o-(α-Benzotriazolylalkyl)phenols: Versatile Intermediates for the Synthesis of Substituted Phenols

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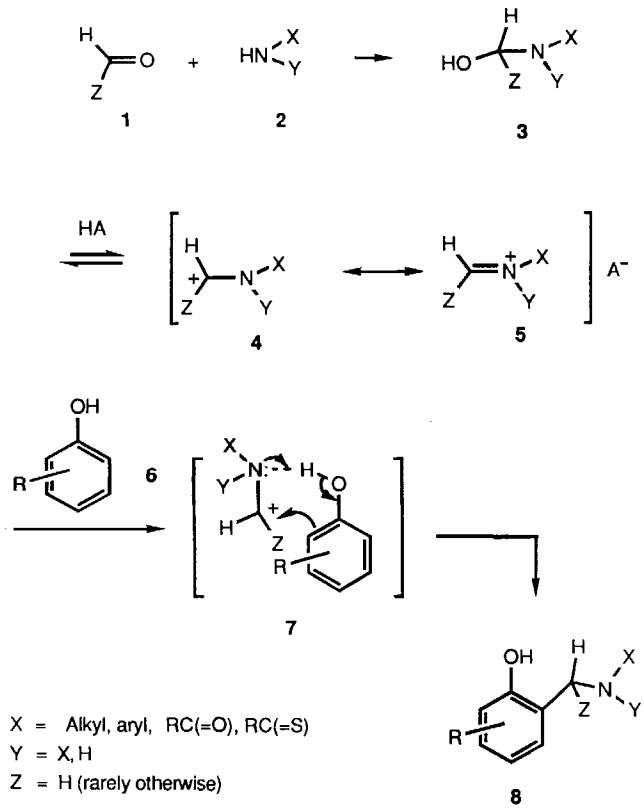
Phenols and naphthols are benzotriazolylmethylated by 1-(hydroxymethyl)-1*H*-benzotriazole (**13**) (a formaldehyde derivative) in the *o*- or (if both *o*-positions are occupied) in the *p*-position. The reaction can be extended to other aldehydes in the case of the naphthols. The methylene group in the *o*-(benzotriazolylmethyl)phenols can be lithiated (but only after trimethylsilyl protection of the hydroxy group) and then substituted by various electrophiles. The benzotriazole residues in both the primary products and in their substituted derivatives can be displaced by the alkyl anions of Grignard reagents or by hydride ions allowing the elaboration of many new types of substituted phenols.

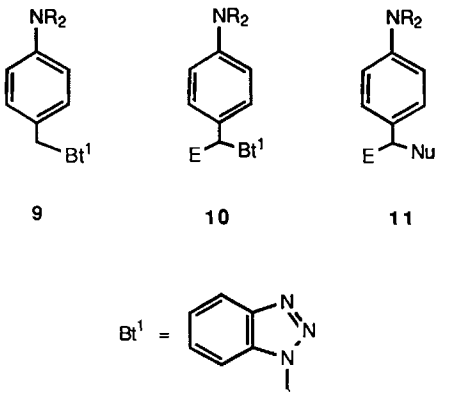
Classical Mannich reactions condense active CH– compounds, including phenols, with formaldehyde and an amine[1]. Important extensions of the Mannich reaction in which amides, imides, ureas, thioureas, etc. replace the amine component are well documented[2]. Phenols have been employed as the active CH– compounds in these Mannich condensations with aldehydes and amides or imides under various conditions[2]. The *ortho*-substituted derivatives are obtained unless both *ortho*-positions are occupied, when the Mannich reaction occurs at the *para*-position[3]. Zaugg[4] attributed the high *ortho*- to *para*-preference to the assistance of the phenolic hydroxy group. The first step of all Mannich reactions is the addition of the NH group to the carbonyl carbon of formaldehyde (or rarely another aldehyde) giving rise to an α-alkylol **3** (Scheme 1). Compound **3** is converted (generally by acid catalysis) into a carbenium/imonium ion (**4** ↔ **5**) which then reacts with the phenol to yield the condensation product **8**. A quasi six-membered chelate ring **7** preceding the carbon–carbon formation is believed to be responsible for the preferred *ortho*-substitution of phenols[5].

The aminols **3** can be isolated prior to use. An example is the Tseherniac-Einhorn reaction[6], where phthalimide reacts with formaldehyde to give an intermediate of type **3**. Other electrophilic reagents that have been isolated prior to use in aromatic substitutions of phenols are *N*-(alkoxyalkyl)amides[7], *N*-(haloalkyl)amides[4], and *N,N'*-(arylmethylene)bisamides[3]. In almost all examples of all of these cases, the carbonyl compound has been formaldehyde.

Previous work in our laboratory[8] has investigated the use of benzotriazole in certain aromatic substitutions. Anilines were readily alkylated with 1-(hydroxymethyl)-1*H*-benzotriazole (**13**) to afford **9** which in turn underwent smooth lithiation and subsequent reaction with an electrophile at the methylene carbon to give derivatives **10**. Subsequent displacement of the benzotriazole group in compounds **9** and **10** by anilines and other electron-rich aromatic compounds such as indoles, pyrroles, etc. gave diarylmethanes (**11**, E = H) and trisubstituted methanes (**11**, E ≠ H), respectively.

Scheme 1





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The displacement of the benzotriazole group is assisted by electron donation from the lone pair on the amino nitrogen atom. We believe that similar alkylation of phenols should occur, and that the subsequent displacement of benzotriazole would also be assisted by the phenolic oxygen lone pair in a manner similar to that established for the aniline system[8]. We now report the realization of these expectations and the development of a new methodology for the convenient synthesis of substituted phenols.

Results and Discussion

Reaction of Phenols with 1-(Hydroxymethyl)-1*H*-benzotriazole (13)

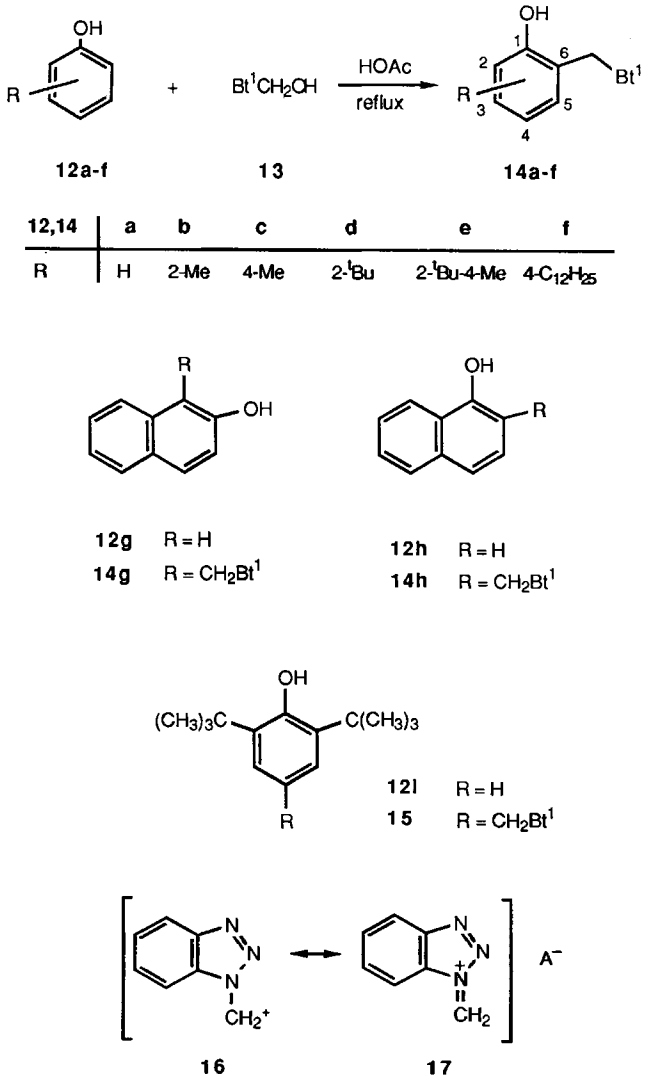
A series of phenols and naphthols (**12a–h**), unsubstituted at the *ortho*-position, when heated with 1-(hydroxymethyl)-1*H*-benzotriazole (**13**) in acetic acid under reflux, afforded the corresponding *ortho*-substituted products **14a–h** in moderate to excellent yields. Protonation of the oxygen in **13**, followed by loss of water would give rise to reactive cations (**16** ↔ **17**). Hydrogen bonding between the phenolic hydrogen and the basic nitrogen of the benzotriazole group would lead to *ortho*-substitution.

In 2,6-di-*tert*-butylphenol (**12i**) where both *ortho*-positions are blocked, more vigorous reaction conditions forced the alkylation to the *para*-position. On heating with **13** under reflux in toluene in the presence of one equivalent of *p*-toluenesulfonic acid monohydrate for two days, the *para*-alkylated product **15** was obtained in a yield of 50%.

Reactions of Naphthols with Benzotriazole and Other Aldehydes

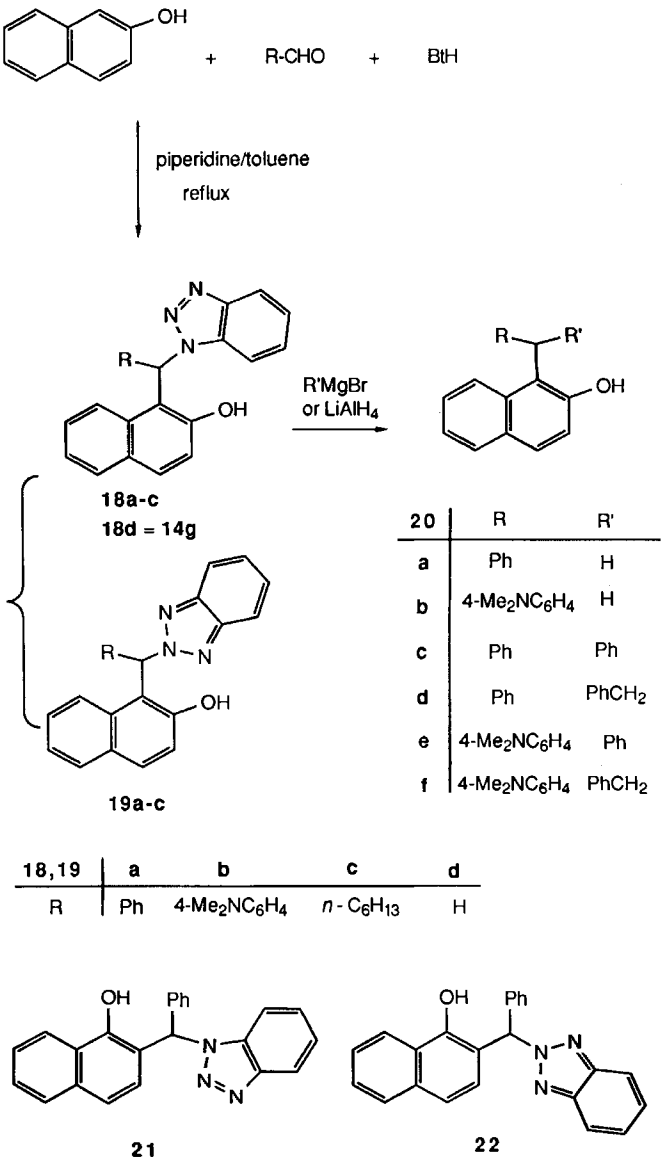
Attempts to condense phenol with benzaldehyde and benzotriazole in the presence of *p*-toluenesulfonic acid, piperidine, or 4-(dimethylamino)pyridine failed even under reflux in toluene for three days. The NMR spectra of the crude products displayed complex mixtures in which the unreacted benzotriazole and phenol resonances were predominant. The absence of the aliphatic Bt–CH signal in the ^{13}C-NMR

Scheme 2



12,14	a	b	c	d	e	f
R	H	2-Me	4-Me	2-^{t}Bu	2-^{t}Bu-4-Me	4-$C_{12}H_{25}$

Scheme 3



20	R	R'
a	Ph	H
b	4-$Me_2NC_6H_4$	H
c	Ph	Ph
d	Ph	$PhCH_2$
e	4-$Me_2NC_6H_4$	Ph
f	4-$Me_2NC_6H_4$	$PhCH_2$

18,19	a	b	c	d
R	Ph	4-$Me_2NC_6H_4$	*n*-C_6H_{13}	H

spectra indicated that the expected products were not formed. However, the high reactivity of 2-naphthol enabled it to react with aromatic aldehydes and benzotriazole in high yields to afford mixtures of benzotriazol-1- and -2-yl isomers **18a,b** and **19a,b**, respectively. The condensation with formaldehyde, on the other hand, gave exclusively the 1-isomer **14g**. The two isomers **18** and **19** were separated by a combination of recrystallization and column chromatography (see Experimental). The isolated isomer ratio was found to be dependent on the reflux time. With benzaldehyde, a reflux time of 24 h gave the 1-isomer **18a** and the 2-isomer **19a** in a ratio of 3:4. Shorter reflux times (cf. 2 h) afforded the 1-isomer **18a** as the predominant product in the ratio of 7:2. The condensation with heptanal and benzotriazole over 23 hours gave the 1-isomer **18c** (10%) and the 2-isomer **19c** (15%) while unreacted 2-naphthol was recovered in 52% yield.

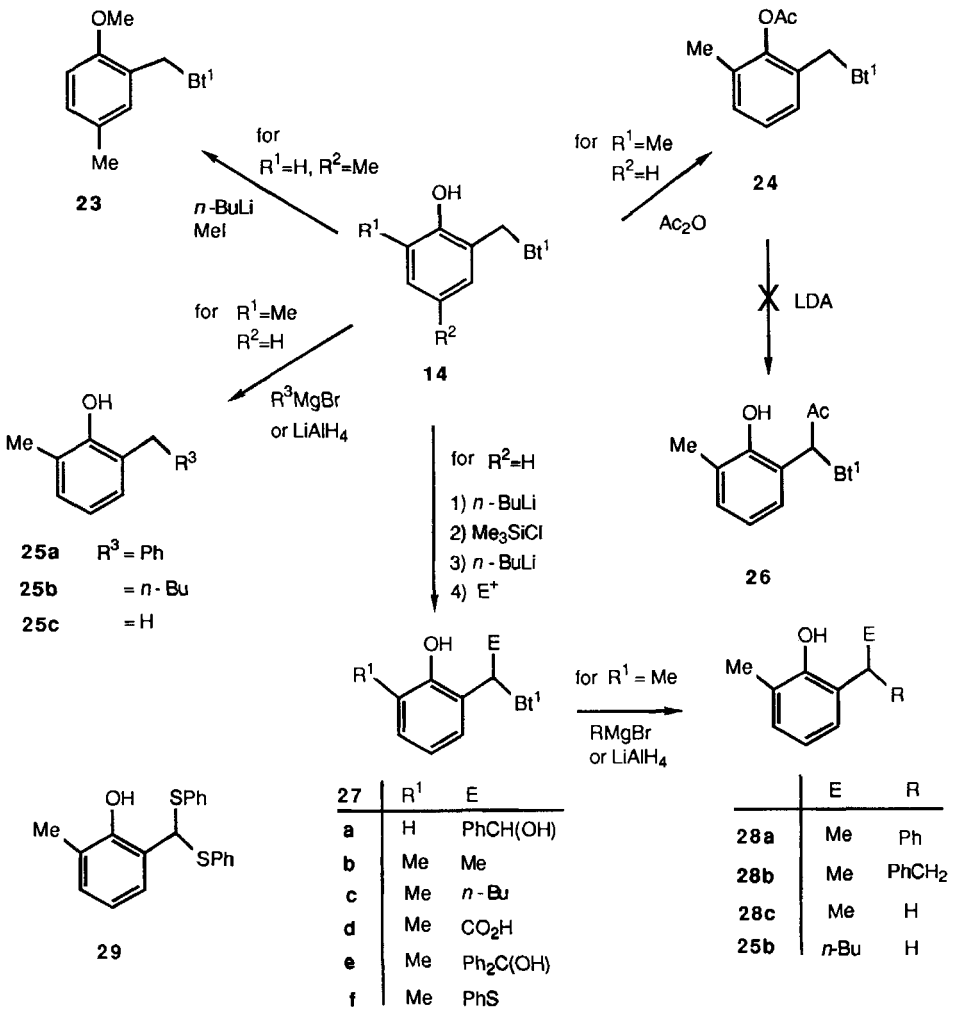
1-Naphthol also condensed with benzaldehyde and benzotriazole to give a mixture of 1- and 2- isomers **21** and **22** in yields of 34 and 23%, respectively.

Lithiation of the Phenol Derivatives 14

Heteroatom-assisted lithiation has received considerable attention recently due to its synthetic utility[9]. The phenolic hydroxy group is relatively ineffective in directing *ortho*-lithiation[9,10]. Posner[11] succeeded in the *ortho*-lithiation of phenol by employing *tert*-butyllithium in tetrahydropyran (THP): the dianion was trapped with various electrophiles to give the *C*-alkylated products (with trimethylsilyl chloride, the *O,C*-disilylated product was observed). However, Morey et al.[12] found that in alkoxyphenols the alkoxy groups usually determined the regioselectivity. MNDO calculations[12] suggest that phenol lithiations are highly dependent on the reaction conditions.

In our compounds of type **14**, the methylene groups are doubly activated: they are benzylic and are also attached to an electron-withdrawing benzotriazole group. Nevertheless, **14c** in THF at −78°C on treatment successively with two equivalents of *n*-butyllithium and one equivalent of methyl iodide gave a mixture of starting material **14c** (24%) and 2-(1*H*-benzotriazol-1-ylmethyl)-4-methylanisole (**23**) through

Scheme 4



O-alkylation (28%). Neither was *C*-alkylation achieved when the hydroxy group of **14b** was protected as its acetyl derivative **24**. Posner's conditions[11] yielded a 1:1 ratio of unreacted **14b** and the *C*-methylation product **27b**. However, when **14b** in THF was treated successively with equimolar amounts of *n*-butyllithium, trimethylsilyl chloride, *n*-butyllithium and finally an electrophile under carefully controlled conditions (vida infra), good yields of *C*-alkylation products were obtained. Workup with ethanolic hydrochloric acid, which removed the protecting trimethylsilyl group, afforded the desired products **27b–e** (Scheme 4, Table 4). Diphenyl disulfide gave the bis(phenylthio) product **29** evidently formed by the displacement of benzotriazole from the initial product **27f** by the phenylthiol anion produced simultaneously. Reaction of the phenol derivative **14a** with benzaldehyde gave the desired product **27a** in a yield of 68%.

Displacement of the Benzotriazole Group

The benzotriazole groups in compounds of type Bt–CRR′Z with Z = NR_2, OR, and SR have been displaced by Grignard or organolithium reagents or by hydride ion to yield amines[13], ethers[14], or thioethers[15], respectively. We speculated that the hydroxy group, after deprotonation, should assist the displacement of the benzotriazole group to form quinone methide intermediates, which upon concomitant addition of nucleophiles should then lead to substituted phenols.

Phenylmagnesium bromide in refluxing diethyl ether, tetrahydrofuran, or 1,2-dimethoxyethane did not react with **14b**. However, heating **14b** with phenylmagnesium bromide or *n*-butylmagnesium bromide in toluene under reflux (as previously used in the reaction of benzotriazolyl ethers with Grignard reagents[14]) afforded the desired products **25a,b**. Compound **14b** was also reduced by $LiAlH_4$ in refluxing toluene to give 2,6-dimethylphenol (**25c**).

As expected, substituents on the methylene carbon increase the reactivity. Thus the methylated substrate **27b** reacted with phenyl- and benzylmagnesium bromides in THF under reflux to give the desired products **28a,b**. In **18a**, the presence of the phenyl substituent enabled the reactions with Grignard reagents to occur at room temperature. Compound **18b** is even more reactive: the Grignard reaction had to be carried out at −78 °C to prevent decomposition. $LiAlH_4$ converted **18a,b** and **27b,c** into the corresponding reduced products **20a,b**, **28c**, and **25b** in good yields.

NMR Spectra of (α-Benzotriazolylalkyl)phenols

The structures of the products **14**, **15**, **18**, **19**, **21**, and **22** are confirmed by ^{1}H- and ^{13}C-NMR spectroscopy and elemental analyses. The ^{13}C-NMR spectra of compounds **14**, **15**, **18**, and **21** (see Table 1) display the characteristic pattern for the 1-substituted benzotriazoles. The quaternary carbons C-3a and C-7a of the benzotriazole moiety resonate between δ = 144.4 and 146.1 and between 131.7 and 133.4, respectively. The methylene carbon in compounds **14** (except for the naphthol analogs **14g**, **14h**) give signals in the region δ = 46.4–48.6 which are shifted upfield due to the mesomeric and steric effects[23] as compared to the *para*-substituted derivative **15** (δ = 52.6). The methylene protons of **14a–f** (see Table 2) are observed at δ = 5.75–6.00. For the naphthyl analogues **14g,h**, the methylene protons resonate downfield at δ = 6.35 and 6.08, respectively. While the chemical shift of the methylene carbon of **14h** is comparable to those of the phenyl derivatives **14a–f**, the signal of the methylene carbon of **14g** is shifted upfield due to the steric effect[23] (see Table 1). For the 1-isomers **18** and **21**, due to the presence of an extra substituent attached to the methylene carbon, both the α-proton (see Table 3) and the α-carbon (see Table 1) resonances are shifted downfield as compared to the methylene protons and carbons in **14** and **15**. For the 2-isomers **19** and **22**, while the α-proton resonances are comparable to those of the corresponding 1-isomers, the α-carbon resonances are shifted further downfield than those of the corresponding 1-isomers due to the presence of two electron-withdrawing N=C bonds.

Experimental

Melting points: Hot-stage microscope. All temperatures quoted are uncorrected. – ^{1}H-NMR: Varian VXR-300 (300 MHz) with TMS [δ(TMS) = 0.00] as the internal reference. – ^{13}C NMR: Varian VXR-300 (75 MHz), referenced to the central line of $CDCl_3$ (δ = 77.00). $CDCl_3$ was used as the solvent for both ^{1}H- and ^{13}C-NMR spectra except when stated otherwise. – High-resolution MS: Kratos/AE1-MS 30 mass spectrometer. – Microanalyses: Carlo Erba 1106 elemental analyzer. – THF and toluene for lithiation and Grignard reactions were distilled from sodium/benzophenone immediately prior to use. – All lithiation and Grignard reactions were carried out under the protection of dry nitrogen. All glassware was dried in an oven overnight prior to use. All moisture-sensitive reagents were transferred by predried syringes.

General Procedure for the Alkylation of Phenols: Preparation of o-(Benzotriazol-1-ylmethyl)phenols **14**: A mixture of 3.75 g (25 mmol) of 1-(hydroxymethyl)-1*H*-benzotriazole (**13**)[8] and the corresponding phenol (25 mmol) in 25 ml of acetic acid was heated under reflux for the appropriate time (see Table 2). The acetic acid was removed under reduced pressure, and to the residue was added sodium hydrogen carbonate solution (10%, 30 ml). The product was extracted with diethyl ether (3 × 30 ml), washed with water, and dried with $MgSO_4$. The solvent was removed in vacuo, and the residue triturated with the appropriate solvent or chromatographed, as indicated below, to give the pure product.

2-(1H-Benzotriazol-1-ylmethyl)phenol (**14a**): The crude product was chromatographed with hexane/ethyl acetate (2:1). – ^{1}H NMR ([D$_6$]DMSO): δ = 5.91 (s, 2H), 6.78 (t, *J* = 7.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 7.1–7.2 (m, 2H), 7.38 (t, *J* = 7.0 Hz, 1H), 7.51 (t, *J* = 7.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 10.00 (s, 1H).

2-(1H-Benzotriazol-1-ylmethyl)-6-methylphenol (**14b**): The crude product was triturated with diethyl ether/hexane. – ^{1}H NMR ([D$_6$]DMSO): δ = 2.20 (s, 3H), 5.92 (s, 2H), 6.74 (t, *J* = 7.0 Hz, 1H), 6.90 (d, *J* = 7.0 Hz, 1H), 7.05 (d, *J* = 7.0 Hz, 1H), 7.38 (t, *J* = 7.0 Hz, 1H), 7.51 (t, *J* = 7.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.90 (s, 1H).

2-(1H-Benzotriazol-1-ylmethyl)-4-methylphenol (**14c**): The crude product was chromatographed with hexane/ethyl acetate (2:1). – ^{1}H NMR ([D$_6$]DMSO): δ = 2.12 (s, 3H), 5.83 (s, 2H), 6.8–6.9 (m,

Table 1. ^{13}C-NMR data[a] for benzotriazole phenol adducts **14, 15, 18, 19, 21,** and **22**

	Benzotriazolyl						Bt-C	Other aliphatic	Other aromatic
	C-4	C-5	C-6	C-7	C-7a	C-3a			
14a	119.1	123.8	127.1	110.9	132.9	145.3	46.5	-	115.5, 119.2, 121.8, 129.5, 129.8, 155.2
14b	119.1[b]	123.7	127.1[b]	110.9	132.9	145.2	47.0	16.6(Me)	119.6, 122.8, 125.1, 127.1, 127.2, 130.9, 153.0
14c	119.0	123.8	127.0	110.9	132.8	145.2	46.4	20.0(Me)	115.3, 121.4, 127.7, 129.9, 130.1, 152.9
14d	120.1[b]	124.4	128.0	109.4	132.5	145.6	48.6	29.7, 34.8(^{t}-Bu)	120.4, 122.4, 128.1, 128.2, 139.1, 154.4
14e	119.2	123.9[b]	128.7	110.6	132.8	145.3	46.9	20.5(Me), 29.8, 34.5 (^{t}-Bu)	124.6, 126.8, 127.2, 138.9, 150.8
14f	119.2	124.2	127.3	110.7	132.9	145.4	47.7	8.5, 12.1, 14.0, 14.1, 14.7, 22.5, 22.6, 29.0, 35.5, 36.9, 37.1, 40.3	116.0, 120.2, 120.3, 127.5, 128.1, 152.4
14g	119.1[b]	123.8[b]	128.5[b]	110.7[b]	132.6	145.2	42.6	-	111.6, 118.0, 122.4, 122.9, 127.0, 127.1, 128.2, 130.7, 133.2, 153.9
14h	119.2[b]	124.3[b]	126.1[b]	109.5	131.8	144.8	46.1	-	115.2, 118.3, 121.4, 122.8, 124.5, 125.4, 125.9, 126.7, 133.4, 149.7
15	119.9	123.7	127.1	109.8	132.8	146.2	52.6	30.1, 34.2 (^{t}-Bu)	124.8, 125.4, 136.4, 153.9
18a	118.8	124.1	128.5	110.5	132.2	144.8	57.9	-	114.1, 117.8, 122.2, 123.3, 125.8, 126.5, 127.1, 127.5, 127.9, 128.1, 130.5, 133.6, 137.3, 153.7
18b	118.1	123.1	127.5	110.4	131.7	144.4	58.1	39.3 (NMe_2)	111.1, 114.3, 117.4, 121.6, 122.5, 123.0, 125.3, 125.6, 127.9, 128.5, 129.5, 133.1, 148.9, 152.7
18c	118.9	123.5	128.5	110.6	132.3	145.5	56.2	13.7, 22.2, 26.6, 28.8, 31.3, 32.0 (n-hexyl)	115.3, 118.0, 122.4, 122.5, 126.3, 126.4, 128.9, 130.1, 133.3, 153.0
21	119.5[b]	124.4[b]	128.0[b]	110.1	133.4	145.0	62.5	-	118.8, 120.5, 122.1, 125.6, 125.7, 126.7, 127.0, 127.3, 127.6, 127.7, 128.6, 134.6, 137.5, 150.6

	C-4(7)	C-5(6)	C-3a(7a)	Bt-C	Other aliphatic	Other aromatic
19a	118.0	127.3	143.5	66.6	-	115.3, 121.0, 121.6, 123.5, 126.0, 127.7, 128.0, 128.6, 129.0, 129.2, 131.9, 133.2, 137.4, 154.8
19b	117.9	127.3	143.4	66.6	40.2 (NMe_2)	112.1, 114.8, 121.1, 121.4, 123.3, 123.9, 127.0, 127.5, 128.9, 129.1, 131.5, 133.1, 150.1, 154.9
19c	117.6	125.7	143.1	63.0	13.6, 22.0, 26.2, 28.6, 31.1, 32.1 (n-hexyl)	116.1, 118.6, 121.9, 122.2, 126.2, 128.4, 128.5, 129.8, 132.2, 153.4
22	117.8	127.1	143.5	73.9	-	116.6, 120.1, 123.0, 125.4, 126.4, 126.7, 127.0, 127.2, 128.1, 128.4, 128.8, 135.1, 137.1, 151.9

[a] Chemical shifts δ. — [b] These signals may be interchangeable.

3H), 7.38 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 9.72 (s, 1H).

2-(1H-Benzotriazol-1-ylmethyl)-6-tert-butylphenol (**14d**): The crude product was triturated with diethyl ether/hexane. — ^{1}H NMR: δ = 1.41 (s, 9H), 5.75 (s, 2H), 6.84 (t, J = 7.6 Hz, 1H), 7.17 (dd, J = 7.5, 1.6 Hz, 1H), 7.28 (dd, J = 8.0, 1.6 Hz, 1H), 7.36 (dt, J = 7.0, 1.0 Hz, 1H), 7.50 (dt, J = 7.0, 1.0 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.76 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H).

2-(1H-Benzotriazol-1-ylmethyl)-6-tert-butyl-4-methylphenol (**14e**): The crude product was triturated with diethyl ether/hexane. — ^{1}H NMR ([D$_6$]DMSO): δ = 1.40 (s, 9H), 2.08 (s, 3H), 6.00 (s, 2H), 6.5–6.6 (m, 1H), 6.9–7.0 (m, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 8.63 (s, 1H).

2-(1H-Benzotriazol-1-ylmethyl)-4-dodecylphenol (**14f**): The crude product was chromatographed with petroleum ether (40–60°C)/ethyl acetate (6:1). — ^{1}H NMR: δ = 0.6–1.7 (m, 25H), 5.95 (s, 2H), 7.0–7.4 (m, 5H), 7.6–7.8 (m, 1H), 8.0 (d, J = 7.0 Hz, 1H), 8.7 (broad, 1H).

1-(1H-Benzotriazol-1-ylmethyl)-2-naphthol (**14g**): The crude product was triturated with diethyl ether. — ^{1}H NMR ([D$_6$]-DMSO): δ = 6.35 (s, 2H), 7.1–7.5 (m, 5H), 7.6–7.8 (m, 4H), 8.28 (d, J = 8.0 Hz, 1H), 10.63 (s, 1H).

Table 2. Preparation of (benzotriazol-1-ylmethyl)phenols **14** and **15**

Comp.	React. time [h]	Yield (%)	Crystal form M.p. [°C]	Molecular formula (Mol. mass)	C	Cald. Found H	N	δ_H Bt–CH_2
14a	72	55	plates 168–170	$C_{13}H_{11}N_3O$ (225.3)	69.32 69.14	4.92 4.93	18.65 18.58	5.91
14b	72	59	micro. 156–158	$C_{14}H_{13}N_3O$ (239.3)	70.28 70.44	5.48 5.49	17.56 17.28	5.92
14c	72	43	micro. 140–142	$C_{14}H_{13}N_3O$ (239.3)	70.28 69.91	5.48 5.44	17.56 17.30	5.83
14d	45	71	prisms 108–110	$C_{17}H_{19}N_3O$ (283.4)	72.57 72.74	6.81 6.93	14.93 15.14	5.75
14e	42	66	needles 132–134	$C_{18}H_{21}N_3O$ (295.4)	73.19 73.27	7.17 7.27	14.23 14.36	6.00
14f	48	46	micro. 87–91	$C_{25}H_{36}N_3O$ (394.6)	76.10 75.72	9.20 9.11	10.65 10.94	5.95
14g	24	93[a]	plates 219–221	$C_{17}H_{13}N_3O$ (275.3)	74.17 74.15	4.76 4.73	15.26 15.20	6.35
14h	4	41	prisms 172–174	$C_{17}H_{13}N_3O$ (275.3)	74.17 74.16	4.76 4.69	15.26 15.10	6.08
15	48	50	micro. 134–136	$C_{21}H_{27}N_3O$ (337.5)	74.74 74.47	8.06 8.22	12.45 12.01	5.74

[a] Compound **14g** was also prepared by the condensation of 2-naphthol with paraformaldehyde and benzotriazole in a yield of 91%.

2-(1H-Benzotriazol-1-ylmethyl)-1-naphthol (**14h**): The crude product was chromatographed with petroleum ether (40–60°C)/ethyl acetate (2:1). – ^{1}H NMR: δ = 6.08 (s, 2H), 7.2–7.5 (m, 6H), 7.63–7.73 (m, 2H), 7.96 (dd, *J* = 8.2, 1.0 Hz, 1H), 8.3–8.4 (m, 1H), 9.59 (broad, 1H).

4-(1H-Benzotriazol-1-ylmethyl)-2,6-di-tert-butylphenol (**15**): A mixture of 2.06 g (10 mmol) of 2,6-di-*tert*-butylphenol, 1.49 g (10 mmol) of 1-(hydroxymethyl)-1*H*-benzotriazole (**13**), and 1.90 g (10 mmol) of *p*-toluenesulfonic acid monohydrate in 30 ml of toluene was heated under reflux for 2 d. The toluene was then removed under reduced pressure and the residue treated with 30 ml of saturated sodium hydrogen carbonate solution and extracted with diethyl ether (3 × 50 ml). The combined extract was dried with $MgSO_4$, the solvent removed in vacuo, and the residue chromatographed with petroleum ether (40–60°C)/ethyl acetate (9:1) to give the desired product (1.68 g, 50%). – ^{1}H NMR: δ = 1.38 (s, 18H), 5.27 (s, 1H), 5.74 (s, 2H), 7.16 (s, 2H), 7.3–7.5 (m, 3H), 8.06 (d, *J* = 8.0 Hz, 1H).

Table 3. Preparation of (benzotriazol-1-ylalkyl)naphthols

Comp.	React. time [h]	Yield (%)	Crystal form M.p. [°C]	Molecular formula (Mol. mass)	C	Calcd. Found H	N	δ_H Bt–*CH*
18a	2	71[a]	micro. 240–242	$C_{23}H_{17}N_3O$ (351.4)	78.61 78.40	4.88 4.83	11.96 11.90	8.31
19a	2	20[a]	micro. 143–145	$C_{23}H_{17}N_3O$ (351.4)	78.61 78.40	4.88 4.77	11.96 11.90	8.36
18b	22	63	micro. 174–176	$C_{25}H_{22}N_4O$ (394.5)	76.12 76.17	5.62 5.63	14.20 14.02	8.17
19b	22	23	micro. 186–188	$C_{25}H_{22}N_4O$ (394.5)	76.12 76.00	5.62 5.67	14.20 14.03	8.33
18c	23	10	needles 155–157	$C_{23}H_{25}N_3O$ (359.5)	76.85 77.02	7.01 7.24	11.69 11.84	6.85
19c	23	15	plates 143–145	$C_{23}H_{25}N_3O$ (359.5)	76.85 77.24	7.01 7.16	11.69 11.79	6.96
21	4	34	micro. 147–149	$C_{23}H_{17}N_3O$ (351.4)	78.61 78.46	4.88 4.88	11.96 11.65	7.74
22	4	23	micro. 68–70	$C_{23}H_{17}N_3O$ (351.4)	78.61 78.68	4.88 4.89	11.96 11.73	7.50

[a] With a reaction time of 24 h, **18a** and **19a** were obtained in 38 and 51%, respectively.

General Procedure for the Condensation of Naphthol, Aldehydes, and Benzotriazole: A mixture of 7.2 g (50 mmol) of naphthol, 5.3 g (50 mmol) of benzotriazole, the corresponding aldehyde (50 mmol) and 0.57 g (6.7 mmol) of piperidine in 100 ml of toluene was heated under reflux for the appropriate time (see Table 3), with azeotropic removal of water. Then toluene was removed under reduced pressure to give the crude product, which was triturated with the appropriate solvent, recrystallized, or chromatographed as indicated to give the pure 1- and 2-isomers.

1-(1H-Benzotriazol-1-ylmethyl)-2-naphthol (**14g**) was thus prepared from paraformaldehyde in a yield of 91% and was identical in all aspects with the sample prepared earlier.

Reaction of 2-Naphthol with Benzaldehyde and Benzotriazole: The crude product was triturated with diethyl ether to give the pure 1-isomer (**18a**), the residue was chromatographed with petroleum ether (40–60°C)/ethyl acetate (10:1) to give the pure 2-isomer (**19a**). With a reaction time of 24 h, **18a** was obtained in a yield of 38% along with 51% of **19a**. With a reaction time of 2 h, **18a** was obtained in a yield of 71% with 20% of **19a**.

1-[α-(1H-Benzotriazol-1-yl)benzyl]-2-naphthol (**18a**): ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 7.1–7.4 (m, 10H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.72 (t, *J* = 8.6 Hz, 2H), 7.97 (d, *J* = 7.7 Hz, 1H), 8.05 (dd, *J* = 7.4, 2.2 Hz, 1H), 8.31 (s, 1H, R_3CH), 10.2 (s, 1H, OH).

1-[α-(2H-Benzotriazol-2-yl)benzyl]-2-naphthol (**19a**): ^{1}H NMR: δ = 6.75–6.85 (m, 2H), 7.15–7.40 (m, 7H), 7.57 (dt, *J* = 7.2, 1.5 Hz, 1H), 7.8–7.9 (m, 4H), 8.35 (d, *J* = 9.6 Hz, 1H), 8.36 (s, 1H, R_3CH), 10.20 (s, 1H, OH).

Reaction of 2-Naphthol with 4-(Dimethylamino)benzaldehyde and Benzotriazole: The crude product was triturated with diethyl ether to give a solid, which was then recrystallized from ethyl acetate to give the pure 1-isomer **18b**. The residues from the trituration and the recrystallization were chromatographed with dichloromethane to give the 2-isomer **19b** in a yield of 23% and more 1-isomer. The total yield of 1-isomer **18b** was 63%.

1-{(1H-Benzotriazol-1-yl)[4-(dimethylamino)phenyl]methyl}-2-naphthol (**18b**): ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 2.91 (s, 6H), 6.63 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 7.16–7.38 (m, 6H), 7.68 (d, *J* = 8.8 Hz, 2H), 7.91–7.97 (m, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 8.17 (s, 1H, R_3CH), 9.75 (s, 1H, OH).

1-{(2H-Benzotriazol-2-yl)[4-(dimethylamino)phenyl]methyl}-2-naphthol (**19b**): ^{1}H NMR: δ = 2.82 (s, 6H), 6.54 (d, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.9 Hz, 2H), 7.25–7.40 (m, 4H), 7.53 (t, *J* = 8.3 Hz, 1H), 7.76–7.90 (m, 4H), 8.32 (d, *J* = 6.4 Hz, 1H), 8.33 (s, 1H, R_3CH), 10.22 (s, 1H, OH).

Reaction of 2-Naphthol with Heptanal and Benzotriazole: The crude product was triturated with diethyl ether/hexane to give a solid, which was washed with 2.5% NaOH solution to give the pure 1-isomer **18c** in a yield of 10%. Acidification of the aqueous solution gave unreacted 2-naphthol in a recovery of 52%. The residue from the trituration was chromatographed with petroleum ether (40–60°C)/ethyl acetate (10:1) to give the pure 2-isomer **19c** in a yield of 15%.

1-[1-(1H-Benzotriazol-1-yl)heptyl]-2-naphthol (**18c**): ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): δ = 0.83 (t, *J* = 6.8 Hz, 3H), 1.2–1.6 (m, 7H), 2.7–3.0 (m, 2H), 3.2–3.3 (m, 1H), 6.85 (t, *J* = 7.1 Hz, 1H,

R_3CH), 7.15–7.40 (m, 5H), 7.51–7.54 (m, 1H), 7.66 (t, J = 6.1 Hz, 2H), 7.93–7.96 (m, 1H), 8.25 (d, J = 8.4 Hz, 1H), 9.73 (s, 1H, OH).

1-[1-(2H-Benzotriazol-2-yl)heptyl]-2-naphthol (**19c**): ^{1}H NMR ($CDCl_3$ + [D_6]DMSO): 0.82 (t, J = 6.8 Hz, 3H), 1.1–1.5 (m, 7H), 2.6–2.8 (m, 1H), 3.1–3.4 (m, 2H), 6.96 (t, J = 8.0 Hz, 1H, R_3CH), 7.2–7.4 (m, 5H), 7.69 (t, J = 9.0 Hz, 2H), 7.82 (q, J = 3.0 Hz, 2H), 7.96 (d, J = 8.7 Hz, 1H), 9.80 (broad, 1H, OH).

Reaction of 1-Naphthol with Benzaldehyde and Benzotriazole: The crude product was chromatographed with hexane/dichloromethane (1:1) to give (1) the 2-isomer **22** in a yield of 23% and (2) the 1-isomer **21** in a yield of 34%.

2-[α-(1H-Benzotriazol-1-yl)benzyl]-1-naphthol (**21**): ^{1}H NMR: δ = 7.0–7.4 (m, 12H), 7.66–7.72 (m, 2H), 7.74 (s, 1H, R_3CH), 8.25–8.31 (m, 1H), 8.90 (broad, 1H, OH).

2-[α-(2H-Benzotriazol-2-yl)benzyl]-1-naphthol (**22**): ^{1}H NMR: δ = 6.85–6.95 (m, 2H), 7.1–7.4 (m, 9H), 7.50 (s, 1H, R_3CH), 7.65–7.85 (m, 3H), 8.4–8.5 (m, 1H), 10.4 (s, 1H, OH).

2-(1H-Benzotriazol-1-ylmethyl)-4-methylanisole (**23**): To a solution of 2.39 g (10 mmol) of **14c** in 50 ml of 1,2-dimethoxyethane at −78°C was added 8.0 ml (20 mmol) of *n*BuLi (2.5 M in hexane). The mixture was stirred at −78°C for 1 h and at room temp. for 2 h, cooled again to −78°C, and 0.62 ml (10 mmol) of iodomethane was added. The reaction was allowed to warm to room temp. and stirred overnight. Water was added, the mixture acidified with 2 N HCl, extracted with diethyl ether (3 × 50 ml) and the combined extract dried with $MgSO_4$. The solvent was removed in vacuo and the residue chromatographed with hexane/ethyl acetate (2:1) to give unreacted **14c** (24%) and compound **23** in a yield of 28%, m.p. 97–99°C. – ^{1}H NMR ([D_6]DMSO): δ = 2.16 (s, 3H), 3.76 (s, 3H), 5.86 (s, 2H), 6.90–7.12 (m, 3H), 7.38 (t, J = 8.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H). – ^{13}C NMR ([D_6]DMSO): δ = 19.9, 46.3, 55.4, 110.7, 111.1, 119.0, 123.1, 123.8, 127.1, 129.2, 130.0, 132.8, 145.1, 154.8.

$C_{15}H_{15}N_3O$ (253.3)
Calcd. C 71.13 H 5.97 N 16.59
Found C 71.48 H 6.04 N 16.70

2-(1H-Benzotriazol-1-ylmethyl)-6-methylphenyl Acetate (**24**): A solution of 1.20 g (5.0 mmol) of **14b** in 20 ml of acetic anhydride was heated under reflux for 30 min and poured into 100 ml of ice/water. The resulting solution was boiled for 30 min. After cooling, the solution was rendered basic with 50% NaOH, extracted with chloroform, and dried with $MgSO_4$. The solvent was removed in vacuo and the residue chromatographed with hexane/ethyl acetate (1:1) to give the pure product, m.p. 74–76°C. – ^{1}H NMR: δ = 2.12 (s, 3H), 2.33 (s, 3H), 5.73 (s, 2H), 7.0–7.4 (m, 6H), 8.02 (d, J = 8.0 Hz, 1H). – ^{13}C NMR: δ = 16.1, 20.4, 48.1, 109.8, 119.8, 123.8, 126.2, 126.8, 127.0, 127.3, 131.4, 131.5, 132.6, 146.1, 147.6, 168.5.

$C_{16}H_{15}N_3O_2$ (281.3)
Calcd. C 68.31 H 5.37 N 14.94
Found C 68.28 H 5.31 N 15.04

General Procedure for the Lithiation of Compounds **14**: To a solution of the substrate (5 mmol) (see Table 4) in 30 ml of THF at −78°C was added 2.0 ml (5 mmol) of *n*BuLi (2.5 M in hexane). The solution was stirred at −78°C for 1 h, then 0.63 ml (5.0 mmol) of trimethylsilyl chloride was added. After stirring at −78°C for 30 min, and at 25°C for 30 min, the solution was recooled to −78°C, and 2.0 ml (5 mmol) of *n*BuLi (2.5 M in hexane) was added. Stirring was continued for 2 h at this temp., and the corresponding electrophile (5 mmol) was added. After allowing the reaction mixture to reach room temp. and stirring overnight, the solution was concentrated under vacuo. Then 15 ml of 95% ethanol and 10 drops of conc. hydrochloric acid were added. After stirring at room temp. for 30 min, the ethanol was removed in vacuo, 30 ml of water added, the mixture extracted with diethyl ether (3 × 40 ml) and the combined extract dried with $MgSO_4$. The solvent was removed in vacuo and the residue recrystallized or chromatographed as indicated below to afford the pure product.

Table 4. Lithiation of compounds **14**

Product	Substrate	Electrophile	Yield (%)	Crystal form M.p. [°C]	Molecular formula (Mol. mass)		Calcd. Found C	H	N
27a	**14a**	PhCHO	68	plates 153–155	$C_{20}H_{17}N_3O_2$ (331.4)		72.49 72.48	5.17 5.14	12.68 12.35
27b	**14b**	MeI	71	prisms 157–159	$C_{15}H_{15}N_3O$ (253.3)		71.13 70.77	5.97 6.05	16.59 16.45
27c	**14b**	*n*BuI	50	plates 125–127	$C_{18}H_{21}N_3O$ (295.4)		73.19 73.10	7.17 7.31	14.23 14.16
27d	**14b**	CO_2	71	micro. 188–190	$C_{15}H_{13}N_3O_3$ (283.3)		63.60 63.31	4.63 4.70	14.83 14.52
27e	**14b**	Ph_2CO	62	micro. 246–248	$C_{27}H_{23}N_3O_2$ (421.5)		76.94 76.97	5.50 5.58	9.97 9.97

2-[1-(1H-Benzotriazol-1-yl)-2-hydroxy-2-phenylethyl]phenol (**27a**): The crude product was chromatographed with petroleum ether (40–60°C)/ethyl acetate (20:1) to give the desired product in a yield of 68%. – ^{1}H NMR: δ = 2.76 (s, 1H), 4.84 (d, J = 5.2 Hz, 1H), 6.02 (dd, J = 5.3, 2.6 Hz, 1H), 6.53 (d, J = 8.1 Hz, 1H), 6.65–6.80 (m, 2H), 6.9–7.5 (m, 8H), 7.62 (d, J = 7.7 Hz, 1H), 7.95 (d, J = 7.9 Hz, 1H), 9.13 (s, 1H). – ^{13}C NMR: δ = 61.9, 74.8, 110.3, 115.3, 118.9, 119.1, 122.5, 123.7, 126.8, 127.2, 127.5, 128.5, 128.9, 133.6, 140.3, 144.9, 154.1.

2-[1-(1H-Benzotriazol-1-yl)ethyl]-6-methylphenol (**27b**): The crude product was recrystallized from methanol. – ^{1}H NMR: δ = 2.12 (d, J = 7.0 Hz, 3H), 2.27 (s, 3H), 6.51 (q, J = 7.0 Hz, 1H, R_3CH), 6.74 (t, J = 7.6 Hz, 1H), 7.01 (t, J = 6.8 Hz, 2H), 7.3–7.5 (m, 3H), 7.95–8.05 (m, 2H). – ^{13}C NMR: δ = 16.4, 19.9, 53.0, 110.2, 119.0, 119.8, 123.4, 124.2, 124.7, 126.5, 126.8, 130.3, 132.4, 145.5, 151.8.

2-[1-(1H-Benzotriazol-1-yl)pentyl]-6-methylphenol (**27c**): The crude product was chromatographed with petroleum ether (40–60°C)/ethyl acetate (8:1). – ^{1}H NMR: δ = 0.83 (t, J = 6.9 Hz, 3H), 1.2–1.4 (m, 4H), 2.29 (s, 3H), 2.40–2.55 (m, 1H), 2.7–2.8 (m, 1H), 6.16 (dd, J = 8.8, 6.6 Hz, 1H), 6.78 (t, J = 7.6 Hz, 1H, R_3CH), 7.06 (d, J = 7.4 Hz, 1H), 7.20 (dd, J = 7.8, 1.3 Hz, 1H), 7.30 (dt, J = 7.0, 1.1 Hz, 1H), 7.39 (dt, J = 7.0, 1.1 Hz, 1H), 7.52 (s, 1H), 7.63 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H). – ^{13}C NMR: δ = 13.8, 16.3, 22.2, 28.8, 33.6, 59.1, 110.0, 119.6, 120.4, 124.1, 125.4, 126.1, 127.3, 130.9, 133.1, 145.4, 152.2.

2-(1H-Benzotriazol-1-yl)-2-(2-hydroxy-3-methylphenyl)acetic Acid (**27d**): The crude product was recrystallized from ethanol/ethyl acetate. – ^{1}H NMR ([D_6]DMSO): δ = 2.20 (s, 3H), 4.70 (broad, 1–2H), 6.87 (t, J = 7.6 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 7.18 (s, 1H, R_3CH), 7.26 (d, J = 6.7 Hz, 1H), 7.34 (t, J = 7.1 Hz, 1H), 7.42 (t, J = 7.0 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H). – ^{13}C NMR ([D_6]DMSO): δ = 16.9, 60.6, 111.2, 119.3, 119.7, 121.2, 124.0, 125.6, 127.4, 127.5, 132.0, 133.1, 145.4, 153.7, 169.9.

2-[1-(1H-Benzotriazol-1-yl)-2-hydroxy-2,2-diphenylethyl]-6-methylphenol (**27e**): The crude product was recrystallized from toluene. – ^{1}H NMR ([D_6]DMSO): δ = 1.74 (s, 3H), 3.11 (s, 1H), 6.30

(t, J = 7.6 Hz, 1H), 6.46 (s, 1H, R_3CH), 6.58 (d, J = 6.7 Hz, 1H), 6.7–7.0 (m, 18H), 7.08 (t, J = 7.1 Hz, 1H), 7.22 (s, 1H), 7.31 (d, J = 7.6 Hz, 2H), 7.50 (d, J = 8.3 Hz, 1H), 7.58 (d, J = 8.3 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 8.70 (s, 1H, OH). – ^{13}C NMR ([D$_6$]DMSO): δ = 16.8, 62.8, 81.3, 112.0, 118.7, 118.8, 123.3, 123.5, 124.5, 125.6, 126.2, 126.6, 126.7, 127.6, 127.7, 129.6, 130.5, 133.4, 144.3, 144.5, 145.7, 153.3.

2-[Bis(phenylthio)methyl]-6-methylphenol (**29**): The crude product was chromatographed with petroleum ether (40–60°C)/ethyl acetate (30:1). – ^{1}H NMR: δ = 2.21 (s, 3H), 5.72 (s, 1H), 6.47 (s, 1H), 6.64 (t, J = 7.6 Hz, 1H), 6.98 (dd, J = 7.4, 2.5 Hz, 2H), 7.16–7.21 (m, 6H), 7.34–7.38 (m, 4H). – ^{13}C NMR: δ = 15.9, 57.1, 120.0, 123.4, 125.4, 127.1, 127.9, 128.8, 130.9, 132.4, 133.6, 152.1.

General Procedure for the Displacement of the Benzotriazolyl Group by Hydride Ion: To a solution of the corresponding benzotriazole adduct (1.0 mmol) in 15 ml of THF (toluene was used as the solvent for **14b**) was added 0.12 g (2.5 mmol) of $LiAlH_4$. The resulting solution was heated under reflux for the time given in Table 5, cooled, and poured into 20 ml of ice/water. This was acidified with 2 N HCl and the mixture extracted with diethyl ether (3 × 30 ml). The combined extract was dried with $MgSO_4$, the solvent removed in vacuo and the residue chromatographed to give the pure product.

1-Benzyl-2-naphthol (**20a**): ^{1}H NMR: δ = 4.40 (s, 2H), 5.09 (s, 1H), 7.00 (d, J = 8.8 Hz, 1H), 7.1–7.2 (m, 5H), 7.28 (t, J = 6.9 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.74 (d, J = 5.1 Hz, 1H), 7.86 (d, J = 8.6 Hz, 1H). – ^{13}C NMR: δ = 30.6, 117.8, 118.1, 123.2, 123.3, 126.1, 126.6, 128.1, 128.4, 128.48, 128.51, 129.4, 133.6, 140.0, 151.1.

1-[4-(Dimethylamino)benzyl]-2-naphthol (**20b**): ^{1}H NMR: δ = 2.84 (s, 6H), 4.33 (s, 2H), 5.25 (s, 1H), 6.63 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 3.7 Hz, 1H), 7.07 (d, J = 3.7 Hz, 2H), 7.30 (dt, J = 8.0, 1.1 Hz, 1H), 7.42 (dt, J = 8.0, 1.1 Hz, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.94 (d, J = 8.5 Hz, 1H). – ^{13}C NMR: δ = 29.7, 40.9, 113.3, 118.0, 118.7, 123.0, 123.3, 126.5, 127.7, 128.2, 128.4, 128.8, 129.4, 133.6, 149.3, 151.4.

2,6-Dimethylphenol (**25c**): ^{1}H NMR: δ = 2.20 (s, 6H), 4.69 (s, 1H), 6.73 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 2H). – ^{13}C NMR: δ = 15.7, 120.2, 123.0, 128.5, 152.1.

2-Ethyl-6-methylphenol (**28c**): ^{1}H NMR: δ = 1.22 (t, J = 7.6 Hz, 3H), 2.23 (s, 3H), 2.61 (q, J = 7.6 Hz, 2H), 4.64 (broad, 1H), 6.78 (t, J = 7.3 Hz, 1H), 6.97 (t, J = 6.8 Hz, 2H). – ^{13}C NMR: δ = 14.0, 15.8, 23.0, 120.3, 123.0, 126.8, 128.4, 129.2, 151.6.

2-Methyl-6-pentylphenol (**25b**): ^{1}H NMR: δ = 0.89 (t, J = 6.9 Hz, 3H), 1.3–1.4 (m, 4H), 1.55–1.65 (m, 2H), 2.22 (s, 3H), 2.58 (t, J = 6.9 Hz, 2H), 6.76 (t, J = 7.4 Hz, 1H), 6.95 (d, J = 7.4 Hz, 2H). – ^{13}C NMR: δ = 14.0, 15.8, 22.5, 29.4, 30.0, 31.7, 120.2, 123.0, 127.7, 127.9, 128.4, 151.7.

Procedure for the Displacement of the Benzotriazolyl Group with Grignard Reagents: To a solution of the appropriate benzotriazole adduct (2 mmol) in 20 ml of THF (toluene was used as the solvent for **14b**) at room temp. (or at –78°C for **18b**) was added the corresponding Grignard reagent (12 mmol) in diethyl ether (see Table 5). The reaction mixture was stirred at room temp. (for substrates **18a,b**) or heated under reflux (for **14b**, diethyl ether was distilled off until the temp. reached the boiling point of toluene) until TLC indicated that the starting material had been consumed. The mixture was poured into 20 ml of ice/water, acidified with 2 N HCl, extracted with diethyl ether (3 × 30 ml) and the combined extract dried with $MgSO_4$. The solvent was removed in vacuo and the residue chromatographed with petroleum ether (40–60°C)/ethyl acetate (except where stated) to give the pure product.

1-(Diphenylmethyl)-2-naphthol (**20c**): ^{1}H NMR: δ = 5.18 (s, 1H), 6.41 (s, 1H), 7.05 (d, J = 8.8 Hz, 1H), 7.2–7.5 (m, 11H), 7.72 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.97 (d, J = 8.6 Hz, 1H). – ^{13}C NMR: δ = 48.6, 119.8, 120.1, 122.8, 123.2, 126.8, 127.2, 128.7, 129.0, 129.1, 129.6, 129.7, 133.4, 141.6, 152.8.

Table 5. Displacement of the benzotriazolyl group by Grignard reagents and $LiAlH_4$

Product	Substrate	Reagent	Reaction time [h]	Yield (%)	M.p. [°C]	Purification solvent[a]	Molecular formula (Mol. mass)	Calcd. / Found C	H	N
20a	**18a**	$LiAlH_4$	22	90	112–114[b]	10:1	$C_{17}H_{14}O$			
20b	**18b**	$LiAlH_4$	3	94	145–147[c]	10:1	$C_{19}H_{19}NO$			
20c	**18a**	PhMgBr	22	66	106–108[d]	10:1	$C_{23}H_{18}O$			
20d	**18a**	$PhCH_2MgBr$	3	86	oil	10:1	$C_{24}H_{20}O$		[e]	
20e	**18b**	PhMgBr	12	68	187–189	12:1	$C_{25}H_{23}NO$	84.95	6.56	3.96
							(353.5)	84.77	6.65	3.65
20f	**18b**	$PhCH_2MgBr$	2	90	118–120	10:1	$C_{26}H_{25}NO$	84.98	6.86	3.81
							(367.5)	84.95	6.90	3.68
25a	**14b**	PhMgBr	72	45	oil[f]	[g]	$C_{14}H_{14}O$		[h]	
25b	**14b**	*n*BuMgBr	24	29	oil	50:1	$C_{12}H_{18}O$	80.85	10.18	
							(178.3)	81.04	10.23	
25b	**27c**	$LiAlH_4$	48	62						
25c	**14b**	$LiAlH_4$	48	50	46–48[i]	50:1	$C_8H_{10}O$			
28a	**27b**	PhMgBr	17	80	oil[j]	20:1	$C_{15}H_{16}O$			
28b	**27b**	$PhCH_2MgBr$	12	66	oil	30:1	$C_{16}H_{18}O$		[k]	
28c	**27b**	$LiAlH_4$	48	59	oil[l]	50:1	$C_9H_{12}O$			
29	**27f**	PhS	12	77	oil	30:1	$C_{20}H_{18}OS_2$	70.97	5.36	
							(338.5)	71.02	5.38	

[a] The ratio indicates that of petroleum ether (40–60°C)/ethyl acetate which is the solvent system used for chromatography. – [b] Ref.[16] m.p. 110–111.5°C. – [c] Ref.[17] m.p. 143°C. – [d] Ref.[18] m.p. 109°C. – [e] Calcd. 324.1508, found 324.1510 (MS). – [f] Ref.[19] m.p. 52°C. – [g] The crude was chromatographed with hexane/dichloromethane (1:1). – [h] Calcd. 198.1042, found 198.1043 (MS). – [i] Ref.[20] m.p. 48–49°C. – [j] Ref.[21] b.p. 166°C/10 Torr. – [k] Calcd. 226.1344, found 226.1347 (MS). – [l] Ref.[22] b.p. 212–214°C.

1-(1,2-Diphenylethyl)-2-naphthol (**20d**): ^{1}H NMR: δ = 3.54 (dd, *J* = 13.4, 9.1 Hz, 1H), 3.76 (dd, *J* = 13.4, 6.4 Hz, 1H), 4.92 (s, 1H), 5.33 (dd, *J* = 8.7, 7.4 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 1H), 6.95–7.05 (m, 4H), 7.1–7.3 (m, 6H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.67 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H). – ^{13}C NMR: δ = 37.7, 42.5, 118.8, 122.2, 122.9, 123.2, 125.8, 126.2, 126.4, 127.6, 127.9, 128.6, 128.7, 128.8, 129.0, 129.5, 133.3, 140.3, 143.3, 151.6.

1-{α-[4-(Dimethylamino)phenyl]benzyl}-2-naphthol (**20e**): ^{1}H NMR: δ = 2.88 (s, 6H), 6.39 (s, 1H), 6.64 (d, *J* = 8.8 Hz, 2H), 7.1–7.3 (m, 11H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.90 (d, *J* = 8.6 Hz, 1H). – ^{13}C NMR: δ = 40.3, 46.7, 112.5, 119.2, 120.8, 122.3, 123.6, 125.8, 125.9, 128.1, 128.3, 128.6, 128.8, 129.1, 129.5, 133.3, 143.1, 149.0, 152.8.

1-{1-[4-(Dimethylamino)phenyl]-2-phenylethyl}-2-naphthol (**20f**): ^{1}H NMR: δ = 2.85 (s, 6H), 3.42 (dd, *J* = 13.9, 8.8 Hz, 1H), 3.70 (dd, *J* = 13.7, 6.8 Hz, 1H), 5.27 (t, *J* = 7.8 Hz, 1H), 5.36 (broad, 1H), 6.64 (d, *J* = 8.8 Hz, 2H), 6.9–7.3 (m, 10H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.67 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H). – ^{13}C NMR: δ = 37.6, 40.6, 41.2, 113.2, 119.2, 122.5, 122.7, 125.7, 126.0, 127.9, 128.3, 128.4, 128.6, 128.8, 129.3, 133.4, 140.3, 149.3, 152.0.

2-Benzyl-6-methylphenol (**25a**): ^{1}H NMR: δ = 2.19 (s, 3H), 3.96 (s, 2H), 4.60 (s, 1H), 6.75–6.82 (m, 1H), 6.95–7.05 (m, 2H), 7.1–7.3 (m, 5H). – ^{13}C NMR: δ = 15.8, 36.6, 120.4, 123.8, 126.4, 128.6, 128.7, 129.3, 129.4, 139.8, 142.5, 152.1.

2-Methyl-6-pentylphenol (**25b**) was obtained in a yield of 29% from reaction of **14b** with *n*BuMgBr and was identical in all aspects with the sample prepared earlier.

2-Methyl-6-(1-phenylethyl)phenol (**28a**): ^{1}H NMR. δ = 1.59 (d, *J* = 7.2 Hz, 3H), 2.13 (s, 3H), 4.30 (q, *J* = 7.2 Hz, 1H), 4.59 (s, 1H), 6.83 (t, *J* = 7.6 Hz, 1H), 6.98 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.1–7.3 (m, 6H). – ^{13}C NMR: δ = 15.8, 21.2, 39.0, 120.3, 124.0, 125.5, 126.4, 127.4, 128.7, 128.9, 131.3, 145.3, 151.6.

2-Methyl-6-(1-methyl-2-phenylethyl)phenol (**28b**): ^{1}H NMR: δ = 1.99 (d, *J* = 7.2 Hz, 3H), 2.17 (s, 3H), 2.71 (dd, *J* = 13.3, 8.5 Hz, 1H), 2.96 (dd, *J* = 13.3, 5.9 Hz, 1H), 3.34 (sext, *J* = 8.1 Hz, 1H), 4.52 (broad, 1H), 6.81 (t, *J* = 7.6 Hz, 1H), 6.9–7.4 (m, 7H). – ^{13}C NMR: δ = 15.9, 19.7, 34.6, 43.7, 120.4, 123.0, 124.7, 125.8, 128.1, 128.2, 129.1, 132.5, 141.0, 151.2.

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12a: 108-95-2 / **12b**: 95-48-7 / **12c**: 106-44-5 / **12d**: 88-18-6 / **12e**: 2409-55-4 / **12f**: 104-43-8 / **12g**: 135-19-3 / **12h**: 90-15-3 / **12i**: 128-39-2 / **13**: 28539-02-8 / **14a**: 132980-32-6 / **14b**: 132980-33-7 / **14c**: 132980-34-8 / **14d**: 132980-35-9 / **14e**: 132980-36-0 / **14f**: 132980-37-1 / **14g**: 28918-29-8 / **14h**: 132980-38-2 / **15**: 132980-39-3 / **18a**: 132377-90-3 / **18b**: 132980-40-6 / **18c**: 132980-41-7 / **19a**: 132980-42-8 / **19b**: 132980-43-9 / **19c**: 132980-44-0 / **21**: 133008-37-4 / **22**: 132980-45-1 / **23**: 132980-46-2 / **24**: 132980-47-3 / **25a**: 1208-45-3 / **25b**: 132980-48-4 / **25c**: 576-26-1 / **27a**: 132980-49-5 / **27b**: 132980-50-8 / **27c**: 132980-51-9 / **27d**: 132980-52-0 / **27e**: 132980-53-1 / **27f**: 132980-54-2 / **28a**: 17959-01-2 / **28b**: 132980-55-3 / **28c**: 1687-64-5 / **29**: 132980-56-4 / BtH: 95-14-7 / RhCHO: 100-52-7 / 4-$Me_2NC_6H_4CHO$: 100-10-7 / PhMgBr: 100-58-3 / $PhCH_2MgBr$: 1589-82-8 / 2-naphthol: 135-19-3 / 1,2-dimethoxyethane: 110-71-4 / MeI: 74-88-4 / *n*BuI: 542-69-8 / CO_2: 124-38-9 / Ph_2CO: 119-61-9 / Me_3SiCl: 75-77-4 / *n*-$C_6H_{13}CHO$: 111-71-7 / 1-naphthol: 90-15-5

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[66/91]