHz): 3.23 (*s*, 6 H); 5.11 (br. *s*, 1 H); 7.21 (br., 1 H); 7.32 (*dd*, *J* = 8.6, 7.6, 1 H); 7.41 (*t*, *J* = 7.6, 1 H); 7.43 (*d*, *J* = 7.6, 1 H); 7.49 (*t*, *J* = 7.6, 1 H); 7.53 (br., 1 H); 7.70 (*d*, *J* = 7.6, 1 H); 7.76 (br., 1 H); 9.47 (br., 1 H). Anal. calc. for $C_{16}H_{16}ClNO_2$ (289.76): C 66.32, H 5.57, N 4.83; found: C 66.13, H 5.54, N 4.90.

1-[4-Chloro-2-(diethoxymethyl)phenyl]-1-phenylmethanimine (**2h**). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.32. IR (neat): 3262, 1605, 1059. ^{1}H-NMR (500 MHz): 1.11 (*t*, *J* = 6.9, 6 H); 3.32–3.38 (*m*, 2 H); 3.50–3.56 (*m*, 2 H); 5.22 (br., 1 H); 7.16 (br., 1 H); 7.35 (*dd*, *J* = 8.4, 2.3. 1 H); 7.39 (*t*, *J* = 8.4, 7.6, 2 H); 7.46 (*d*, *J* = 7.6, 1 H); 7.47 (*t*, *J* = 7.6, 1 H); 7.67 (br. *d*, *J* = 8.4, 1 H); 7.74 (*d*, *J* = 2.3, 1 H); 9.68 (br., 1 H). Anal. calc. for $C_{18}H_{20}ClNO_2$ (317.81): C 68.03, H 6.34, N 4.41; found: C 67.75, H 6.30, N 4.21.

1-[4-Chloro-2-(diethoxymethyl)phenyl]-1-(3-chlorophenyl)methanimine (**2i**). Yellow oil. R_f (AcOEt/hexane 1:5) 0.33. IR (neat): 3262, 1606, 1060. ^{1}H-NMR (500 MHz): 1.12 (*t*, *J* = 6.9, 6 H); 3.33–3.40 (*m*, 2 H); 3.49–3.57 (*m*, 2 H); 5.18 (br., 1 H); 7.13 (br., 1 H); 7.32 (*dd*, *J* = 8.4, 7.6, 1 H); 7.36 (*dd*, *J* = 8.4, 2.3, 1 H); 7.44 (*d*, *J* = 7.6, 1 H); 7.53 (br., 1 H); 7.73 (*d*, *J* = 2.3, 1 H); 7.75 (br., 1 H); 9.80 (br., 1 H). Anal. calc. for $C_{18}H_{19}Cl_2NO_2$ (352.26): C 61.37, H 5.44, N 3.98; found: C 61.15, H 5.47, N 3.90.

1-[2-(Diethoxymethyl)-4-methoxyphenyl]-1-phenylmethanimine (**2j**). Pale-yellow oil. R_f (AcOEt/hexane 1:3) 0.32. IR (neat): 3262, 1607, 1061. ^{1}H-NMR (500 MHz): 1.13 (*t*, *J* = 7.6, 6 H); 3.32–3.38 (*m*, 2 H); 3.52–3.59 (*m*, 2 H); 3.87 (*s*, 3 H); 5.24 (br. *s*, 1 H); 6.89 (*dd*, *J* = 8.4, 3.1, 1 H); 7.14 (*d*, *J* = 8.4, 1 H); 7.28 (*d*, *J* = 3.1, 1 H); 7.38 (*t*, *J* = 7.6, 2 H); 7.45 (*t*, *J* = 7.6, 1 H); 7.67 (br. *d*, *J* = 7.6, 2 H); 9.69 (br., 1 H). Anal. calc. for $C_{19}H_{23}NO_3$ (313.39): C 72.82, H 7.40, N 4.47; found: C 72.60, H 7.45, N 4.43.

1-(3-Chlorophenyl)-1-[2-(diethoxymethyl)-4-methoxyphenyl]methanimine (**2k**). Pale-yellow oil. R_f (AcOEt/hexane 1:4) 0.39. IR (neat): 3262, 1607, 1061. ^{1}H-NMR (500 MHz): 1.14 (*t*, *J* = 7.6, 6 H); 3.39–4.00 (*m*, 2 H); 3.53–3.59 (*m*, 2 H); 3.87 (*s*, 3 H); 5.21 (br., 1 H); 6.89 (*dd*, *J* = 8.4, 3.1, 1 H); 7.10 (*d*, *J* = 8.4, 1 H); 7.28 (*d*, *J* = 3.1, 1 H); 7.31 (*dd*, *J* = 8.4, 7.6, 1 H); 7.42 (*dd*, *J* = 8.4, 2.3, 1 H); 7.54 (br., 1 H); 7.71 (br., 1 H); 9.78 (br., 1 H). Anal. calc. for $C_{19}H_{22}ClNO_3$ (347.84): C 65.61, H 6.38, N 4.03; found: C 65.70, H 6.29, N 3.92.

1-[2-(Diethoxymethyl)-4,5-dimethoxyphenyl]-1-phenylmethanimine (**2l**). Yellow oil. R_f (AcOEt/hexane 1:2) 0.32. IR (neat): 3262, 1603, 1058. ^{1}H-NMR (500 MHz): 1.14 (*t*, *J* = 6.9, 6 H); 3.30–3.36 (*m*, 2 H); 3.52–3.58 (*m*, 2 H); 3.90 (*s*, 3 H); 3.96 (*s*, 3 H); 5.17 (br. *s*, 1 H); 6.69 (br. *s*, 1 H); 7.25 (*s*, 1 H); 7.40 (*dd*, *J* = 8.4, 7.6, 2 H); 7.47 (*t*, *J* = 7.6, 1 H); 7.70 (br., 2 H); 9.71 (br., 1 H). Anal. calc. for $C_{20}H_{25}NO_4$ (343.42): C 69.95, H 7.34, N 4.08; found: C 69.98, H 7.31, N 4.03.

1-(3-Chlorophenyl)-1-[2-(diethoxymethyl)-4,5-dimethoxyphenyl]methanimine (**2m**). Yellow oil. R_f (AcOEt/hexane 2:5) 0.30. IR (neat): 3259, 1604, 1059. ^{1}H-NMR (500 MHz): 1.15 (*t*, *J* = 7.6, 6 H); 3.32–3.38 (*m*, 2 H); 3.53–3.59 (*m*, 2 H); 3.83 (*s*, 3 H); 3.96 (*s*, 3 H); 5.15 (br., 1 H); 6.64 (br., 1 H); 7.25 (*s*, 1 H); 7.32 (*dd*, *J* = 8.4, 7.6, 1 H); 7.44 (*d*, *J* = 7.6, 1 H); 7.56 (br., 1 H); 7.76 (br., 1 H); 9.79 (br., 1 H). Anal. calc. for $C_{20}H_{24}ClNO_4$ (377.86): C 63.57, H 6.40, N 3.71; found: C 63.59, H 6.42, N 3.44.

1-(4-Chlorophenyl)-1-[2-(diethoxymethyl)-4,5-dimethoxyphenyl]methanimine (**2n**). Yellow oil. R_f (AcOEt/hexane 1:2) 0.31. IR (neat): 3262, 1605, 1059. ^{1}H-NMR (500 MHz): 1.14 (*t*, *J* = 6.9, 6 H); 3.32–3.38 (*m*, 2 H); 3.53–3.59 (*m*, 2 H); 3.82 (*s*, 3 H); 3.95 (*s*, 3 H); 5.46 (br. *s*, 1 H); 6.63 (br. *s*, 1 H); 7.24 (*s*, 1 H); 7.36 (*d*, *J* = 8.4, 2 H); 7.66 (br. *d*, *J* = 8.4, 2 H); 9.71 (br., 1 H). Anal. calc. for $C_{20}H_{24}ClNO_4$ (377.86): C 63.57, H 6.40, N 3.71; found: C 63.29, H 6.21, N 3.80.

1-(4-Chlorophenyl)-1-[2-(1,1-diethoxyethyl)phenyl]methanimine (**6a**).White solid. M.p. 76–77° (hexane). IR (KBr): 3262, 1610, 1051. ^{1}H-NMR (500 MHz): 0.93 (*t*, *J* = 7.6, 6 H); 1.45 (*s*, 3 H); 3.26 (*q*, *J* = 7.6, 4 H); 7.08 (*d*, *J* = 6.9, 1 H); 7.30–7.34 (*m*, 3 H); 7.41 (*td*, *J* = 6.9, 1.5, 1 H); 7.54 (*d*, *J* = 7.6, 1 H); 7.60 (br. *d*, *J* = 6.9, 2 H); 9.05 (br., 1 H). Anal. calc. for $C_{19}H_{22}ClNO_2$ (331.84): C 68.77, H 6.68, N 4.22; found: C 68.66, H 6.67, N 4.16.

1-[2-(1,1-Diethoxyethyl)-4-methoxyphenyl]-1-phenylmethanimine (**6b**). Light-brown oil. R_f (AcOEt/hexane 1:3) 0.41. IR (neat): 3261, 1607, 1059. ^{1}H-NMR (500 MHz): 0.94 (*t*, *J* = 6.9, 6 H); 1.41 (*s*, 3 H); 3.23–3.32 (*m*, 4 H); 3.86 (*s*, 3 H); 6.87 (*dd*, *J* = 8.4, 3.1, 1 H); 7.06 (*d*, *J* = 8.4, 1 H); 7.08 (*d*, *J* = 3.1, 1 H); 7.33 (*dd*, *J* = 7.6, 6.9, 2 H); 7.37 (*t*, *J* = 7.6, 1 H); 7.63 (br. *d*, *J* = 6.9, 2 H); 9.16 (br., 1 H). Anal. calc. for $C_{20}H_{25}NO_3$ (327.42): C 73.37, H 7.70, N 4.28; found: C 73.08, H 7.75, N 4.19.

1-(3-Chlorophenyl)-1-[2-(1,1-diethoxyethyl)-4-methoxyphenyl]methanimine (**6c**). Pale-yellow oil. R_f (AcOEt/hexane 1:4) 0.30. IR (neat): 3264, 1608, 1060. ^{1}H-NMR (500 MHz): 0.95 (*t*, *J* = 6.9, 6 H); 1.43 (*s*, 3 H); 3.23–3.31 (*m*, 4 H); 3.86 (*s*, 3 H); 6.87 (*dd*, *J* = 8.4, 2.3, 1 H); 7.02 (*d*, *J* = 8.4, 1 H); 7.08 (*d*, *J* = 2.3, 1 H); 7.26 (*t*, *J* = 7.6, 1 H); 7.35 (*dd*, *J* = 7.6, 1.5, 1 H); 7.53 (br. *d*, *J* = 7.6, 1 H); 7.65 (br. *s*, 1 H); 9.17 (br., 1 H). Anal. calc. for $C_{20}H_{24}ClNO_3$ (361.86): C 66.38, H 6.69, N 3.87; found: C 66.16, H 6.80, N 3.86.

*1-(3-Chlorophenyl)-3-ethoxy-1*H*-isoindole* (**4b**). *Representative Procedure.* A soln. of **2b** (0.19 g, 0.61 mmol) in $CHCl_3$ (4 ml) containing TsOH · H_2O (12 mg, 0.061 mmol) was heated at reflux temp. for 8 h. The cooled mixture was diluted with CH_2Cl_2 (25 ml) and washed with sat. aq. $NaHCO_3$ (10 ml). The org. layer was dried (Na_2SO_4) and concentrated by evaporation. The residue was purified by CC (SiO_2; AcOEt/hexane 1:4) to afford **4b** (0.13 g, 76%). Pale-yellow solid. M.p. 99–101° (hexane/Et_2O). IR (KBr): 1621, 1598, 1575, 1345. ^{1}H-NMR (500 MHz): 1.50 (*t*, *J* = 6.9, 3 H); 4.53–4.60 (*m*, 2 H); 5.66 (*s*, 1 H); 7.147 (*d*, *J* = 6.9, 1 H); 7.153 (*d*, *J* = 1.5, 1 H); 7.21–7.25 (*m*, 2 H); 7.32 (*dd*, *J* = 8.4, 2.3, 1 H); 7.37–7.42 (*m*, 2 H); 7.61–7.62 (*m*, 1 H). ^{13}C-NMR (125 MHz): 14.5; 64.3; 71.8; 120.8; 122.8; 125.5; 127.1; 127.6; 127.7; 129.6; 129.8; 132.4; 134.3; 141.3; 153.3; 170.3. HR-MS: 272.0831 ($[M+H]^+$, $C_{16}H_{15}ClNO^+$; calc. 272.0842). Anal. calc. for $C_{16}H_{14}ClNO$ (271.74): C 70.72, H 5.19, N 5.15; found: C 70.48, H 5.49, N 5.10.

*3-Ethoxy-1-phenyl-1*H*-isoindole* (**4a**) [12a]. Pale-yellow solid. M.p. 91–92° (hexane; [12a]: 88–89°). IR (KBr): 1618, 1599, 1570, 1343. ^{1}H-NMR (500 MHz): 1.49 (*t*, *J* = 6.9, 3 H); 4.51–4.62 (*m*, 2 H); 5.70 (*s*, 1 H); 7.20 (*dd*, *J* = 6.9, 1.5, 2 H); 7.25 (*d*, *J* = 6.9, 1 H); 7.28–7.33 (*m*, 3 H); 7.34–7.39 (*m*, 2 H); 7.60 (*dd*, *J* = 6.9, 2.3, 1 H). ^{13}C-NMR (125 MHz): 14.6; 64.1; 72.4; 120.6; 122.8; 127.1; 127.4; 127.4; 128.6; 129.4; 132.5; 139.2; 154.0; 169.9.

*1-(4-Chlorophenyl)-3-ethoxy-1*H*-isoindole* (**4c**). Pale-yellow solid. M.p. 103–104° (hexane/Et_2O; [2]: 100–101°). IR (KBr): 1620, 1599, 1570, 1346. ^{1}H-NMR (500 MHz): 1.49 (*t*, *J* = 6.9, 3 H); 4.50–4.60 (*m*, 2 H); 5.66 (*s*, 1 H); 7.14 (*d*, *J* = 8.4, 2 H); 7.26 (*d*, *J* = 8.4, 2 H); 7.28 (*dd*, *J* = 8.4, 2.3, 1 H); 7.36–7.41 (*m*, 2 H); 7.61 (*dd*, *J* = 7.6, 2.3, 1 H). ^{13}C-NMR (125 MHz): 14.5; 64.2; 71.7; 120.7; 122.7; 127.6; 128.5; 128.7; 129.6; 132.5; 133.1; 137.8; 153.6; 170.2.

*3-Ethoxy-1-(4-methoxyphenyl)-1*H*-isoindole* (**4d**) [13]. Pale-yellow solid. M.p. 61–63° (hexane/Et_2O; [13]: 64–65°). IR (KBr): 1621, 1599, 1571, 1345. ^{1}H-NMR (600 MHz): 1.48 (*t*, *J* = 7.1, 3 H); 3.77 (*s*, 3 H); 4.50–4.60 (*m*, 2 H); 5.66 (*s*, 1 H); 6.83 (*d*, *J* = 8.6, 2 H); 7.11 (*d*, *J* = 8.6, 2 H); 7.31 (*dd*, *J* = 8.4, 1.7, 1 H); 7.35–7.39 (*m*, 2 H); 7.60 (*dd*, *J* = 8.4, 1.7, 1 H). ^{13}C-NMR (150 MHz): 14.6; 55.3; 64.1; 72.0; 114.0; 120.6; 122.9; 127.3; 128.3; 129.5; 131.3; 132.6; 154.4; 159.0; 169.7. HR-MS: 268.1329 ($[M+H]^+$, $C_{17}H_{18}NO_2^+$; calc. 268.1337). Anal. calc. for $C_{17}H_{17}NO_2$ (267.32): C 76.38, H 6.41, N 5.24; found: C 76.28, H 6.44, N 5.10.

*1-(1,1-Dimethylethyl)-3-ethoxy-1*H*-isoindole* (**4e**). Yellow oil. R_f (AcOEt/hexane 1:12) 0.39. IR (neat): 1626, 1599, 1577, 1344. ^{1}H-NMR (500 MHz): 1.01 (*s*, 9 H); 1.46 (*t*, *J* = 6.9, 3 H); 4.41–4.45 (*m*,

including *s* at 4.22, 2 H); 4.53–4.60 (*m*, 1 H); 7.34–7.37 (*m*, 2 H); 7.51–7.58 (*m*, 2 H). ^{13}C-NMR (125 MHz): 14.6; 27.1; 35.3; 63.4; 77.8; 120.2; 123.8; 126.9; 128.2; 133.8; 152.2; 168.4. HR-MS: 218.1535 ($[M+H]^+$, $C_{14}H_{20}NO^+$; calc. 218.1545). Anal. calc. for $C_{14}H_{19}NO$ (217.31): C 77.38, H 8.81, N 6.45; found: C 77.28, H 8.52, N 6.42.

*3-Methoxy-1-phenyl-1*H-*isoindole* (**4f**) [12]. Pale-yellow solid. M.p. 112–114° (hexane; [12b]: 111–113°). IR (KBr): 1623, 1600, 1574, 1372. ^{1}H-NMR (500 MHz): 4.15 (*s*, 3 H); 5.71 (*s*, 1 H); 7.20 (*dd*, *J* = 8.4, 2.3, 2 H); 7.25 (*t*, *J* = 7.6, 1 H); 7.29–7.33 (*m*, 3 H); 7.35–7.40 (*m*, 2 H); 7.59 (*dd*, *J* = 8.4, 2.3, 1 H). ^{13}C-NMR (125 MHz): 55.5; 72.4; 120.6; 122.9; 127.2; 127.4; 127.5; 128.6; 129.5; 132.2; 139.0; 154.1; 170.6.

*1-(3-Chlorophenyl)-3-methoxy-1*H-*isoindole* (**4g**). Pale-yellow solid. M.p. 85–86° (hexane/CH_2Cl_2). IR (KBr): 1623, 1599, 1577, 1373. ^{1}H-NMR (500 MHz): 4.16 (*s*, 3 H); 5.67 (*s*, 1 H); 7.15 (br. *s*, 2 H); 7.24–7.27 (*m*, 2 H); 7.33 (*dd*, *J* = 8.4, 3.1, 1 H); 7.37–7.42 (*m*, 2 H); 7.59 (*d*, *J* = 8.4, 1 H). ^{13}C-NMR (125 MHz): 55.6; 71.7; 120.7; 122.8; 125.5; 127.1; 127.7; 127.7; 129.7; 129.9; 132.1; 134.4; 141.2; 153.4; 170.9. HR-MS: 258.0675 ($[M+H]^+$, $C_{15}H_{13}ClNO^+$; calc. 258.0685). Anal. calc. for $C_{15}H_{12}ClNO$ (257.71): C 69.91, H 4.69, N 5.43; found: C 69.80, H 4.40, N 5.30.

*5-Chloro-3-ethoxy-1-phenyl-1*H-*isoindole* (**4h**). Pale-yellow solid. M.p. 90–92° (hexane). IR (KBr): 1618, 1596, 1571, 1336. ^{1}H-NMR (500 MHz): 1.48 (*t*, *J* = 6.9, 3 H); 4.50–4.60 (*m*, 2 H); 5.68 (*s*, 1 H); 7.17 (*dd*, *J* = 8.4, 1.5, 2 H); 7.22–7.26 (*m*, 2 H); 7.28–7.33 (*m*, 3 H); 7.58 (*d*, *J* = 1.5, 1 H). ^{13}C-NMR (125 MHz): 14.5; 64.4; 72.3; 120.9; 123.9; 127.1; 127.7; 128.7; 129.6; 133.6; 134.2; 138.5; 152.3; 168.8. HR-MS: 272.0836 ($[M+H]^+$, $C_{16}H_{15}ClNO^+$; calc. 272.0842). Anal. calc. for $C_{16}H_{14}ClNO$ (271.74): C 70.72, H 5.19, N 5.15; found: C 70.65, H 5.17, N 5.09.

*5-Chloro-1-(3-chlorophenyl)-3-ethoxy-1*H-*isoindole* (**4i**). Pale-yellow solid. M.p. 97–100° (hexane/CH_2Cl_2). IR (KBr): 1618, 1596, 1575, 1338. ^{1}H-NMR (500 MHz): 1.49 (*t*, *J* = 7.6, 3 H); 4.50–4.60 (*m*, 2 H); 5.64 (*s*, 1 H); 7.11 (*dd*, *J* = 6.9, 1.5, 1 H); 7.13 (br. *s*, 1 H); 7.22–7.24 (*m*, 3 H); 7.35 (*dd*, *J* = 8.4, 1.5, 1 H); 7.59 (*d*, *J* = 1.5, 1 H). ^{13}C-NMR (125 MHz): 14.5; 64.6; 71.6; 121.1; 123.8; 125.4; 127.1; 127.9; 129.8; 123.0; 133.9; 134.2; 134.5; 140.7; 151.6; 169.1. HR-MS: 306.0446 ($[M+H]^+$, $C_{16}H_{14}Cl_2NO^+$; calc. 306.0452). Anal. calc. for $C_{16}H_{13}Cl_2NO$ (306.19): C 62.76, H 4.28, N 4.57; found: C 62.54, H 4.05, N 4.39.

*3-Ethoxy-5-methoxy-1-phenyl-1*H-*isoindole* (**4j**). White solid. M.p. 110–111° (hexane/CH_2Cl_2). IR (KBr): 1624, 1575, 1345. ^{1}H-NMR (500 MHz): 1.49 (*t*, *J* = 7.6, 3 H); 3.85 (*s*, 3 H); 4.50–4.61 (*m*, 2 H); 5.64 (*s*, 1 H); 6.93 (*dd*, *J* = 8.4, 2.3, 1 H); 7.08 (*d*, *J* = 2.3, 1 H); 7.17–7.20 (*m*, 3 H); 7.23 (*t*, *J* = 7.6, 1 H); 7.29 (*t*, *J* = 7.6, 2 H). ^{13}C-NMR (125 MHz): 14.6; 55.6; 64.2; 71.9; 104.2; 117.2; 123.5; 127.1; 127.4; 128.5; 133.9; 139.5; 146.5; 159.7; 169.5. HR-MS: 268.1329 ($[M+H]^+$, $C_{17}H_{18}NO_2^+$; calc. 268.1337). Anal. calc. for $C_{17}H_{17}NO_2$ (267.32): C 76.38, H 6.41, N 5.24; found: C 76.18, H 6.38, N 5.20.

*1-(3-Chlorophenyl)-3-ethoxy-5-methoxy-1*H-*isoindole* (**4k**). Pale-yellow solid. M.p. 89–90° (hexane/Et_2O). IR (KBr): 1626, 1577, 1339. ^{1}H-NMR (500 MHz): 1.50 (*t*, *J* = 6.9, 3 H); 3.86 (*s*, 3 H); 4.50–4.60 (*m*, 2 H); 5.60 (*s*, 1 H); 6.94 (*dd*, *J* = 7.6, 2.3, 1 H); 7.09 (*d*, *J* = 2.3, 1 H); 7.12–7.14 (*m*, 2 H); 7.18 (*d*, *J* = 8.4, 1 H); 7.20–7.25 (*m*, 2 H). ^{13}C-NMR (125 MHz): 14.5; 55.7; 64.3; 71.2; 104.4; 117.4; 123.4; 125.4; 127.1; 127.6; 129.8; 133.9; 134.3; 141.7; 145.7; 159.9; 169.9. HR-MS: 302.0942 ($[M+H]^+$, $C_{17}H_{17}ClNO_2^+$; calc. 302.0948). Anal. calc. for $C_{17}H_{16}ClNO_2$ (301.77): C 67.66, H 5.34, N 4.64; found: C 67.43, H 5.28, N 4.55.

*3-Ethoxy-5,6-dimethoxy-1-phenyl-1*H-*isoindole* (**4l**). Pale-yellow solid. M.p. 113–114° (hexane/CH_2Cl_2). IR (KBr): 1623, 1602, 1569, 1342. ^{1}H-NMR (500 MHz): 1.48 (*t*, *J* = 7.6, 3 H); 3.83 (*s*, 3 H); 3.94 (*s*, 3 H); 4.48–4.59 (*m*, 2 H); 5.60 (*s*, 1 H); 6.79 (*s*, 1 H); 7.07 (*s*, 1 H); 7.18 (*d*, *J* = 6.9, 2 H); 7.25 (*t*, *J* = 7.6, 1 H); 7.30 (*dd*, *J* = 7.6, 6.9, 2 H). ^{13}C-NMR (125 MHz): 14.6; 56.1; 56.2; 64.1; 72.3; 102.6; 105.4; 124.9; 127.3; 127.4; 128.6; 139.5; 147.7; 149.2; 151.1; 169.7. HR-MS: 298.1438 ($[M+H]^+$, $C_{18}H_{20}NO_3^+$; calc. 298.1443). Anal. calc. for $C_{18}H_{19}NO_3$ (297.35): C 72.71, H 6.44, N 4.71; found: C 72.77, H 6.59, N 4.60.

*1-(3-Chlorophenyl)-3-ethoxy-5,6-dimethoxy-1*H-*isoindole* (**4m**). White solid. M.p. 102–105° (hexane/CH_2Cl_2). IR (KBr): 1622, 1601, 1567, 1340. ^{1}H-NMR (500 MHz): 1.49 (*t*, *J* = 6.9, 3 H); 3.85 (*s*, 3 H); 3.95 (*s*, 3 H); 4.50–4.57 (*m*, 2 H); 5.55 (*s*, 1 H); 6.77 (*s*, 1 H); 7.08 (*s*, 1 H); 7.11 (*dd*, *J* = 7.6, 1.5, 1 H); 7.13 (br. *s*, 1 H); 7.22–7.25 (*m*, 2 H). ^{13}C-NMR (125 MHz): 14.6; 56.1; 56.2; 64.3; 71.6; 102.7; 105.3; 124.8; 125.6; 127.3; 127.6; 129.9; 134.4; 141.7; 147.0; 149.4; 151.3; 170.1. HR-MS: 332.1044 ($[M+H]^+$, $C_{18}H_{19}ClNO_3^+$; calc. 332.1053). Anal. calc. for $C_{18}H_{18}ClNO_3$ (331.79): C 65.16, H 5.47, N 4.22; found: C 64.99, H 5.46, N 4.27.

*1-(4-Chlorophenyl)-3-ethoxy-5,6-dimethoxy-1*H-*isoindole* (**4n**). Pale-yellow solid. M.p. 131–132° (hexane/CH_2Cl_2). IR (KBr): 1622, 1601, 1567, 1339. ^{1}H-NMR (500 MHz): 1.48 (*t*, *J* = 6.9, 3 H); 3.84 (*s*,

3 H); 3.95 (*s*, 3 H); 4.47–4.57 (*m*, 2 H); 5.56 (*s*, 1 H); 6.75 (*s*, 1 H); 7.07 (*s*, 1 H); 7.12 (*d*, *J* = 8.4, 2 H); 7.27 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (125 MHz): 14.6; 56.1; 56.2; 64.2; 71.5; 102.6; 105.3; 124.8; 128.6; 128.8; 133.1; 138.1; 147.2; 149.3; 151.3; 169.9. HR-MS: 332.1045 ($[M+H]^+$, $C_{18}H_{19}ClNO_3^+$; calc. 332.1053). Anal. calc. for $C_{18}H_{18}ClNO_3$ (331.79): C 65.16, H 5.47, N 4.22; found: C 65.27, H 5.56, N 4.07.

*3-(4-Chlorophenyl)-1-ethoxy-1-methyl-1*H-*isoindole* (**7a**). Pale-yellow solid. M.p. 85–86° (hexane/CH_2Cl_2). IR (KBr): 1596, 1138. ^{1}H-NMR (500 MHz): 1.13 (*t*, *J* = 7.6, 3 H); 1.72 (*s*, 3 H); 2.92–2.99 (*m*, 1 H); 3.21–3.28 (*m*, 1 H); 7.42–7.48 (*m*, 2 H); 7.51 (*d*, *J* = 8.4, 2 H); 7.59 (*d*, *J* = 6.9, 1 H); 7.66 (*d*, *J* = 6.9, 1 H); 7.93 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (125 MHz): 15.5; 25.2; 59.2; 103.0; 122.7; 122.8; 128.9; 129.0; 129.5; 129.7; 132.3; 136.5; 136.8; 153.3; 168.8. HR-MS: 286.0992 ($[M+H]^+$, $C_{17}H_{17}ClNO^+$; calc. 286.0998). Anal. calc. for $C_{17}H_{16}ClNO$ (285.77): C 71.45, H 5.64, N 4.90; found: C 71.31, H 5.60, N 4.91.

*1-Ethoxy-6-methoxy-1-methyl-3-phenyl-1*H-*isoindole* (**7b**). Brown oil. R_f (AcOEt/hexane 1:4) 0.29. IR (neat): 1607, 1349, 1137. ^{1}H-NMR (500 MHz): 1.14 (*t*, *J* = 6.9, 3 H); 1.71 (*s*, 3 H); 2.95–3.01 (*m*, 1 H); 3.26–3.32 (*m*, 1 H); 3.90 (*s*, 3 H); 6.93 (*dd*, *J* = 8.4, 2.3, 1 H); 7.11 (*d*, *J* = 2.3, 1 H); 7.52–7.53 (*m*, 3 H); 7.61 (*d*, *J* = 8.4, 1 H); 7.97 (*dd*, *J* = 7.6, 1.5, 2 H). ^{13}C-NMR (125 MHz): 15.5; 25.4; 55.7; 59.0; 102.2; 108.3; 114.4; 123.9; 128.3; 128.6; 129.9; 130.6; 134.0; 155.9; 161.3; 169.5. HR-MS: 282.1486 ($[M+H]^+$, $C_{18}H_{20}NO_2^+$; calc. 282.1494). Anal. calc. for $C_{18}H_{19}NO_2$ (281.35): C 76.84, H 6.81, N 4.98; found: C 76.75, H 6.73, N 5.12.

*3-(3-Chlorophenyl)-1-ethoxy-6-methoxy-1-methyl-1*H-*isoindole* (**7c**). Brown oil. R_f (AcOEt/hexane 1:5) 0.34. IR (neat): 1607, 1343, 1138. ^{1}H-NMR (500 MHz): 1.15 (*t*, *J* = 7.6, 3 H); 1.70 (*s*, 3 H); 2.95–3.01 (*m*, 1 H); 3.24–3.30 (*m*, 1 H); 3.91 (*s*, 3 H); 6.94 (*dd*, *J* = 8.4, 2.3, 1 H); 7.11 (*d*, *J* = 2.3, 1 H); 7.46 (*dd*, *J* = 8.4, 7.6, 1 H); 7.51 (*dd*, *J* = 8.4, 1.5, 1 H); 7.57 (*d*, *J* = 8.4, 1 H); 7.84 (*dt*, *J* = 7.6, 1.5, 1 H); 7.96 (*t*, *J* = 1.5, 1 H). ^{13}C-NMR (125 MHz): 15.5; 25.4; 55.7; 59.1; 102.4; 108.5; 114.5; 123.6; 126.4; 128.4; 129.4; 123.0; 130.6; 134.8; 135.7; 156.0; 161.5; 168.3. HR-MS: 316.1096 ($[M+H]^+$, $C_{18}H_{19}ClNO_2^+$; calc. 316.1104). Anal. calc. for $C_{18}H_{18}ClNO_2$ (315.79): C 68.46, H 5.75, N 4.44; found: C 68.30, H 5.86, N 4.60.

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