Benzotriazole-Mediated Synthesis of α-Di- and α-Trisubstituted Ethers and Sulfides

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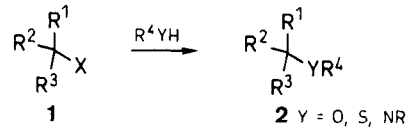
Ethylaryl- and diethylaryl(benzotriazol-1-yl)methanes, obtained by mono- or dialkylation of substituted (benzotriazol-1-ylmethyl)benzenes, react with sodium alkoxides, phenol and thiophenol to yield the corresponding α-di- and α-trisubstituted ethers and sulfides. With amines, instead of nucleophile displacement, products arising from reduction or elimination are formed.

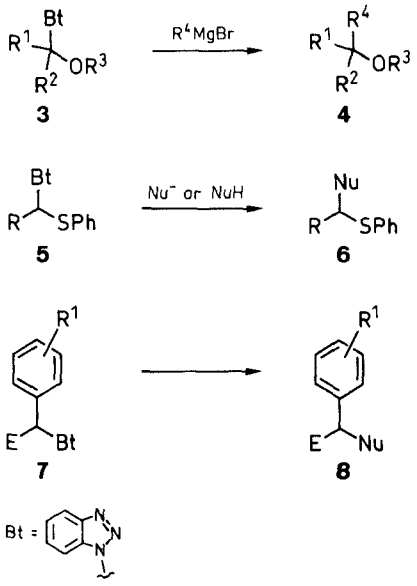
Classical methods for the synthesis of ethers, sulfides and amines generally involve formation of the respective C–O, C–S, and C–N bonds by nucleophilic substitution in compounds of type **1** (Scheme 1). For ethers (Y = O), the Williamson synthesis[1] works well for primary alkyl ethers ($R^1 = R^2 = H$); for *sec*-alkyl ethers the yields are low while *tert*-alkyl ethers cannot be prepared by this method (because of elimination). Sulfides (Y = S) can be similarly prepared by treatment of alkyl halides with salts of thiols,[2] but as above, this method fails for the *tert*-alkyl sulfides. This method is not satisfactory for primary and secondary amines since the products are themselves strong bases and attack the substrate.[3]



Scheme 1

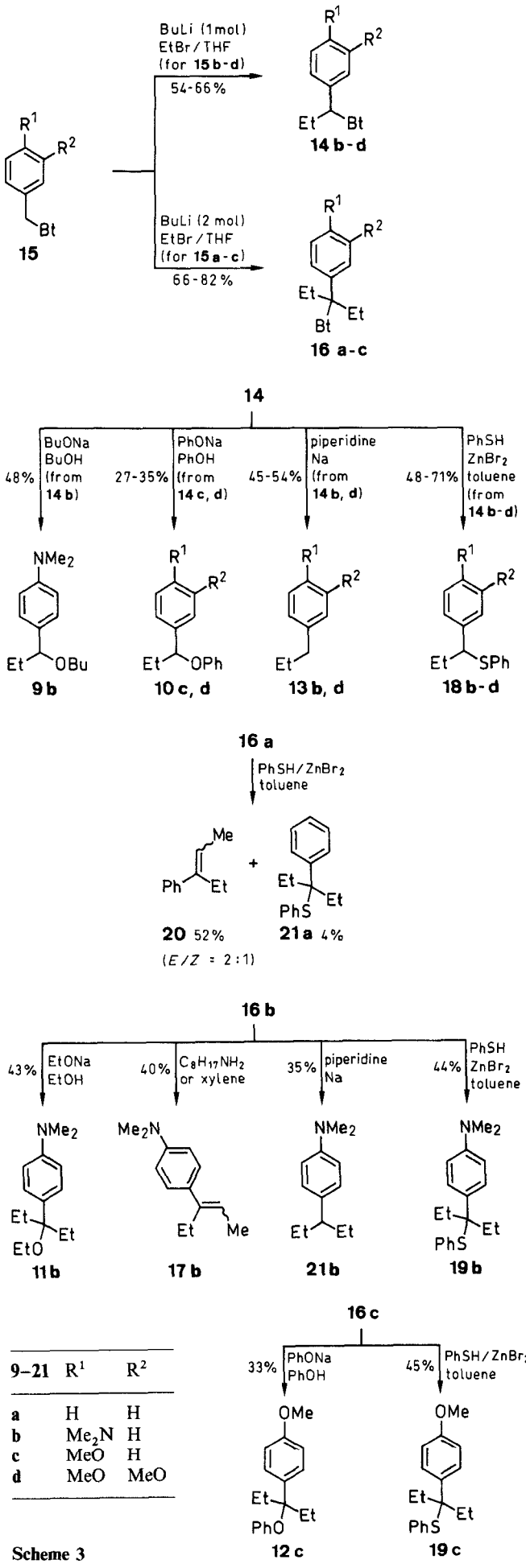
Alternative synthesis for these substituted ethers and thioethers generally involve transformations on the C-α atom in molecules where the C–O–C or C–S–C bond already exists. This approach has been exploited in our laboratory by invoking the use of benzotriazole as a synthetic auxiliary.[4] We have reported that *N*-(α-alkoxyalkyl)benzotriazoles of type **3** react with Grignard reagents with the replacement of benzotriazole to afford α-di- and α-trisubstituted ethers **4**[5,6] (Scheme 2). The starting α-benzotriazolylalkyl alkyl/aryl ethers **3** can be obtained by several routes[5–7] and thus the sequence **3** → **4** offers a versatile route for ether synthesis. Similarly, the α-(benzotriazol-1-yl)alkyl phenyl sulfides **5**,[8,9] react with Grignard reagents to give sulfides, and also with thioalkylated electron-rich aromatic compounds[10] to afford α-disubstituted phenyl sulfides **6** (Scheme 2). Derivatives of type **7** where the aryl group possesses electron-donor substituents, assist in the displacement of benzotriazole by electron-rich aromatic compounds such as anilines, pyrroles, indoles, etc. to give trisubstituted methanes **8** (Scheme 2).

The displacement of the benzotriazole group in the reactions described above is assisted by electron donation from the lone pair on an oxygen (**3**) or sulfur (**5**) atom, or from the electron-rich aromatics (**7**). We anticipated that the activation through an aromatic ring by electron-donating substituents should assist displacement of the benzotriazole group in compounds of type **7** by sodium alkoxides or by thiophenol. This in effect would enable synthesis of α-substituted and α,α-disubstituted ethers and thioethers along the lines depicted in Scheme 1, i.e. via formation of the C–O and C–S bonds rather than by the previously described methods involving modifications on the C-α atom. We now report the development of a novel approach to α-alkylaryl- and α-dialkylaryl-substituted ethers and phenyl sulfides and of trisubstituted methanes based on these considerations.



Scheme 2

Benzotriazole derivatives of type **15** (Scheme 3) were readily prepared by methods developed in our laboratory.[11–14] The methylene groups in compounds **15b–d** are relatively acidic and underwent deprotonation with butyllithium. Treatment of the anion with ethyl bromide gave the expected monoethylated derivatives **14b–d** in 54–66% yield (Table 1). The use of 2-fold excesses of butyllithium and ethyl bromide gave the diethylated compounds **16a–c** in 66–82% yield (Table 1). The structures of the products obtained were confirmed by their NMR spectra (Tables 2 and 3). The methine carbons were observed in the ^{13}C NMR spectra at δ = 64.9–65.1 for compounds **14b–d**, whereas the signals of the tertiary substituted carbon atoms in **16a–c** appear at δ = 70.8–71.1. The methine protons in the ^1H NMR spectra of compounds **14b–d** resonated at δ = 5.64–5.67 as doublets of doublets. The methylene protons of the ethyl groups both in compounds **14b–d** and **16a–c** were magnetically non-equivalent and appeared as two one-proton multiplets in the range δ = 2.40–2.77 for **14b–d** and at δ = 2.40–2.81 for **16a–c**.



9–21	R^1	R^2
a	H	H
b	Me_2N	H
c	MeO	H
d	MeO	MeO

Scheme 3

Table 1. Prepared Substituted Aryl(Benzotriazol-1-yl)methanes **14** and **16**

Product	Yield (%)	mp (°C)	Purification Solvent
14b	66	108	MeOH
14c	60	oil	10:1[b]
14d	54	oil	6:1[b]
16a	66	138	Et_2O
16b	82	103	6:1[b]
16c	81	129	10:1[b]

[a] The microanalyses or high-resolution MS data were in satisfactory agreement with the calculated values: C ± 0.22, H ± 0.30, N ± 0.29; $m/z = 0.0008$ (M^+).

[b] The ratio indicates hexane to EtOAc.

The displacement of benzotriazole from substituted products **14b–d** and **16a–c** was effected by oxygen nucleophiles such as sodium phenoxide and alkoxides, by sulfur nucleophiles, e. g. thiophenol with zinc bromide catalysis, and also by primary and secondary amines.

The treatment of the diethyl derivative **16b** with sodium ethoxide and **16c** with sodium phenoxide gave the alkoxy-substituted compounds **11b** and **12c**, respectively (Tables 4–6). Attempted isolation of **11b** from the reaction mixture led to a 3:1 mixture of **11b** and **17b**. Furthermore, **11b** was unstable and completely decomposed to **17b** within a few days. The use of sodium butoxide in boiling butanol smoothly gave the monoethyl compound **9b** by benzotriazole displacement from **14b** in 48% yield. A similar reaction of **14c,d** with sodium phenoxide in boiling phenol lead to phenoxy-substituted derivatives **10c,d**. Attempted purification of compound **10d** by column chromatography lead to decomposition of the product. The reaction mixture was characterized by GC/LRMS and from the NMR spectral data (Tables 5 and 6).

Reaction of **14b–d** with thiophenol afforded the α-disubstituted phenyl sulfides **18b–d** in 48–71% yield (Table 4). The methine proton signals in these compounds were shielded in comparison with the benzotriazole derivatives **14b–d** (cf. Tables 2 and 5). This, along with the absence of benzotriazole resonances, confirmed the displacement of the electron-withdrawing group.

The diethyl substituted compounds **16b,c** gave phenyl sulfides **19b,c** in yields (44 and 45%, respectively) lower than for the sulfides **18b,c** (48 and 56%, respectively) obtained from monoethylated compounds **14b,c** (Tables 4–6). With the diethylphenyl derivative **16a**, formation of **21a** in 4% yield was accompanied by elimination of benzotriazole to give the *E*- and *Z*-isomers of 3-phenylpent-2-ene (**20**)[15] in a 2:1 ratio (52% yield). The mixture was characterized by GC/LRMS and by the NMR spectral data. The ^1H NMR spectrum of the mixture exhibited the aliphatic signals for **21a** at $\delta = 0.75$ (t, $J = 7.5$ Hz, 6H, $2 \times \underline{CH_3}CH_2$) and 1.82–2.00 (m, 4H, $2 \times CH_3\underline{CH_2}$). The signals of the *E*-(*Z*)-isomers **20** appeared at $\delta = 0.98$ (0.94) (t, $J = 7.0$ Hz, 3H, $CH_2\underline{CH_3}$), 1.88 (1.55) (d, $J = 7.0$ Hz, 1H, CH_3), 2.52 (2.35) (q, $J = 7.0$ Hz, 2H, $\underline{CH_2}CH_3$) and 5.69 (5.49) (q, $J = 7.0$ Hz, 1H, =CH), and these chemical shifts agreed with the literature values

Table 2. ^{1}H NMR Data of Substituted Aryl(Benzotriazol-1-yl)methanes **14b–d** and **16a–c** [δ, J (Hz)]

Compound	Et	CH	R^1	R^2	Benzotriazolyl and Aromatic Protons
14b	0.94 (t, J = 7.3, 3H), 2.40–2.54 (m, 1H), 2.67–2.77 (m, 1H)	5.64 (dd, J = 8.6, 6.9)	2.9 (s, 6H)	–	6.63 (d, J = 8.8, 2H), 7.24 (d, J = 8.6, 2H), 7.24–7.40 (m, 3H), 8.03 (d, J = 8.2, 1H)
14c	0.94 (t, J = 7.3, 3H), 2.47–2.54 (m, 1H), 2.69–2.76 (m, 1H)	5.67 (dd, J = 8.7, 6.7)	3.72 (s, 3H)	–	6.83 (d, J = 8.7, 2H), 7.25–7.40 (m, 5H), 8.03 (d, J = 8.1, 1H)
14d	0.96 (t, J = 7.3, 3H), 2.40–2.60 (m, 1H), 2.65–2.75 (m, 1H)	5.66 (dd, J = 8.6, 6.8)	3.79 (s, 3H)	3.83 (s, 3H)	6.81 (d, J = 8.3, 1H), 6.85–7.00 (m, 2H), 7.25–7.45 (m, 3H), 8.05 (d, J = 7.9, 1H)
16a	0.67 (t, J = 7.5, 6H), 2.53–2.67 (m, 2H), 2.69–2.81 (m, 2H)	–	–	–	6.64 (d, J = 8.3, 1H), 7.08–7.32 (m, 7H), 8.04 (d, J = 8.3, 1H)
16b	0.66 (t, J = 7.4, 6H), 2.40–2.80 (m, 4H)	–	2.93 (s, 6H)	–	6.64 (d, J = 9.0, 2H), 6.72 (d, J = 8.4, 1H), 7.02 (d, J = 9.0, 2H), 7.07 (m, 1H), 7.2 (m, 1H), 8.02 (d, J = 8.3, 1H)
16c	0.66 (t, J = 7.5, 6H), 2.52–2.59 (m, 2H), 2.69–2.76 (m, 2H)	–	3.79 (s, 3H)	–	6.67 (d, J = 8.4, 1H), 6.84 (d, J = 9.0, 2H), 7.05–7.30 (m, 4H), 8.04 (d, J = 8.3, 1H)

Table 3. ^{13}C NMR Data of Substituted Aryl(Benzotriazol-1-yl)methanes **14b–d** and **16a–c** (δ)

Compound	Benzotriazolyl						Bt-C	Other Aliphatic Protons	Other Aromatic Protons
	C-4	C-5	C-6	C-7	C-7a	C-3a			
14b	119.8	123.6	127.8	110.2	132.6	146.2	65.1	11.3, 27.7 (C_2H_5), 40.5 [$(CH_3)_2N$]	112.2, 126.4, 126.7, 150.2
14c	119.9	123.8	127.0	110.0	132.7	146.2	64.9	11.3, 28.0 (C_2H_5), 55.2 (CH_3O)	114.1, 127.0, 131.2, 159.4
14d	119.0	123.6	126.7	109.7	132.5	145.9	64.9	11.0, 27.8 (C_2H_5), 55.6 (CH_3O)	109.6, 110.7, 119.5, 131.4, 148.6, 149.0
16a	119.8	123.4	126.5	112.2	132.2	146.8	71.1	7.64, 28.9, 29.0 (C_2H_5)	126.1, 126.2, 127.7, 128.5, 142.3
16b	119.6	123.2	127.3	111.9	132.4	146.7	70.8	7.7, 29.0 (C_2H_5), 40.2 [$(CH_3)_2N$]	112.7, 126.0, 129.6, 149.5
16c	119.8	123.4	127.7	112.4	132.3	146.8	70.7	7.7, 29.0 (C_2H_5), 55.1 (CH_3O)	113.7, 126.1, 134.4, 158.8

Table 4. Displacement of Benzotriazole in **14** and **16** by Sodium Alkoxides and by Thiophenol

Substrate	Reagent	Reaction Conditions (°C, h)	Solvent	Product	Yield (%)	mp (°C)	Eluent (hexane/EtOAc)
14b	BuONa	120, 144	BuOH	**9b**	48	oil[b]	10:1
14c	PhONa	180, 96	PhOH	**10c**	35	oil	4:1[b]
14d	PhONa	180, 96	PhOH	**10d**	27	oil	–[c]
16d	EtONa	80, 72	EtOH	**11b**	43	oil	6:1
16c	PhONa	180, 96	PhOH	**12c**	33	oil	2:1[b]
14b	PhSH	80, 24	toluene	**18b**	71	59–60	2:1[b]
14c	PhSH	80, 24	toluene	**18c**	48	41–42	20:1
14d	PhSH	40, 48	Et_2O	**18d**	56	oil	6:1
16b	PhSH	40, 24	Et_2O	**19b**	44	71	10:1
16c	PhSH	80, 48	toluene	**19c**	45	oil	6:1

[a] The microanalyses or HRMS data were in satisfactory agreement with the calculated values: C ± 0.22, H ± 0.30, N ± 0.29; m/z = 0.0008 (M^+).
[b] Hexane/Et_2O.
[c] Decomposes during purification.

for the isomeric mixture of 3-phenylpent-2-enes.[15] The overlapped signals of the phenyl protons for **20** and **21a** resonated at δ = 6.96–7.48. GC analysis showed a mixture of three major compounds in a 13:9:1 ratio, and LRMS for these components reveals M^+ peaks at 146 [(*E*- and *Z*-) **20**], 218 (PhSSPh), and $[M-1]^+$ at 255 (**21a**), respectively. Since the yield of the desired phenyl sulfide **21a** was only 4%, the compound was not isolated from the mixture. The low yields in the benzotriazole displacement in diethylated derivatives **16a–c** may have been caused by steric compression at the tertiary substituted carbon atom.

Nitrogen nucleophiles gave a different outcome. Reaction of compounds **14b,d** and **16b** with piperidine in the presence of sodium afforded the reduced products **13b,d** and **21b**, respectively in yields of 35–55%. For compounds **13b** and **13d**, the protons on the carbon atom α to the

Table 5. ^{1}H NMR Data of Ethers **9–12** and Phenyl Sulfides **18**, **19** [δ, J (Hz)]

Compound	Et	CH	R^1	R^2	Aromatic Protons	Others
9b	0.87 (t, J = 7.2, 3H), 1.54 (m, 2H)	3.99 (t, J = 6.8)	2.90 (s, 6H)	–	6.69 (d, J = 9.0, 2H), 7.14 (d, J = 9.0, 2H)	1.35 (m, 2H), 1.54 (m, 2H), 1.57–1.67 (m, 1H), 1.77–1.86 (m, 1H), 3.15–3.22 (m, 1H), 3.27–3.35 (m, 1H)
10c	0.90 (t, J = 7.3, 3H), 2.0 (m, 2H)	4.02 (t, J = 7.6)	3.73 (s, 3H)	–	6.70–7.30 (m, 9H)	–
10d	0.93 (t, J = 7.2, 3H), 1.98 (m, 2H)	4.15 (t, J = 7.8)	3.81 (s, 3H)	3.82 (s, 3H)	6.76–7.48 (m, 8H)	–
11b[a]	0.72 (t, J = 7.2, 6H), 1.80 (m, 4H)	–	2.90 (s, 6H)	–	6.69 (d, J = 9.0, 2H), 7.23 (d, J = 9.0, 2H)	1.14 (t, J = 7.0, 3H), 3.12 (q, J = 7.0, 2H)
12c	0.59 (t, J = 7.2, 6H), 2.00 (q, J = 7.2, 4H)	–	3.74 (s, 3H)	–	6.68–7.19 (m, 9H)	–
18b	0.89 (t, J = 7.3, 3H), 1.94 (m, 2H)	4.01 (dd, J = 8.8, 5.9)	2.90 (s, 6H)	–	6.63 (d, J = 8.5, 2H), 7.10–7.30 (m, 7H)	–
18c	0.89 (t, J = 7.4, 3H), 1.81–2.02 (m, 2H)	4.03 (dd, J = 8.8, 5.9)	3.74 (s, 3H)	–	6.79 (d, J = 8.8, 2H), 7.16–7.30 (m, 7H)	–
18d	0.91 (t, J = 7.3, 3H), 1.84–2.02 (m, 2H)	4.00 (dd, J = 9.0, 6.0)	3.80 (s, 3H)	3.82 (s, 3H)	6.74 (d, J = 9.0, 2H), 6.88 (m, 1H), 7.16–7.27 (m, 5H)	–
19b	0.80 (t, J = 7.2, 3H), 1.70–1.87 (m, 4H)	–	2.81 (s, 6H)		6.53 (d, J = 9.0, 2H), 6.94–7.12 (m, 7H)	–
19c	0.90 (t, J = 7.5, 6H), 1.77–1.96 (m, 4H)	–	3.74 (s, 3H)	–	6.80 (d, J = 9.0, 2H), 6.98–7.25 (m, 7H)	–

[a] Signals arising from the elimination product **17b** are not included.

Table 6. ^{13}C NMR Data of Ethers **9–12** and Phenyl Sulfides **18**, **19** (δ)

Compound	Et	CH	C	R^1	R^2	Aromatic Protons	Others
9b	10.4, 31.0	68.0	–	40.4	–	112.2, 127.4, 130.7, 149.8	13.8, 19.3, 32.0, 83.3
10c	12.6, 27.7	45.3	–	55.2	–	113.9, 115.9, 120.7, 127.2, 127.9, 129.0, 131.3, 136.2, 153.45, 157.9	–
10d	12.7, 27.9	55.8	–	45.3	45.3	109.2, 115.8, 120.2, 124.1, 127.0, 127.4, 127.7, 128.7, 137.4, 154.1	–
11b	7.5, 28.1	–	80.7	40.4	–	111.8, 127.2, 132.5, 149.0	15.6, 56.3
12c	8.3, 29.3	–	48.5	55.1	–	113.0, 114.5, 129.0, 129.1, 141.0, 141.2, 152.9, 156.8	–
18b	12.3, 29.4	54.6	–	40.6	–	112.4, 126.5, 128.5, 129.3, 131.9, 135.9, 149.6	–
18c	12.2, 29.4	55.1	–	54.5	–	113.6, 126.7, 128.5, 128.8, 132.1, 133.8, 135.3, 158.4	–
18d	12.1, 29.2	55.0	–	55.6	55.6	110.5, 111.1, 119.9, 120.6, 126.8, 128.4, 132.3, 134.2, 135.0, 147.8, 148.6	–
19b	8.5, 28.1	–	59.9	40.6	–	111.9, 127.9, 128.0, 128.2, 132.3, 132.8, 136.2, 148.8	–
19c	8.4, 27.9	–	59.5	55.0	–	112.9, 127.3, 128.0, 128.1, 128.4, 128.5, 132.4, 136.1, 136.5, 157.6	–

phenyl ring appeared as a triplet at about δ = 2.5 and integrated for two hydrogens indicating it was a methylene group which was not attached to a heteroatom. The diethyl derivative **16b** also formed the corresponding reduced product **21b** as indicated by a septet at δ = 2.2. Reaction of **16b** with pyrrolidine alone gave back the starting materials only even after refluxing for 2 days. Starting material was recovered also from the reaction mixture when **16b** was refluxed in butylamine. However, heating **16b** with octylamine yielded **17b** arising from thermal elimination of benzotriazole and no displacement by the amine. The same product was formed when **16b** was refluxed in xylene alone. Compound **17b** was characterized by elemental and spectral analysis.

Compounds **13b,d** and **21b** have been described in the literature. Although the three compounds are quite similar, they were made by diverse methods and apparently there is no general method for the synthesis of these derivatives. (4-Dimethylaminophenyl)propane **(13b)** has been prepared[16] by the Wolff–Kishner reduction of (4-dimethylaminophenyl)propan-2-one; a byproduct (ca. 9%) in the reaction of dimethylaniline *N*-oxide with diketene. The authors prove the authenticity of this product by comparing it to that obtained by an alternative synthesis involving nitration of 1-phenylpropane followed by reduction of the corresponding *p*-nitro isomer. Friedel–Crafts acylation of 1,2-dimethoxybenzene in carbon disulfide in the presence of a Lewis acid affords the corresponding 4-acyl derivatives.[17] Clemmensen reduction of the ketones afforded 4-alkyl-1,2-dimethoxybenzenes of type **13d**. The reduction occurred in moderate yields, but the low yield in the first step detracts from the method. Typically, the overall yield was < 25%. With polyphosphoric acid as a catalyst and the use of appropriate alkyl carboxylic acid, the yields of the acyl-3,4-dimethoxyphenones were much higher.[18] As above, Clemmensen reduction afforded the alkyl derivatives. The diethyl de-

rivative **21b** was obtained by the solvolysis of an *N*-ethyldibenzoacridinium cation prepared in situ from 1-ethylpropylamine and a xanthylium ion in the presence of the nucleophilic solvent *N,N*-dimethylaniline.[19] Similar nucleophilic displacements with heterocycles as leaving groups were carried out with other secondary amines and with phenol or *p*-cresol; the products (mixtures of *o*- and *p*-substituted or of *O*- and *C*-alkylation) were analyzed by GC/MS. This seemed to be a mechanistic investigation utilizing procedures of questionable synthetic value. 4-Alkenylanilines have previously been prepared by the reaction of Wittig reagents with carbonyl compounds.[20] A variety of such propenylbenzenes have been prepared with various substituents on the benzene ring. In all cases, the yields of the products were low, and *E*/*Z* mixtures were obtained. The trisubstituted alkenes of type **17b** are less common. Studies in the mesolytic cleavage of C–C bonds[21] afford **17b** from either an anion, a cation or a radical precursor depending upon the cleavage process. However, there was no characterization or data given for this compound.

In summary, displacement of benzotriazole by alkoxides, phenol and thiophenol in alkyl(dialkyl)aryl(benzotriazol-1-yl)methanes proceeded smoothly in fair yield and enabled synthesis of a wide variety of α-di- and trisubstituted ethers and phenyl sulfides via formation of the C–O and C–S bonds which are otherwise difficult to prepare. Although the reactions with amines did not effect the expected displacement, they gave products with linear or branched alkyl or alkenyl groups in useful yields and these methods appear to be those of choice for the preparation of such compounds.

Melting points were determined on a hot-stage microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR 300 spectrometer (300 and 75 MHz, respectively), using $CDCl_3$ as solvent and TMS as an internal reference. HRMS were recorded on a Kratos AEI MS 30 spectrometer. Elemental analyses were performed on a Carbo erba 1106 elemental analyzer. Commercially available reagent grade solvents were distilled from sodium/benzophenone immediately prior to use. All lithiation and benzotriazole displacement reactions were carried out under dry N_2. All glassware was dried in an oven overnight prior to use. All moisture-sensitive reagents were transferred by pre-dried syringes. Flash chromatography was run over silica gel (E. Merck 60, 230–400 mesh).

(Benzotriazol-1-yl)arylmethanes **15a–c** were prepared according to the reported procedures.[11,14,22]

(Benzotriazol-1-yl)(3,4-dimethoxyphenyl)methane (15d):
A mixture of 1-(hydroxymethyl)-1*H*-benzotriazole[23] (1.49 g, 10 mmol), 1,2-dimethoxybenzene (1.38 g, 10 mmol) and TsOH (1.90 g, 10 mmol) in toluene (30 mL) was refluxed for 24 h. The solvent was removed under reduced pressure, and sat. $NaHCO_3$ solution (50 mL) was added to the residue. The product was extracted with $CHCl_3$ (3 × 50 mL), and the combined extract was washed with H_2O and dried with ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed (hexane/EtOAc; 6:1 as eluent) to give pure microcrystals **15d**; yield: 2.02 g (74%); mp 74–75°C.

$C_{15}H_{15}N_3O_2$	calc.	C 66.90	H 5.61	N 15.60
(269.3)	found	66.81	5.58	15.88

^{1}H NMR: δ = 3.79 (s, 3H), 3.85 (s, 3H), 5.78 (s, 2H), 6.81–6.88 (m, 3H), 7.35–7.39 (m, 3H), 8.05 (d, *J* = 8.1 Hz, 1H).

^{13}C NMR: δ = 52.2, 55.8, 109.8, 110.7, 111.1, 119.8, 120,2, 124.0, 127.0, 127.4, 132.6, 149.3.

Substituted Aryl(Benzotriazol-1-yl)methanes (14b–d and 16a–c; General Procedure:
BuLi (2.5 M in hexane; 1.0 mL, 2.5 mmol for **14b–d**, or 2.0 mL, 5.0 mmol for **16a–c**) was added dropwise to a solution of the appropriate substrate **15** (2.5 mmol) in THF (80 mL) at −78°C. The mixture was stirred at −78°C for 2 h, and a solution of bromoethane (2.5 mmol for **14b–d**, or 5.0 mmol for **16a–c**) in THF (5 mL) was added slowly. The mixture was kept at −78°C for 3 h, allowed to warm to r.t. and stirred overnight. H_2O (30 mL) was added to quench the reaction, and the solution was extracted with $CHCl_3$ (3 × 15 mL). The combined $CHCl_3$ extracts were washed with H_2O and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified by recrystallization or by column chromatography. The analytical and spectroscopic data are presented in Tables 1–3.

Displacement of Benzotriazole in 14b–d and 16a–c by Alkoxides; General Procedure:
The appropriate benzotriazole compound **14b–d, 16a–c** (3 mmol) was added to a stirred solution of Na (3.3 mmol) in the appropriate alcohol (20 mL) under N_2. The mixture was refluxed for the time indicated in Table 4 followed by distillation of the alcohol under reduced pressure. H_2O (15 mL) was added, the mixture extracted with $CHCl_3$ (3 × 20 mL), the combined organic layer dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography (Tables 4–6).

Displacement of Benzotriazole in 14c,d and 16c by Phenol; General Procedure:
The appropriate benzotriazole compound **14c,d, 16c** (3 mmol) was added to a stirred warm solution of Na (3.3 mmol) in phenol (8.5 g, 90 mmol) under N_2. The mixture was refluxed for 4 d followed by distillation of phenol under reduced pressure. H_2O (25 mL) was added and the mixture was extracted with Et_2O (3 × 20 mL). The combined organic layer was washed with aq NaOH solution (5%, 2 × 20 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (Tables 4–6).

Displacement of Benzotriazole in 14b–d and 16b,c by Thiophenol; General Procedure:
To a stirred solution of the appropriate benzotriazole compound **14b–d, 16b,c** (3 mmol) in a suitable solvent (Table 3) under N_2 was added PhSH (6 mmol, 0.62 mL) and $ZnBr_2$ (3.0 M in Et_2O, 2 mL, 6 mmol). When toluene was the solvent, the Et_2O was distilled from the mixture during the reaction. The resulting mixture was heated at the temperature and for the time given in Table, cooled and aqueous NaOH solution (5%, 10 mL) was added. The aqueous layer was extracted with $CHCl_3$ (2 × 20 mL), and the combined organic layers were washed with H_2O (2 × 20 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified either by recrystallization or by column chromatography (Tables 4–6).

Reaction of Benzotriazole Derivatives 14b,d and 16b with Sodium in Piperidine; General Procedure:
The appropriate benzotriazole compound **14b,d**, or **16b** (3 mmol) was added to a stirred solution of Na (3.3 mmol) in piperidine (15 mL) under N_2. The mixture was heated overnight at 100°C followed by distillation of piperidine under reduced pressure. H_2O (25 mL) was added and the mixture was washed with Et_2O (3 × 20 mL). The combined organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The crude material was purified by column chromatography.

1-(4-N,N-Dimethylaminophenyl)propane **(13b)**: Purification by column chromatography (hexane) gave pure oil; yield: 0.22 g (45%) (Lit.[16] bp 116–118°C/13 Torr).

^{1}H NMR: δ = 0.93 (t, *J* = 7.3 Hz, 3H), 1.60 (sextet, *J* = 7.6 Hz, 2H), 2.49 (t, *J* = 8.1 Hz, 2H), 2.90 (s, 6H), 6.7 (d, *J* = 8.74, 2H), 7.1 (d, *J* = 8.74, 2H).

^{13}C NMR: δ = 13.9, 24.8, 37.0, 41.0, 113.0, 129.0, 131.1, 149.0.

1,2-Dimethoxy-4-propylbenzene **(13d)**: Purification by column chromatography ($CHCl_3$) gave pure oil; yield: 0.19 g (54%) (Lit.[17] bp 112–114 °C/4 Torr).

^{1}H NMR: δ = 0.94 (t, J = 7.3 Hz, 3 H), 1.62 (sextet, J = 7.4 Hz, 2 H), 2.53 (t, J = 7.3 Hz, 2 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 6.65–6.95 (m, 3 H).

^{13}C NMR: δ = 13.7, 24.7, 37.6, 55.7, 55.9, 111.1, 111.8, 120.2, 135.3, 147.0, 148.7.

3-(4-N,N-Dimethylaminophenyl)pentane **(21b)**: Purification by column chromatography (hexane/Et_2O, 4:1) gave pure oil; yield: 0.20 g (35%).

HRMS: m/z calculated for $C_{13}H_{21}N$ 191.1674; found 191.1673.

^{1}H NMR: δ = 0.77 (t, J = 7.2 Hz, 6 H), 1.4–1.7 (m, 4 H), 2.15–2.25 (m, 1 H), 2.89 (s, 6 H), 6.69 (d, J = 8.7 Hz, 2 H), 7.00 (d, J = 8.7 Hz, 2 H).

^{13}C NMR: δ = 12.2, 29.3, 40.8, 48.6, 112.7, 128.3, 133.9, 148.9.

3-(4-*N,N*-Dimethylaminophenyl)pent-2-ene (17b):
A stirred solution of **16b** (3.0 mmol) in octylamine (15 mL) under N_2 was refluxed for 1 d. The octylamine was removed by vacuum distillation, and 10% aq $NaHCO_3$ solution (30 mL) was added to the residue. The mixture was extracted with Et_2O (3 × 30 mL), washed with H_2O (2 × 20 mL), and the combined organic layer was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue purified by column chromatography (hexanes/EtOAc, 50:1) to give an oil; yield: 0.22 g (40%).

^{1}H NMR: δ = 0.99 (t, J = 7.6 Hz, 3 H), 1.76 (d, J = 6.8 Hz, 3 H), 2.48 (q, J = 7.5 Hz, 2 H), 2.91 (s, 6 H), 5.64 (q, J = 6.8 Hz, 1 H), 6.69 (d, J = 8.9 Hz, 2 H), 7.25 (d, J = 9.0 Hz, 2 H).

^{13}C NMR: δ = 13.3, 13.8, 22.4, 40.6, 112.4, 118.9, 126.6, 131.3, 141.7, 149.3.

(1) Feuer, H.; Hooz, J. In *Chemistry of the Ether Linkage*, Ed.; Patai, S., Interscience: New York, 1967; pp 446 and 468.
(2) Peach, M. In *The Chemistry of the Thiol Group*, Patai, S., Ed.; Wiley: New York, Part 2, p 721.
(3) Gibson, M.S. In *The Chemistry of the Amino Group*, Patai, S., Ed.; Interscience: New York, 1968, p 45.
(4) Katritzky, A.R.; Rachwal, S.; Hitchings, G.J. *Tetrahedron* **1991**, *47*, 2683.
(5) Katritzky, A.R.; Rachwal, S.; Rachwal, B. *J. Org. Chem.* **1989**, *54*, 6022.
(6) Katritzky, A.R.; Zhao, X.; Shcherbakova, I.V. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3295.
(7) Katritzky, A.R.; Rachwal, S.; Rachwal, B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 791.
(8) Katritzky, A.R.; Afridi, A.S.; Kuzmierkiewicz, W. *Helv. Chim. Acta* **1991**, *74*, 1924.
(9) Katritzky, A.R.; Afridi, A.S.; Kuzmierkiewicz, W. *Helv. Chim. Acta* **1991**, *74*, 1931.
(10) Katritzky, A.R.; Xie, L.; Afridi, A.S.; Fan, W.-Q.; Kuzmierkiewicz, W. *Synthesis* **1993**, 47.
(11) Katritzky, A.R.; Lan, X.; Lam, J.N. *Synthesis* **1990**, *341*.
(12) Katritzky, A.R.; Lan, X.; Lam, J.N. *J. Org. Chem.* **1991**, *56*, 4397.
(13) Katritzky, A.R.; Lan, X.; Lam, J.N. *Chem. Ber.* **1991**, *124*, 1809.
(14) Katritzky, A.R.; Lan, X.; Lam, J.N. *Chem. Ber.* **1991**, *124*, 1819.
(15) Uijttewaal, A.P.; Jonkers, F.L.; van der Gen, A. *J. Org. Chem.* **1979**, *44*, 3157.
(16) Taylor, G.A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 376.
(17) Kachru, C.N.; Pathak, B. *J. Indian Chem. Soc.* **1957**, *34*, 611.
(18) Horton, W.J.; Paul, E.G. *J. Am. Chem. Soc.* **1957**, *79*, 2264.
(19) Katritzky, A.R.; Lopez-Rodriguez, M.L.; Keay, J.G.; King, R.W. *J. Chem. Soc., Perkin Trans. 2* **1985**, 165.
(20) Cabiddu, S.; Maccioni, A.; Secci, M. *Ann. Chim.* **1964**, *54*, 1153; *Chem. Abstr.* **1965**, *63*, 4190.
(21) Maslak, P.; Narvaez, J.N. *Angew. Chem.* **1990**, *102*, 302; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 283.
(22) Märky, M.; Schmid, H.; Hansen, H.-J. *Helv. Chim. Acta* **1979**, *62*, 2129.
(23) Burckhalter, J.H.; Stephens, V.C.; Hall, L.A.R. *J. Am. Chem. Soc.* **1952**, *74*, 3868.