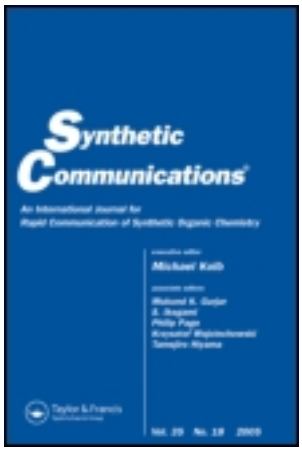

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CONVENIENT PREPARATION OF SOME N-SUBSTITUTED 1,2,3,4-TETRAHYDROISOQUINOLINES LACKING ELECTRON-DONATING SUBSTITUENTS

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CONVENIENT PREPARATION OF SOME *N*-SUBSTITUTED 1,2,3,4-TETRAHYDROISOQUINOLINES LACKING ELECTRON-DONATING SUBSTITUENTS

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ABSTRACT

N,*N*-*Bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines **3** are cyclised intramolecularly in conc. H_2SO_4 to the corresponding *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines **4**. The remaining benzotriazolyl-moiety can be replaced by nucleophiles, leading to *N*-substituted 1,2,3,4-tetrahydroisoquinolines **5–8**.

INTRODUCTION

The preparation of 1,2,3,4-tetrahydroisoquinolines with electron-withdrawing substituents on the aromatic moiety is a challenging task.

Classic methods, such as the Pictet–Spengler,[1,2] Bischler–Napieralski[3–5] or the Pomeranz–Fritsch[6] syntheses often fail[7–9] due to the decreased activity of the aromatic ring in the intramolecular cyclisation step. These compounds are, however, of particular interest, since they have been shown[10] to inhibit phenylethanolamine *N*-methyltransferase (PNMT); an interference with this key enzyme in the biosynthesis of epinephrine is likely to be of therapeutic value, particularly in the treatment of anxiety and ischemic heart conditions.[11] Some attempts have been made to develop synthetic routines suitable for the preparation of deactivated tetrahydroisoquinolines. Deady and co-workers,[12] for instance, reported the preparation of the 6-chloro-1,2,3,4-tetrahydroisoquinoline from the corresponding *N*-(2-bromoethyl)-4-chloro-benzylamine by refluxing with $AlCl_3$ in decalin. Quallich et al.[9] developed a synthesis for 6-nitro-1,2,3,4-tetrahydro-isoquinoline by double displacement of a diol with a nitrogen nucleophile. In this multi-step approach a diacid, obtained by malonate displacement and subsequent hydrolysis and decarboxylation, is reduced to the corresponding diol, which is then cyclised in the presence of an amine. Further, various chloro- and bromo-substituted 1,2,3,4-tetrahydroisoquinolines are accessible by one-pot cyclisation from their corresponding 2-benzylamino-1-ethanol hydrochloride by heating in the presence of ammonium chloride and aluminium chloride. Obtained yields are, however, only in the 40–80% range.[10] Stokker[8] introduced an interesting method, which is exclusively applicable to the synthesis of tetrahydroisoquinolines lacking electron-donating substituents. It involves the intramolecular reaction of an α-amido alcohol, prepared *in situ* from paraformaldehyde and *N*-trifluoroacylated β-phenylethylamines. Yields are good for deactivated β-phenylethylamines, but the reaction fails if the starting material is activated by any methoxy-substituent; applied to the synthesis of unsubstituted 1,2,3,4-tetrahydroisoquinoline the obtained yield is poor.

This paper describes an approach, which is related to the Pictet–Spengler reaction but must be seen as complementary to it, since it gives high yields for 1,2,3,4-tetrahydroisoquinolines with electron-withdrawing aromatic substituents, but fails for unsubstituted or activated derivatives. It involves the intramolecular Friedel–Crafts cyclisation of *N*,*N*-*bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines **3** which are easily accessible from the reaction between 1-hydroxymethylbenzotriazole **1** and the corresponding β-phenylethylamines **2**. After ring-closure, the remaining benzotriazolyl moiety in the resulting *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines **4** can be replaced with different nucleophiles to yield various *N*-substituted deactivated derivatives **5–8** (Scheme 1).

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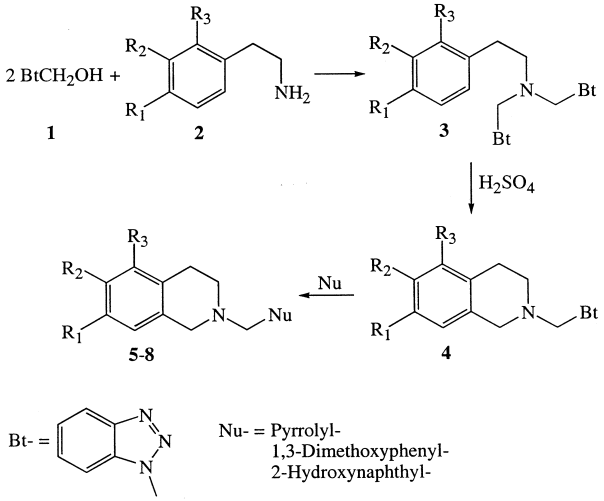

Scheme 1.

RESULTS AND DISCUSSION

Reaction of 1-Hydroxymethylbenzotriazole with β-Phenylethylamines

In the first step of the reaction the *N*,*N*-*bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines **3a–f** are synthesised from 1-hydroxymethylbenzotriazole **1**, prepared according to a well-known procedure from benzotriazole and formaldehyde,[13] and the β-phenylethylamines **2a–f** by heating in EtOH for 1 h. The crystalline products are characterised by a resonance of approx. δ_H 5.6 for the benzotriazolylmethylene group [$BtCH_2N$] (Table 1). The reaction between **1** and primary amines in a 2:1 ratio to the corresponding *bis*-adducts is well established in the literature[14] and has been employed before for the preparation of various *N*,*N*-*bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines.[15]

Cyclisation of *N*,*N*-*Bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines in H_2SO_4

In a previous paper,[15] the intramolecular ring-closure of some *N*,*N*-*bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines with $AlCl_3$ at RT

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Table 1. *N,N-Bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines **3a–f**

Compound	Formula	R_1	R_2	R_3	Yield (%)	Mp (°C, EtOH)	δ_H [$BtCH_2N$]
3a	$C_{22}H_{20}BrN_7$	Br	H	H	92	143–145	5.63 (s, 4H)
3b	$C_{22}H_{20}FN_7$	F	H	H	89	117–118	5.64 (s, 4H)
3c	$C_{22}H_{20}FN_7$	H	H	F	98	116–117	5.66 (s, 4H)
3d	$C_{22}H_{20}ClN_7$	Cl	H	H	92	149–150	5.62 (s, 4H)
3e	$C_{22}H_{20}ClN_7$	H	H	Cl	80	116–118	5.68 (s, 4H)
3f	$C_{22}H_{19}Cl_2N_7$	Cl	H	Cl	88	125–126	5.68 (s, 4H)

Table 2. *N*-Benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines **4a–f**

Compound	Formula	R_1	R_2	R_3	Yield (%)	Mp (°C, EtOH)	δ_H [$BtCH_2N$]	δ_H [$ArCH_2N$]
4a	$C_{16}H_{15}BrN_4$	Br	H	H	82	145–146	5.63 (s, 2H)	3.83 (s, 2H)
4b	$C_{16}H_{15}FN_4$	F	H	H	83	147–148	5.64 (s, 2H)	3.84 (s, 2H)
4c	$C_{16}H_{15}FN_4$	H	H	F	69	134–135	5.65 (s, 2H)	3.86 (s, 2H)
4d	$C_{16}H_{15}ClN_4$	Cl	H	H	83	146–148	5.62 (s, 2H)	3.80 (s, 2H)
4e	$C_{16}H_{15}ClN_4$	H	H	Cl	73	144–145	5.61 (s, 2H)	3.81 (s, 2H)
4f	$C_{16}H_{14}Cl_2N_4$	Cl	H	Cl	86	149–150	5.63 (s, 2H)	3.80 (s, 2H)

was reported. Employing that mild Friedel–Crafts catalyst prevented, however, the successful cyclisation of the stronger deactivated *N,N-bis*(benzotriazol-1-ylmethyl)-5,7-dichloro-β-phenylethylamine **3f** and caused also some difficulties for compound **3e**. In contrast, the use of conc. H_2SO_4 as catalyst and 'solvent' is straightforward and yields the corresponding crystalline *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines **4a–f** in high quantities. After alkaline work-up the successful intramolecular ring-closure is evident in a characteristic resonance at approx. δ_H 3.8 [$ArCH_2N$] (Table 2).

It can be assumed that the intramolecular cyclisation of compounds **3a–f** proceeds *via* an iminium ion after removal of one benzotriazolyl moiety from the molecule (Scheme 2).

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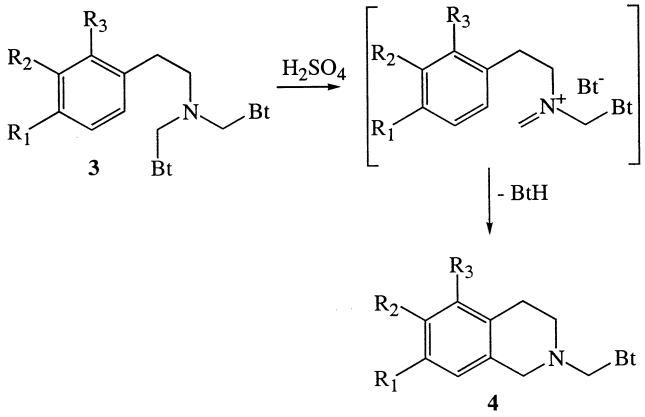
As briefly mentioned before, the method can be seen as complementary to the Pictet–Spengler reaction, since it fails with unsubstituted and methoxy-substituted *N,N-bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines. Under the conditions described, these compounds yield the corresponding *bis*(*N*-1,2,3,4-tetrahydroisoquinolinyl)methanes **9**, even when treated with conc. H_2SO_4 for only 15 min at 4°C.

The formation of *bis*(*N*-1,2,3,4-tetrahydroisoquinolinyl)methanes **9a–f** (Figure 1) also occurs to a small extent during the cyclisation of **3a–f** to **4a–f**, evident in a minor peak in the products' crude ^{13}C NMR-spectra at δ_C 80, stemming from the *bis*(*N*-tetrahydroisoquinolinyl)methylene group [NCH_2N]. An adherence to the reaction conditions, not only with respect to temperature, but the ratio of starting material to H_2SO_4 is essential for a successful preparation of compounds **4a–f**. If the conditions are, for instance, changed from a 45:1 to a considerably higher ratio, the corresponding *bis*(*N*-1,2,3,4-tetrahydroisoquinolinyl)methanes **9a–f** are obtained as the exclusive product of the reaction[16] (Table 3).



Scheme 2.

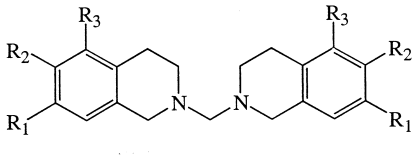


Figure 1.

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Table 3. *Bis*(*N*-1,2,3,4-Tetrahydroisoquinolinyl)methanes **9a–g**[16]

Compound	Formula	R_1	R_2	R_3	Ratio (H_2SO_4 to 3)	Conditions	Yield (%)	δ_C [NCH_2N]
9a	$C_{19}H_{20}Br_2N_2$	Br	H	H	100:1	25°C, 4 h	87	80.0
9b	$C_{19}H_{20}F_2N_2$	F	H	H	100:1	25°C, 4 h	85	80.2
9c	$C_{19}H_{20}F_2N_2$	H	H	F	100:1	25°C, 4 h	90	80.3
9d	$C_{19}H_{20}Cl_2N_2$	Cl	H	H	100:1	25°C, 4 h	96	80.1
9e	$C_{19}H_{20}Cl_2N_2$	H	H	Cl	100:1	25°C, 4 h	99	80.1
9f	$C_{19}H_{18}Cl_4N_2$	Cl	H	Cl	200:1	80°C, 30 h	93	79.5
9g	$C_{19}H_{22}N_2$	H	H	H	100:1	4°C, 30 min	96	80.7
					45:1	4°C, 15 min	83	

Replacement of the Benzotriazolyl-Moiety by Nucleophiles

Benzotriazole is a very versatile auxiliary, which can be replaced under mild conditions by a variety of nucleophiles.[17–19] In this case, $AlCl_3$ is employed as Friedel–Crafts catalyst and the benzotriazolyl substituted by pyrrole (**5b**, **5c**, **5g**), 1,3-dimethoxybenzene (**6d**, **6g**) and 2-hydroxynaphthalene (**7a**, **7e**, **7g**). The reduction of **4f** to *N*-methyl-5,7-dichloro-1,2,3,4-tetrahydroisoquinoline **8f** with $NaBH_4$ further underlines the versatility of the replacement (Scheme 3, Table 4). To establish the ideal conditions for the various substitutions, *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinoline **4g**, which can easily be prepared from the reaction between 1,2,3,4-tetrahydroisoquinoline and **1**,[20] was used as a lead compound.

It is found that pyrrole reacts readily at RT with compounds **4b**, **4c** and **4g** in the presence of the catalyst. After alkaline work-up the corresponding *N*-(2′-pyrrolylmethyl)-1,2,3,4-tetrahydroisoquinolines **5b**, **5c** and **5g** are obtained as sole products of the reaction. The replacement of the benzotriazolyl moiety with 1,3-dimethoxybenzene in compounds **4d** and **4g** at RT is, however, incomplete and more reliable results are obtained when the mixture is refluxed in $CHCl_3$. The respective *N*-(2′,4′-dimethoxybenzyl)-1,2,3,4-tetrahydroisoquinolines **6d** and **6g** are isolated after alkaline work-up. As anticipated, due to steric hindrance the *N*-(2′,6′-dimethoxybenzyl)-isomer is not formed in this reaction. Refluxing in $CHCl_3$ was also found to be a successful procedure in the preparation of the *N*-(2′-hydroxy-1′-naphthylmethyl)-1,2,3,4-tetrahydroisoquinolines **7a**, **7e** and **7g**. Further, stirring compound **4f** or **4g** and $NaBH_4$ at RT in MeOH following an earlier reported procedure[15] yields high quantities of the *N*-methyl-1,2,3,4-tetrahydroisoquinolines **8f** and **8g**.

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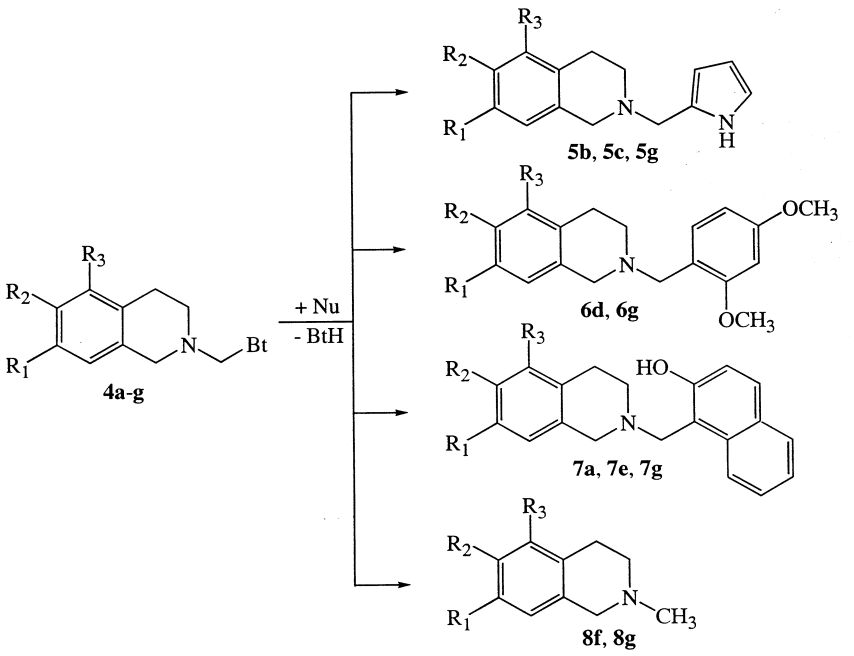

Scheme 3.

CONCLUSION

The method described in this paper is a convenient approach to the preparation of some deactivated *N*-substituted 1,2,3,4-tetrahydroisoquinolines. Although related to the Pictet–Spengler reaction, it must be seen as complementary to it, since it is exclusively applicable to 1,2,3,4-tetrahydroisoquinolines with electron-withdrawing substituents on the aromatic moiety. In a two-step reaction, β-phenylethylamines **2a–f** and 1-hydroxymethylbenzotriazole **1** are converted into the stable intermediates *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines **4a–f**, employing conc. H_2SO_4 as catalyst and 'solvent' for the intramolecular ring-closure. A strict adherence to the established conditions for the cyclisation step with respect to temperature and concentration of **4** in the acid is important, otherwise the corresponding *bis*(*N*-1,2,3,4-tetrahydroisoquinolinyl)methanes **9a–f** are obtained. The replacement of the benzotriazolyl moiety in compounds **4a–g** opens the way to the synthesis of a wide range of *N*-substituted 1,2,3,4-tetrahydroisoquinolines, exemplified by the replacement with pyrrole (**5b**, **5c**, **5g**), 1,3-dimethoxybenzene (**6d**, **6g**)

Table 4. *N*-Substituted 1,2,3,4-Tetrahydroisoquinolines **5–8**

Compound	Nucleophile	R_1	R_2	R_3	Mp (°C)	Yield (%)	δ_H [NCH_2Nu]
7a	C	Br	H	H	127–128	93	4.33 (s, 2H)
5b	A	F	H	H	100–102	95	3.67 (s, 2H)
5c	A	H	H	F	86–89	86	3.69 (s, 2H)
6d	B	Cl	H	H	126–129[a]	93	3.67 (s, 2H)
7e	C	H	H	Cl	130–132	97	4.34 (s, 2H)
8f	D	Cl	H	Cl	133–135[a]	83	2.45 (s, 3H)
5g	A	H	H	H	88–89	98	3.67 (s, 2H)
6g	B				133–135[a]	96	3.67 (s, 4H)[b]
7g	C				154–156	85	4.32 (s, 2H)
8g	D				150–153[a]	70	2.44 (s, 3H)

A: Pyrrole; B: 1,3-Dimethoxybenzene; C: 2-Hydroxynaphthalene; D: Reduction with $NaBH_4$.
[a]As picrate; [b]Signal collapsed with [$ArCH_2N$].

and 2-hydroxynaphthalene (**7a**, **7e**, **7g**), as well as the reduction with $NaBH_4$ to the corresponding *N*-methyl-1,2,3,4-tetrahydroisoquinolines (**8f**, **8g**). All steps of the established procedure work under mild conditions and yield high to excellent quantities of the final product.

EXPERIMENTAL

General

All reagents used were AR grade. Melting points were determined on a Gallenkamp Melting Point Apparatus and are uncorrected. FTIR-spectra were taken on a Mattson Polaris FTIR-Spectrophotometer in Nujol and UV/VIS-data on a Varian Cary 1 UV Visible Spectrophotometer, using

ethanol as solvent. ^{1}H- and ^{13}C-NMR spectra were recorded with a Varian Gemini 200 (200 MHz/50 MHz) in deuteriochloroform ($CDCl_3$) with tetramethylsilane (TMS) as internal reference. ^{1}H-NMR chemical shifts δ are reported in parts per million (ppm, $\delta_{TMS} = 0.00$) and ^{13}C-NMR results (in ppm) are measured relative to $CDCl_3$ ($\delta = 77.0$ for centerline). Coupling patterns are indicated as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). GC/MS spectra were obtained on a Varian Star 3400 CX spectrometer with a SGE 30QC2.5/BPX1.0 column. Elemental analyses were performed in the Research School of Chemistry, Australian National University, Canberra, Australia.

Preparation of *N*,*N*-*Bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines. General Method

A solution of the β-phenylethylamines **2a–f** (1.0 equiv.) in EtOH was added to 1-hydroxymethylbenzotriazole **1** (2.0 equiv.). The mixture was heated with stirring for 1 h. The *N*,*N*-*bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines **3a–f** crystallised from the solution and were recrystallised from EtOH. The preparation of compounds **3d–f** was already reported elsewhere.[15]

N,*N*-*Bis*(*benzotriazol*-1-*ylmethyl*)-4-*bromo*-*β*-*phenylethylamine* **3a**. 1.00 g 4-Bromo-β-phenylethylamine **2a** (5.0 mmol) was reacted with 1.49 g (10.0 mmol) 1-hydroxymethylbenzotriazole **1** in 20 mL EtOH. Product **3a** was obtained as very fine, white crystals (2.12 g, 92%). Mp. 143–145°C (EtOH); δ_H 8.10 (d, 2H, 9 Hz), 7.51–7.40 (m, 6H), 7.22 (d, 2H, 7 Hz), 6.82 (d, 2H, 7 Hz), 5.63 (s, 4H, NCH_2N), 3.12 (t, 2H, 6 Hz, NCH_2CH_2), 2.77 (t, 2H, 6 Hz, NCH_2CH_2); δ_C 146.2, 137.8, 133.2, 131.6, 130.3, 128.1, 124.4, 120.2, 109.7, 64.4 (NCH_2N), 51.5 (NCH_2CH_2), 33.1 (NCH_2CH_2); λ_{max} (nm/dm^3 mol^{-1} cm^{-1}) 284 (1320), 256 (2880), 210 (7740); ν_{max} (cm^{-1}, Nujol) 1330, 1275, 1225, 1200, 1145, 1060, 1010, 975, 750, 525; Anal. calc. for $C_{22}H_{20}BrN_7$: C 57.2; H 4.4; N 21.2; Found: C 57.4, H 4.1, N 21.3%.

N,*N*-*Bis*(*benzotriazol*-1-*ylmethyl*)-4-*fluoro*-*β*-*phenylethylamine* **3b**. Product **3b** (2.56 g, 89%) was obtained from the reaction between 4-fluoro-β-phenylethylamine **2b** (1.00 g, 7.2 mmol) and 1-hydroxymethylbenzotriazole **1** (2.14 g, 14.4 mmol) as very fine white powder. Mp. 117–118°C (EtOH); δ_H 8.11 (d, 2H, 8 Hz), 7.53–7.41 (m, 6H), 6.97–6.77 (m, 4H), 5.64 (s, 4H, NCH_2N), 3.13 (t, 2H, 7 Hz, NCH_2CH_2), 2.79 (t, 2H, 7 Hz, NCH_2CH_2); δ_C 161.7 (239 Hz), 146.3, 134.4, 133.2, 130.1 (8 Hz), 128.1, 124.4, 120.2, 115.3 (16 Hz), 109.8, 64.4 (NCH_2N), 52.0 (NCH_2CH_2), 33.0 (NCH_2CH_2); .λ_{max} (nm/dm^3 mol^{-1} cm^{-1}) 272 (11200), 259 (13920), 210 (19040); ν_{max} (cm^{-1}, Nujol) 1505, 1225, 1200, 1150, 1140, 1075, 990, 840,

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745, 660, 580, 560, 510; Anal. calc. for $C_{22}H_{20}FN_7$: C 65.8; H 5.0; N 24.4; Found: C 66.1, H 5.4, N 24.4%.

N,*N*-*Bis*(*benzotriazol*-1-*ylmethyl*)-2-*fluoro*-*β*-*phenylethylamine* **3c**. The reaction between 2-fluoro-β-phenylethylamine **2c** (1.00 g, 7.2 mmol) and 1-hydroxymethylbenzotriazole **1** (2.14 g, 14.4 mmol) yielded product **3c** (2.82 g, 98%) as fine white crystals. Mp. 116–117°C (EtOH); δ_H 8.10 (d, 2H, 8 Hz), 757–7.36 (m, 6H), 7.11–6.85 (m, 4H), 5.66 (s, 4H, NCH_2N), 3.18 (t, 2H, 6 Hz, NCH_2CH_2), 2.90 (t, 2H, 6 Hz, NCH_2CH_2); δ_C 161.3 (245 Hz), 146.2, 133.3, 130.9 (4 Hz), 128.3, 128.0, 125.6 (15 Hz), 124.3, 120.1, 115.2 (19 Hz), 109.8, 64.3 (NCH_2N), 50.6 (NCH_2CH_2), 27.2 ($ArCH_2$); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 280 (9760), 258 (15360), 212 (20000); ν_{max} (cm^{-1}, Nujol) 1275, 1225, 1175, 1155, 1130, 1075, 1025, 970, 825, 755, 745, 670; Anal. calc. for $C_{22}H_{20}FN_7$: C 65.8; H 5.0; N 24.4; Found: C 66.1, H 5.3, N 24.5%.

Preparation of *N*-Benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines. General Method

The *N*,*N*-*Bis*(benzotriazol-1-ylmethyl)-β-phenylethylamines **3a–e** (1.0 equiv.) were slowly added to conc. H_2SO_4 (45.0 equiv.) at 4°C with stirring. After 2 h, the mixture was slowly brought to RT and stirred for another 2 h. The stronger deactivated compound **3f** required more vigorous conditions and was heated at approx. 80°C for 30 h. The solution was then in all cases quenched with crushed ice, its pH adjusted to 12 with NaOH 10 M and exhaustively extracted with DCM. The combined organic extracts were washed with NaOH 2 M, dried with anhydrous $MgSO_4$, filtered and evaporated under reduced pressure. The corresponding *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines **4a–f** crystallised from an oily solution and were recrystallised from EtOH. The identity of compounds **4d** and **4e** was confirmed by comparison with the literature[15] (Mp., ^1H and ^{13}C NMR data). Compound **4g** was obtained from the reaction between 1-hydroxymethylbenzotriazole **1** and 1,2,3,4-tetrahydroisoquinoline.[20] An alternative preparation uses compound **3g** and $AlCl_3$.[15]

N-*Benzotriazol*-1-*ylmethyl*-7-*bromo*-1,2,3,4-*tetrahydroisoquinoline* **4a**. *N*,*N*-*Bis*(benzotriazol-1-ylmethyl)-4-bromo-β-phenylethylamine **3a** (0.50 g, 1.1 mmol) was reacted in conc. H_2SO_4 (2.8 mL, 50.4 mmol) to yield product **4a** (0.31 g, 82%) as white crystals. Mp. 145–146°C (EtOH); δ_H 8.09 (d, 1H, 8 Hz), 7.69 (d, 1H, 8 Hz), 7.53 (t, 1H, 7 Hz), 7.40 (t, 1H, 7 Hz), 7.24–7.16 (m, 2H), 6.94 (d, 1H, 6 Hz), 5.63 (s, 2H, NCH_2N), 3.83 (s, 2H, $ArCH_2N$), 2.95 (t, 2H, 4 Hz, NCH_2CH_2), 2.87 (t, 2H, 4 Hz, NCH_2CH_2); δ_C 135.9, 134.0, 132.7, 130.5, 129.5, 127.9, 126.7, 124.2, 120.2, 119.4, 118.4, 109.9, 68.8 (NCH_2N), 51.9 (NCH_2CH_2), 48.1 ($ArCH_2N$), 28.5 (NCH_2CH_2); λ_{max}

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($nm/dm^3\,mol^{-1}\,cm^{-1}$) 273 (3010), 259 (3460), 212 (9110); ν_{max} (cm^{-1}, Nujol) 1330, 1205, 1150, 1080, 1050, 960, 940, 820, 750, 725; Anal. calc. for $C_{16}H_{15}BrN_4$: C 56.0; H 4.4; N 16.3; Found: C 56.3, H 4.5, N 16.4%.

N-Benzotriazol-1-*ylmethyl*-7-*fluoro*-1,2,3,4-*tetrahydroisoquinoline* **4b**. Product **4b** (0.59 g, 83%) was obtained from the reaction of *N*,*N-bis*(benzotriazol-1-ylmethyl)-4-fluoro-β-phenylethylamine **3b** (1.00 g, 2.5 mmol) in conc. H_2SO_4 (6.4 mL, 115.2 mmol) as white crystals. Mp. 147–148°C (EtOH); δ_H 8.09 (d, 1H, 9 Hz), 7.70 (d, 1H, 8 Hz), 7.53 (t, 1H, 7 Hz), 7.39 (t, 1H, 7 Hz), 7.02 (t, 1H, 7 Hz), 6.85–6.68 (m, 2H), 5.64 (s, 2H, NCH_2N), 3.84 (s, 2H, $ArCH_2N$), 2.96 (t, 2H, 5 Hz, NCH_2CH_2), 2.87 (t, 2H, 5 Hz, NCH_2CH_2); δ_C 161.2 (239 Hz), 146.1, 135.6 (4 Hz), 134.0, 130.3 (4 Hz), 127.8, 126.7, 124.1, 120.2, 118.4, 113.3 (22 Hz/33 Hz), 109.9, 68.8 (NCH_2N), 52.2 (NCH_2CH_2), 48.4 ($ArCH_2N$), 28.3 (NCH_2CH_2); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 276 (3410), 260 (3720), 211 (6730); ν_{max} (cm^{-1}, Nujol) 1315, 1250, 1225, 1150, 1085, 1050, 975, 950, 870, 750, 725, 620, 575; Anal. calc. for $C_{16}H_{15}FN_4$: C 68.1; H 5.4; N 19.9; Found: C 68.5, H 5.4, N 20.1%.

N-Benzotriazol-1-*ylmethyl*-5-*fluoro*-1,2,3,4-*tetrahydroisoquinoline* **4c**. *N*,*N-Bis*(benzotriazol-1-ylmethyl)-2-fluoro-β-phenylethylamine **3c** (1.00 g, 2.5 mmol) was reacted in conc. H_2SO_4 (6.4 mL, 115.2 mmol). After alkaline work-up, compound **4c** (0.49 g, 69%) was obtained as white crystals. Mp. 134–135°C (EtOH); δ_H 8.09 (d, 1H, 9 Hz), 7.70 (d, 1H, 9 Hz), 7.53 (t, 1H, 7 Hz), 7.40 (t, 1H, 7 Hz), 7.07 (q, 1H, 7 Hz/15 Hz), 6.82 (t, 2H, 9 Hz), 5.65 (s, 2H, NCH_2N), 3.86 (s, 2H, $ArCH_2N$), 2.97 (t, 2H, 4 Hz, NCH_2CH_2), 2.89 (t, 2H, 4 Hz, NCH_2CH_2); δ_C 161.6 (245 Hz), 146.1, 136.4 (4 Hz), 134.0, 127.8, 127.0 (11 Hz), 124.2, 122.0, 120.2, 118.4, 112.7 (12 Hz), 110.0, 69.0 (NCH_2N), 51.9 (NCH_2CH_2), 47.7 ($ArCH_2N$), 22.5 (NCH_2CH_2); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 270 (4060), 259 (5070), 212 (7630); ν_{max} (cm^{-1}, Nujol) 1345, 1250, 1205, 1180, 1150, 1010, 955, 795, 780, 525, 500; Anal. calc. for $C_{16}H_{15}FN_4$: C 68.1; H 5.4; N 19.9; Found: C 67.8, H 5.5, N 19.5%.

N-Benzotriazol-1-*ylmethyl*-7-*chloro*-1,2,3,4-*tetrahydroisoquinoline* **4d**. The reaction of *N*,*N-bis*(benzotriazol-1-ylmethyl)-4-chloro-β-phenylethylamine **3d** (5.00 g, 12.0 mmol) in conc. H_2SO_4 (30.0 mL, 540.0 mmol) yielded compound **3d** (2.96 g, 83%) as white needles.

N-Benzotriazol-1-*ylmethyl*-5-*chloro*-1,2,3,4-*tetrahydroisoquinoline* **4e**. Product **4e** (1.56 g, 73%) was obtained as white needles after alkaline work-up from the reaction of *N*,*N-bis*(benzotriazol-1-ylmethyl)-2-chloro-β-phenylethylamine **3e** (3.00 g, 7.2 mmol) in conc. H_2SO_4 (18.0 mL, 324.0 mmol).

N-Benzotriazol-1-*ylmethyl*-5,7-*dichloro*-1,2,3,4-*tetrahydroisoquinoline* **4f**. *N*,*N-Bis*(benzotriazol-1-ylmethyl)-2,4-dichloro-β-phenylethylamine **3f** (5.00 g, 11.1 mmol) was reacted in conc. H_2SO_4 (31.0 mL, 558.0 mmol).

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Product **4f** (3.18 g, 86%) crystallised from the oily solution upon contact with EtOAc and was recrystallised from EtOH to yield fine white crystals. Mp. 149–150°C (EtOH); δ_H 8.10 (d, 1H, 9 Hz), 7.68 (d, 1H, 8 Hz), 7.54 (t, 1H, 7 Hz), 7.40 (t, 1H, 7 Hz), 7.20 (s, 1H), 6.92 (s, 1H), 5.63 (s, 2H, NCH_2N), 3.80 (s, 2H, $ArCH_2N$), 2.98 (t, 2H, 4 Hz, NCH_2CH_2), 2.85 (t, 2H, 4 Hz, NCH_2CH_2); δ_C 146.1, 137.3, 135.1, 133.9, 131.9, 130.6, 127.9, 127.1, 125.2, 124.2, 120.2, 109.8, 68.5 (NCH_2N), 52.0 (NCH_2CH_2), 47.9 ($ArCH_2N$), 26.8 (NCH_2CH_2); λ_{max} (nm/dm^3 mol^{-1} cm^{-1}) 274 (1790), 254 (2230), 210 (7840); ν_{max} (cm^{-1}, Nujol) 1560, 1205, 1175, 1160, 1145, 1095, 1050, 970, 870, 830, 750, 620, 570; Anal. calc. for $C_{16}H_{14}Cl_{l2}N_4$: C 57.7; H 4.2; N 16.8; Found: C 57.7, H 4.4, N 16.7%.

Preparation of *N*-(2′-Pyrrolylmethyl)-1,2,3,4-tetrahydroisoquinolines. General Method

The respective *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines (**1** equiv.) were dissolved in DCM (20 mL). Anhydrous $AlCl_3$ (**4** equiv.) and pyrrole (1 equiv.) were added. The mixture was stirred at RT for 5 h with a drying tube (anhydrous $CaCl_2$) attached, then poured onto crushed ice and brought to pH 12 with NaOH 2 M. The layers were separated and the aqueous solution exhaustively extracted with DCM. The combined organic extracts were washed with NaOH 2 M, dried with anhydrous $MgSO_4$, filtered and evaporated under reduced pressure. The products crystallised slowly from an oily solution and were recrystallised.

N-(2′-*Pyrrolylmethyl*)-7-*fluoro*-1,2,3,4-*tetrahydroisoquinoline* **5b**. The reaction between *N*-benzotriazol-1-ylmethyl-7-fluoro-1,2,3,4-tetrahydroisoquinoline **4b** (0.50 g, 1.8 mmol), anhydrous $AlCl_3$ (0.95 g, 7.1 mmol) and pyrrole (0.12 g, 1.8 mmol) yielded product **5b** (0.39 g, 95%) as colourless crystals. Mp. 100–102°C (EtOAc : hexane 1:9); δ_H 8.77 (broad s, 1H, NH), 7.09–7.02 (m, 1H), 6.86 (d, 1H, 8 Hz), 6.72–6.66 (m, 2H), 6.14 (t, 1H, 5 Hz), 6.10 (s, 1H), 3.67 (s, 2H, NCH_2), 3.57 (s, 2H, $ArCH_2N$), 2.83 (t, 2H, 5 Hz, NCH_2CH_2), 2.74 (t, 2H, 5 Hz, NCH_2CH_2); δ_C 161.2 (245 Hz), 136.5 (11 Hz), 130.2 (11 Hz), 129.8, 128.3, 117.9, 113.5 (21 Hz), 112.8, 107.9, 107.8, 55.7 (NCH_2), 54.9 ($ArCH_2N$), 50.4 (NCH_2CH_2), 28.1 (NCH_2CH_2); λ_{max} (nm/dm^3 mol^{-1} cm^{-1}) 276 (1590), 270 (1560), 223 (6550); ν_{max} (cm^{-1}, Nujol) 3480, 3210, 1255, 1130, 1075, 1025, 950, 875, 725, 605, 575; Anal. calc. for $C_{14}H_{15}FN_2$: C 73.0; H 6.6; N 12.2; Found: C 73.4, H 7.3, N 12.2%.

N-(2′-*Pyrrolylmethyl*)-5-*fluoro*-1,2,3,4-*tetrahydroisoquinoline* **5c**. Compound **5c** (0.24 g, 86%) was obtained from the reaction between *N*-benzotriazol-1-ylmethyl-5-fluoro-1,2,3,4-tetrahydroisoquinoline**4c**(0.35 g,

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1.2 mmol), anhydrous $AlCl_3$ (0.66 g, 5.0 mmol) and pyrrole (0.08 g, 1.2 mmol), crystallising as colourless prisms from a brown oily solution. Mp. 86–89°C (Et_2O : hexane 1:2); δ_H 8.62 (broad s, 1H, NH), 7.09 (q, 1H, 7 Hz, 14 Hz), 6.90–6.76 (m, 3H), 6.15 (t, 1H, 2 Hz), 6.10 (s, 1H), 3.69 (s, 2H, NCH_2), 3.60 (s, 2H, $ArCH_2N$), 2.83 (t, 2H, 5 Hz, NCH_2CH_2), 2.76 (t, 2H, 5 Hz, NCH_2CH_2); δ_C 161.1 (245 Hz), 137.3 (9 Hz), 128.3, 126.9 (11 Hz), 122.1, 121.8, 117.9, 112.6 (21 Hz), 108.0, 107.8, 55.3 (NCH_2), 55.0 ($ArCH_2N$), 49.7 (NCH_2CH_2), 22.4 (NCH_2CH_2); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 276 (2230), 270 (2180), 225 (7100); ν_{max} (cm^{-1}, Nujol) 3180, 1250, 1230, 1110, 1070, 1005, 910, 775, 725; Anal. calc. for $C_{14}H_{15}FN_2$: C 73.0; H 6.6; N 12.2; Found: C 73.0, H 6.9, N 12.1%.

N-(2′-*Pyrrolylmethyl*)-1,2,3,4-*tetrahydroisoquinoline* **5g**. *N*-Benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinoline **4g** (0.50 g, 1.9 mmol), anhydrous $AlCl_3$ (1.00 g, 7.5 mmol) and pyrrole (0.13 g, 1.9 mmol) were reacted at RT for 5 h. Compound **5g** (0.39 g, 98%) was obtained from the reaction as white crystals. Mp. 88–89°C (hexane); δ_H 8.75 (broad s, 1H, NH), 7.13–7.04 (m, 3H), 7.00–6.97 (m, 1H), 6.71 (s, 1H), 6.13 (t, 1H, 2 Hz), 6.09 (s, 1H), 3.67 (s, 2H, NCH_2), 3.60 (s, 2H, $ArCH_2N$), 2.90 (t, 2H, 5 Hz, NCH_2CH_2), 2.74 (t, 2H, 5 Hz, NCH_2CH_2); δ_C 134.7, 134.3, 128.8, 128.6, 126.8, 126.4, 125.8, 117.7, 107.9, 107.6, 55.9 (NCH_2), 55.1 ($ArCH_2N$), 50.5 (NCH_2CH_2), 28.9 (NCH_2CH_2); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 273 (550), 266 (590), 220 (11100); ν_{max} (cm^{-1}, Nujol) 3180, 1330, 1235, 1125, 1075, 1025, 745, 710, 610; Anal. calc. for $C_{14}H_{16}N_2$: C 79.2; H 7.6; N 13.2; Found: C 78.9, H 7.5, N 13.0%.

Preparation of *N*-(2′,4′-Dimethoxybenzyl)-1,2,3,4-tetrahydroisoquinolines and *N*-(2′-Hydroxy-1′-naphthylmethyl)-1,2,3,4-tetrahydroisoquinolines. General Method

The respective *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinolines (1 equiv.) were dissolved in $CHCl_3$ (30 mL). Anhydrous $AlCl_3$ (4 equiv.) and 1,3-dimethoxybenzene or 2-hydroxynaphthalene (1 equiv.) were added. The mixture was refluxed for 24 h, then quenched with crushed ice and brought to pH 12 with NaOH 2 M. The layers were separated and the aqueous solution exhaustively extracted with DCM. The combined organic extracts were washed with NaOH 2 M, dried with anhydrous $MgSO_4$, filtered and evaporated under reduced pressure.

N-(2′,4′-*Dimethoxybenzyl*)-7-*chloro*-1,2,3,4-*tetrahydroisoquinoline* **6d**. The reaction between *N*-benzotriazol-1-ylmethyl-7-chloro-1,2,3,4-tetrahydroisoquinoline **4d** (0.50 g, 1.7 mmol), anhydrous $AlCl_3$ (0.89 g, 6.7 mmol) and 1,3-dimethoxybenzene (0.23 g, 1.7 mmol) yielded product **6d** (0.50 g,

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93%) as slightly yellow oil, which crystallised upon triturating with ether and cooling. Due to a presumably low melting point, the solid could not be isolated at RT and was converted into the corresponding picrate. Mp. (picrate) 126–129°C (EtOH); δ_H 7.28 (d, 1H, 8 Hz), 7.05–6.99 (m, 3H), 6.50–6.46 (m, 2H), 3.82 (s, 6H, OCH_3), 3.67 (s, 2H, NCH_2), 3.63 (s, 2H, $ArCH_2N$), 2.83 (t, 2H, 4 Hz, NCH_2CH_2), 2.78 (t, 2H, 4 Hz, NCH_2CH_2); δ_C 160.3, 159.1, 137.0, 133.0, 131.5, 131.1, 130.1, 126.6, 126.3, 118.2, 104.1, 98.5, 55.4 and 55.2 and 55.1 (OCH_3 and $ArCH_2N$ and NCH_2), 50.1 (NCH_2CH_2), 28.3 (NCH_2CH_2); *m*/*z* (%) 317 (M^+, 13), 179 (20), 166 (12), 152 (14), 151 (100), 121 (29), 91 (16), 77 (16); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 280 (3110), 224 (9590); ν_{max} (cm^{-1}, Nujol) 1620, 1505, 1295, 1205, 1160, 1040, 940, 840, 800; Anal. calc. for $C_{24}H_{23}ClN_4O_9$: C 52.7; H 4.2; N 10.2; Found: C 53.1, H 4.5, N 10.2%.

N-(2′,4′-*Dimethoxybenzyl*)-1,2,3,4-tetrahydroisoquinoline **6g**. *N*-Benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinoline **4g** (0.50 g, 1.9 mmol), anhydrous $AlCl_3$ (1.00 g, 7.5 mmol) and 1,3-dimethoxybenzene (0.26 g, 1.9 mmol) were refluxed for 24 h in $CHCl_3$. Product **6g** (0.52 g, 96%) was obtained as colourless oil, which crystallised upon contact with either at 4°C. Since the solid could not be isolated at RT, the corresponding picrate was obtained. Mp. (picrate) 133–135°C (EtOH); δ_H 7.31 (d, 1H, 9 Hz), 7.09 (d, 3H, 2 Hz), 7.01–6.98 (m, 1H), 6.15–6.45 (m, 2H), 3.81 (s, 6H, OCH_3), 3.67 (s, 4H, $ArCH_2$ and $ArCH_2N$), 2.89 (t, 2H, 5 Hz, NCH_2CH_2), 2.77 (t, 2H, 4 Hz, NCH_2CH_2); δ_C 160.2, 159.1, 135.4, 134.6, 131.4, 128.8, 126.8, 126.1, 125.6, 118.8, 104.0, 98.5, 55.9 (OCH_3), 55.4 (NCH_2 and $ArCH_2N$), 50.4 (NCH_2CH_2), 29.0 (NCH_2CH_2); *m*/*z* (%) 283 (M^+, 14), 207 (21), 151 (100), 145 (28), 132 (20), 121 (33), 91 (23), 77 (21); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 278 (600), 207 (4730); ν_{max} (cm^{-1}, Nujol) 1620, 1500, 1295, 1215, 1155, 1050, 745, 670; Anal. calc. for $C_{24}H_{24}N_4O_9$: C 56.3; H 4.7; N 10.9; Found: C 55.9, H 4.6, N 10.7%.

N-(2′-*Hydroxy*-1′-*naphthylmethyl*)-7-*bromo*-1,2,3,4-*tetrahydroisoquinoline* **7a**. The reaction between *N*-benzotriazol-1-ylmethyl-7-bromo-1,2,3,4-tetrahydroisoquinoline **4a** (0.70 g, 2.0 mmol), anhydrous $AlCl_3$ (1.09 g, 8.2 mmol) and 2-hydroxynaphthalene (0.29 g, 2.0 mmol) yielded compound **7a** (0.69 g, 93%) as creamy white crystals. Mp. 127–128°C (EtOH); δ_H 7.87–7.70 (m, 3H), 7.47 (t, 1H, 6 Hz), 7.35–7.26 (m, 2H), 7.17–7.00 (m, 3H), 4.33 (s, 2H, NCH_2), 3.82 (s, 2H, $ArCH_2N$), 2.94 (bs, 4H, NCH_2CH_2); δ_C 156.7, 135.6, 132.8, 132.6, 130.5, 129.9, 129.6, 129.1, 128.7, 126.6, 122.7, 121.1, 119.7, 119.3, 110.7, 55.8 (NCH_2), 54.9 ($ArCH_2N$), 49.9 (NCH_2CH_2), 28.0 (NCH_2CH_2); λ_{max} ($nm/dm^3\,mol^{-1}\,cm^{-1}$) 335 (1910), 290 (2790), 279 (3750), 230 (11770); ν_{max} (cm^{-1}, Nujol) 3400, 1625, 1315, 1270, 1245, 1225, 1160, 1100, 950, 895, 820, 750, 670; Anal. calc. for $C_{20}H_{18}BrNO$: C 65.2; H 4.9; N 3.8; Found: C 65.5, H 5.1, N 3.6%.

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N-(2′-*Hydroxy*-1′-*naphthylmethyl*)-5-*chloro*-1,2,3,4-*tetrahydroisoquinoline* **7e**. *N*-Benzotriazol-1-ylmethyl-5-chloro-1,2,3,4-tetrahydroisoquinoline **4e** (0.60 g, 2.0 mmol), anhydrous $AlCl_3$ (1.07 g, 8.0 mmol) and 2-hydroxynaphthalene (0.29 g, 2.0 mmol) were refluxed in $CHCl_3$ for 24 h. After alkaline work-up, compound **7e** (0.63 g, 97%) was obtained as white crystals. Mp. 130–132°C (EtOH : EtOAc 1:1); δ_H 7.88–7.70 (m, 3H), 7.47 (t, 1H, 9 Hz), 7.31 (t, 1H, 8 Hz), 7.26 (d, 1H, 3 Hz), 7.15–7.07 (m, 2H), 6.93 (d, 1H, 8 Hz), 4.34 (s, 2H, NCH_2), 3.84 (s, 2H, $ArCH_2N$), 3.00 (bs, 4H, NCH_2CH_2); δ_C 156.7, 135.6, 134.5, 132.8, 131.9, 129.5, 129.1, 128.7, 127.6, 127.1, 126.6, 125.2, 122.7, 121.1, 119.4, 110.7, 55.7 (NCH_2), 55.3 ($ArCH_2N$), 50.0 (NCH_2CH_2), 26.8 (NCH_2CH_2); λ_{max} (nm/dm^3 mol^{-1} cm^{-1})) 335 (1390), 290 (2130), 279 (2770), 269 (2420), 233 (10230); ν_{max} (cm^{-1}, Nujol) 3400, 1625, 1425, 1325, 1275, 1270, 1240, 1130, 820, 775, 750, 705; Anal. calc. for $C_{20}H_{18}ClNO$: C 74.2; H 5.6; N 4.3; Found: C 73.8, H 5.6, N 4.0%.

N-(2′-*Hydroxy*-1′-*naphthylmethyl*)-1,2,3,4-*tetrahydroisoquinoline* **7g**. The reaction between *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinoline **4g** (0.50 g, 1.9 mmol), anhydrous $AlCl_3$ (1.01 g, 7.6 mmol) and 2-hydroxynaphthalene (0.27 g, 1.9 mmol) yielded compound **7g** (0.47 g, 85%) as white solid. Mp. 154–156°C (EtOH); δ_H 7.88–7.68 (m, 3H), 7.46 (t, 1H, 8 Hz), 7.30 (t, 1H, 8 Hz), 7.17–6.99 (m, 5H), 4.32 (s, 2H, NCH_2), 3.86 (s, 2H, $ArCH_2N$), 2.97 (bs, 4H, NCH_2CH_2); δ_C 156.8, 133.6, 133.4, 132.9, 129.4, 129.0, 128.8, 128.7, 126.8, 126.5, 126.1, 122.6, 121.1, 119.4, 110.9, 56.0 (NCH_2), 55.4 ($ArCH_2N$), 50.2 (NCH_2CH_2), 28.5 (NCH_2CH_2); λ_{max} (nm/dm^3 mol^{-1} cm^{-1}) 335 (750), 290 (1300), 279 (1680), 268 (1620), 230 (8760); ν_{max} (cm^{-1}, Nujol) 3400, 1625, 1580, 1525, 1270, 1245, 1160, 1080, 975, 925, 750, 735, 535; Anal. calc. for $C_{20}H_{19}NO$: C 83.0; H 6.6; N 4.8; Found: C 83.4, H 6.4, N 4.6%.

Preparation of *N*-Methyl-1,2,3,4-tetrahydroisoquinolines. General Method

The respective *N*-benzotriazol-1-ylmethyl-1,2,3,4-tetrahydroisoquinoline (1 equiv.) was slowly added to $NaBH_4$ (2.5 equiv.) dissolved in MeOH (20 mL). The mixture was stirred at RT for 7 h with a drying tube (anhydrous $CaCl_2$) attached. After evaporation of the solvent under reduced pressure, the residue was partitioned between NaOH 2 M (10 mL) and DCM (10 mL). The aqueous solution was extracted with DCM (3×10 mL) and the combined organic extracts washed with NaOH 2 M (30 mL). The organic solution was dried with anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to yield the corresponding

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N-methyl-1,2,3,4-tetrahydroisoquinoline as oil. The preparation of compound **8g** was already described elsewhere.[15]

5,7-*Dichloro-N-methyl*-1,2,3,4-*tetrahydroisoquinoline* **8f**. *N*-Benzotriazol-1-ylmethyl-5,7-dichloro-1,2,3,4-tetrahydroisoquinoline **4f** (0.10 g, 0.3 mmol) was reduced with $NaBH_4$ (0.03 g, 0.8 mmol) to yield compound **8f** (0.05 g, 83%) as pale yellow oil. Mp. (picrate) 133–135°C (EtOH); δ_H 7.22 (s, 1H), 6.94 (s, 1H), 3.51 (s, 2H, $ArCH_2N$), 2.84 (t, 2H, 6 Hz, NCH_2CH_2), 2.69 (t, 2H, 6 Hz, NCH_2CH_2), 2.45 (s, 3H, NCH_3); δ_C 138.4, 135.0, 131.6, 130.9, 126.9, 125.0, 57.5 ($ArCH_2N$), 52.3 (NCH_2CH_2), 45.6 (NCH_3), 26.9 (NCH_2CH_2); *m*/*z* (%) 215 (M^+, 35), 214 (100), 180 (22), 174 (19), 172 (30), 137 (32), 102 (31); Anal. calc. for $C_{16}H_{14}Cl_2N_4O_7$: C 43.2; H 3.2; N 12.6; Found: C 42.8, H 3.3, N 12.3%.

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