Benzotriazol-1-ylmethylammonium Salts Synthesis and Reactivity [1]

Alan R. Katritzky*, Craig V. Hughes and Stanislaw Rachwal

Department of Chemistry, University of Florida,
Gainesville, FL 32611

Received February 22, 1989

Benzotriazol-1-ylmethylamines on treatment with alkylating agents afford benzotriazol-1-ylmethylammonium salts, also available from reactions of chloromethylbenzotriazole with tertiary amines. In deuterated solvents under basic conditions the methylene protons of these salts exchange with deuterium. At elevated temperatures, an alkyl group substituent migrated from the ammonium center to the benzotriazolyl N-3. Reactions of the salts with Grignard reagents afforded various products arising from substitution of the ammonium moiety and/or from attack on the benzenoid ring.

J. Heterocyclic Chem., **26**, 1579 (1989).

Introduction.

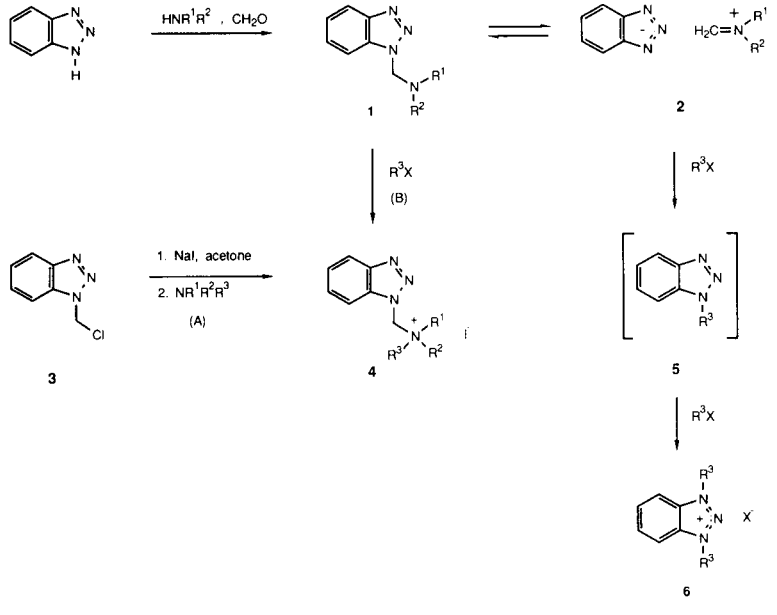
Homolytic cleavage or alkylation by activated Grignard reagents have been observed for a variety of quaternary ammonium salts [2-4]. Strong bases cause both Stevens [5-7] and Sommelet-Hauser [7-10] rearrangements of quaternary ammonium salts when none of the groups attached to the quaternary center contain β-H, whereas those which do contain β-H usually undergo Hofmann elimination [11].

N-Mannich bases have been prepared from a variety of heterocyclic [12a-16] and aliphatic [17a,17b] systems. Several heterocyclic *N*-Mannich bases have been converted into their quaternary ammonium salts by treatment with alkylating agents. In some cases, these salts exhibit potent pharmacological activity [18-20]. Two other approaches for the preparation of *N*-Mannich base quaternary salts are treatment of a tertiary amine either with an iminium salt [21a,21b] or with an α-chloromethylamine [22].

The ammonium moiety of 2-(trimethylammoniomethyl)-phthalimide iodide can be attached to diphenylphosphine or to diphenylarsine [13], or (using their alkali metal salts) to activated methylene compounds [15]. Kalcheva prepared a series of quaternary derivatives of *N*-Mannich bases from 5-chlorobenzoxazolone which upon hydrolysis with aqueous acetic acid gave the corresponding *N*-hydroxymethyl derivatives [14]. *N*-Substituted quaternary ammoniomethyl derivatives of pyrrole and indole undergo dissociation at elevated temperatures to 5-azoniafulvene cation and its benzo-annellated analog, respectively [12a,12b].

Recent work in our laboratory has shown that benzotriazole readily condenses with equimolar quantities of an aldehyde and primary amine [23a-24], secondary amine [23a,25], amide [26,27], thioamide [27,28], or sulfonamide

Scheme 1



[29] to afford analogs of *N*-Mannich bases. Further synthetic utilization of these adducts was achieved by substitutive replacement of the benzotriazolyl moiety by alkyl and aryl groups or protons (using Grignard reagents or sodium borohydride). Our present work focuses upon the synthesis of benzotriazolylmethylammonium salts and the investigation of their reactivity toward nucleophiles and anion donors.

Preparation.

Benzotriazolylmethylamines:

Secondary alkylamines were *N*-benzotriazolylmethylated by benzotriazole-formaldehyde in methanol or ether, applying a procedure developed recently in our laboratory [23a-25]. The less reactive amines, 4-*N*-methylaminopyridine and *N*-methylaniline were reacted under Dean-Stark conditions using benzene as the solvent to give 4-*N*-(benzotriazol-1'-yl)methyl-*N*-methylaminopyridine, and *N*-(benzotriazol-1'-yl)methyl-*N*-methylaniline, respectively.

Quaternization of Benzotriazol-1-ylmethylamines.

Several of the salts **4** were prepared by treatment of benzotriazol-1-ylmethylamines **1** with 1.5 equivalents of an alkylating agent in dry acetonitrile (Method A, Scheme 1). The salts precipitated from the solution and were purified by recrystallization. The choice of electrophile appeared to be limited to methyl iodide, ethyl iodide or 1-chloromethylbenzotriazole. Ethyl bromoacetate and benzyl bromide were also investigated, however they failed to give the expected benzotriazolylmethylammonium salts in either acetonitrile or when heated as a neat mixture with a benzotriazolylmethylamine. Methyl tosylate did give the corresponding salt, **4b**, with benzotriazol-1-ylmethylpyrrolidine, however it did not react with any of the other adducts.

We suspect that the reason why so many benzotriazolylmethylamine adducts failed to undergo quaternization with an electrophile is because these adducts are in equilibrium with ion-pair **2** in solution [25]. The benzotriazolyl anion can frequently compete successfully with amine **1** in the reaction with electrophiles, thus decreasing the concentration of **2** and shifting the equilibrium towards further ionization of **1**. In several cases the 1,3-dialkylbenzo-

Table 1

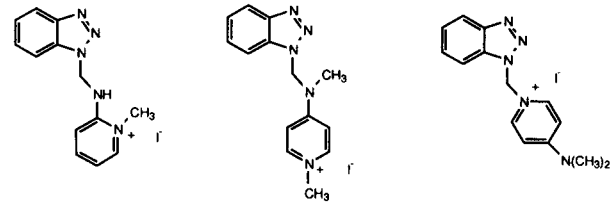
Benzotriazol-1-ylmethylammonium Salts

Compound No.	R^1	R^2	R^3	X^-	Method	% Yield	mp °C	Crystal form (recryst solv)	Elemetal Analysis found/(required) % C	% H	% N
4a	$-(CH_2)_4-$		Me	I	A:B	64:94	178-180	microcryst (MeOH)	41.60 (41.87)	4.82 (4.98)	16.2O (16.28)
4b	$-(CH_2)_4-$		Et	I	A	60	185-188	prisms (MeOH)	43.37 (43.59)	5.34 (5.35)	15.53 (15.64)
4c	$-(CH_2)_4-$		$BtCH_2$	Cl	A	53	170-172	microcryst (MeOH)	58.33 (58.45)	5.44 (5.45)	26.58 (26.51)
4d	$-CH_2CH_2OCH_2CH_2-$		Me	I	A	40	197-200	microcryst ——	39.79 (40.01)	4.72 (4.76)	15.45 (15.55)
4e	$-(CH_2)_4$		Me	TsO	A	46	170-172	prisms (MeOH)	58.59 (58.74)	6.27 (6.23)	14.32 (14.42)
4f	Me	Me	Me	I	B	79	196-198	microcryst (MeOH)	37.49 (37.75)	4.67 (4.75)	17.53 (17.61)
4g	$-(CH_2)_5-$		Me	I	B	92	207-208	needles (MeOH)	43.53 (43.59)	5.37 (5.35)	15.29 (15.64)
4h	$-CH_2CH_2-N(CH_2CH_2-)CH_2CH_2-$			I	B	86	183-187	microcryst (MeOH)	42.08 (42.06)	4.90 (4.89)	18.89 (18.87)
4i	Me	Me	Ph	I	B	34	116-120	prisms (MeOH)	47.37 (47.38)	4.51 (4.51)	14.62 (14.73)
4j	Et	Et	Et	I	B	96	177-180	prisms (EtOAc:MeOH)	42.95 (43.34)	5.90 (5.88)	15.41 (15.55)
4k	$-(CH_2)_4-$		$PhCH_2$	I	B	99	138-140	prisms (acetone)	51.53 (51.44)	5.19 (5.04)	13.07 (13.33)
4l	$-(CH_2)_4-$		$PhCH_2CH_2$	I	B	100	173-175	prisms (MeOH)	52.57 (52.94)	5.38 (5.34)	12.78 (12.90)

triazolium salts **6** precipitated from the reaction mixtures. They formed *via* 1-alkylbenzotriazole **5**, which reacted further with an excess of the alkylating agent.

Quaternization of the benzotriazolylmethylaminopyridines occurred on the *N*-atom of the pyridyl ring to afford **7-8**. This phenomenon can be explained in terms of higher basicity of the pyridylamine heterocyclic nitrogen compared to the exocyclic nitrogen [30] and is related to the fact that 4-dimethylaminopyridine undergoes protonation and methylation by methyl iodide exclusively on the heterocyclic nitrogen atom [31].

Chart 1



7 8 9

Reaction of Iodomethylbenzotriazole with Tertiary Amines.

An alternative method which was found to be more general (Method B) for preparation of **4** is the reaction of chloromethylbenzotriazole activated by sodium iodide with tertiary amines (Scheme 1). The purpose of the sodium iodide was to prepare a highly reactive intermediate, iodomethylbenzotriazole, which could react faster (because of higher polarization of the C-I bond), and form less soluble and less hygroscopic ammonium salts in comparison with analogous chlorides. 4-Dimethylaminopyridine reacts at the pyridyl *N*-atom rather than the amine nitrogen to afford 1-(benzotriazol-1'-yl)methyl-4-*N*,*N*-dimethylaminopyridinium iodide **9**. An attempt to extend this method to 1-(α-chlorobutyl)benzotriazole [32] led only to dehydrochlorination to 1-(benzotriazol-1'-yl)butene. Pyrrolidine

Table 2

^{1}H NMR Chemical Shiftes (ppm) of Quarternary Salts in DMSO-d_6

Compound No.	Benzotriazole Ring Protons 4-H	5-H [a]	6-H [a]	7-H	$BtCH_2$	Other H
4a	8.20 d, J = 8.3	7.53 J = 7.7	7.75 J = 7.7	8.20 d, J = 8.3	6.45	3.70-3.90 (m, 2H), 3.54-3.70 (m, 2H) 3.10 (s, 3H), 2.05-2.26 (m, 4H)
4b	8.19 t, J = 8.5	7.55 J = 7.7	7.78 J = 7.7	8.19 t, J = 8.5	6.45	3.55-3.85 (m, 4H), 3.32-3.50 (q, 2H, J = 7.1) 2.00-2.24 (m, 4H), 1.35-1.50 (t, 3H, J = 7.1)
4c	8.48 d, J = 8.6	7.55 J = 7.6	7.75 J = 7.6	8.22 d, J = 8.1	6.85	3.90-4.02 (m, 4H), 1.78-1.90 (m, 4H)
4d	8.22 t, J = 8.1	7.57 J = 7.7	7.79 J = 7.7	8.22 t, J = 8.1	6.50	3.90-4.15 (m, 4H), 3.72-3.90 (m, 2H) 3.45-3.62 (m, 2H), 3.29 (s, 3H)
4e	8.14-8.24 m	7.48-7.60 m [b]	7.73 J = 7.4	8.14-8.24 m	6.45	7.48-7.60 (2H [c]), 7.06-7.15 (d, 2H, J = 8.7) 3.70-3.91 (m, 2H), 3.51-3.70 (m, 2H) 3.08 (s, 3H), 2.29 (s, 3H), 2.08-2.22 (m, 4H)
4f	8.22 t, J = 8.4	7.57 J = 7.7	7.78 J = 7.7	8.22 t, J = 8.4	6.41	3.22-3.36 (br s, 9H)
4g	8.22 d, J = 8.1	7.56 J = 8.1	7.76 J = 7.8	8.22 d, J = 8.1	6.45	3.48-3.73 (m, 4H), 3.18 (s, 3H), 1.87-2.03 (m, 4H), 1.44-1.78 (m, 2H)
4h	8.14-8.27 m	7.56 J = 7.4	7.76 J = 7.4	8.14-8.27 m	6.40	3.45-3.63 (m, 6H), 2.96-3.13 (m, 6H)
4i	8.08 d, J = 8.3	7.38-7.57 m [d]	7.38-7.57 m [d]	7.87-7.95 m [d]	6.86	7.87-7.95 (1H [e]), 7.38-7.57 (4H [f] 3.90 (s, 6H)
4j	8.16-8.26 m [g]	7.56 J = 7.6	7.77 J = 7.6	8.16-8.26 m [g]	6.45	3.40-3.55 (q, 6H, J = 7.2), 1.36-1.50 (t, 9H, J = 7.2)
4k	8.22-8.34 m [g]	7.56 J = 7.7	7.76 J = 7.7	8.22-8.34 m [g]	6.50	7.74-7.88 (2H [h]), 7.50-7.68 (3H [c]), 4.90 (s, 2H), 3.60-3.90 (m, 4H), 1.85-2.20 (m, 4H)
4l	8.22 d, J = 8.3	7.57 J = 7.7	7.76 J = 7.7	8.22 d, J = 8.3	6.61	7.29-7.37 (m, 4H), 7.21-7.29 (m, 1H), 3.78-3.88 (m, 4H), 3.49-3.60 (m, 2H) 3.26-3.36 (m, 2H), 2.09-2.24 (m, 4H)

[a] Triplet unless otherwise specified. [b] Overlaps with tosylate group. [c] Overlaps with 6-H of benzotriazole. [d] Overlaps with phenyl ring. [e] Overlaps with 7-H of benzotriazole. [f] Overlaps with 5-H and 6-H of benzotriazole. [g] Overlapping doublets, J = 8.4. [h] Overlaps with 5-H of benzotriazole.

failed to add across the carbon-carbon double bond of this product.

Spectroscopy.

The spectral data of a few examples of the quaternary benzotriazol-1-ylmethylammonium salts were compared with their methyl analogs (*i.e.* where proton is substituted for benzotriazole). In general, benzotriazole has little effect on the chemical shifts of the residual atoms attached to the ammonium center. In the case of cyclic secondary amines (pyrrolidine and piperidine), the resonances arising from protons and carbons adjacent to N^+ are shifted slightly downfield, whereas the remaining ring atoms are virtually unaffected. Where bis(benzotriazol-1-yl) substitution is present (**4c**, Table 1), the β-protons and β-carbons were more shielded than in 1,1-dimethylpyrrolidinium iodide.

A larger difference in chemical shifts was observed upon comparison of the benzotriazol-1-ylmethylamines with their corresponding quaternized derivatives. The most pronounced difference occurs on the methylene group situated between benzotriazole and the ammonium nitrogen. These methylene protons are significantly deshielded with $\Delta\ \delta$ in the range of 0.7-1.1 ppm. In the carbon spectra, the largest chemical shift difference is observed for carbons directly attached to N^+. Other C-atoms in the ammonium moieties are deshielded in some cases and shielded in others with respect to the amine adducts with no particular trend discernable.

Protons on the benzotriazolyl ring resonate further downfield in the quaternary ammonium salts compared to their benzotriazol-1-ylmethylamine precursors. The difference in chemical shifts are in the range of 0.15-0.25 ppm for 4-H, 5-H and 6-H in DMSO-d_6, but the chemical shift of the 7-H differs by a greater margin (0.30-0.60 ppm). In most cases, the 4-H and 7-H of salts **4** either overlap or are superimposed in DMSO-d_6, where in the free amines these two hydrogens give distinct signals. However, a ^{1}H nmr spectrum of **4a** in deuteriochloroform gave four separate resonances for each of the benzotriazolyl protons at δ 8.42, 7.50, 7.68 and 8.09 in comparison with DMSO-d_6 (δ 8.20, 7.53, 7.75 and 8.20), for H-4, H-5, H-6 and H-7, respectively. Clearly the polarity of DMSO has a pronounced effect upon the ionizability of **4**. The ^{1}H nmr spectra of the other ammonium salts were not obtained in deuteriochloroform owing to their low solubility.

Reactivity.

Acidity - Reactivity of *N*-ylides.

Ylide-like species have been suggested as reaction intermediates in both the Stevens [5] and Sommelet-Hauser [8] rearrangements. Babayan and coworkers [33] observed under basic conditions (sodium in DMSO), that phenacylmethyltrimethylammonium iodide forms a stable, non-rearranged *N*-ylide. Treatment of this ylide with diethyl malonate, followed by excess allyl bromide gave diethyl allylmalonate, diethyl diallylmalonate, and a small quantity of alkylated ylide. The ylide derived from 1-(benzoylmeth-

Table 3

^{13}C NMR Chemical Shifts (ppm) of Quaternary Salts in DMSO-d_6

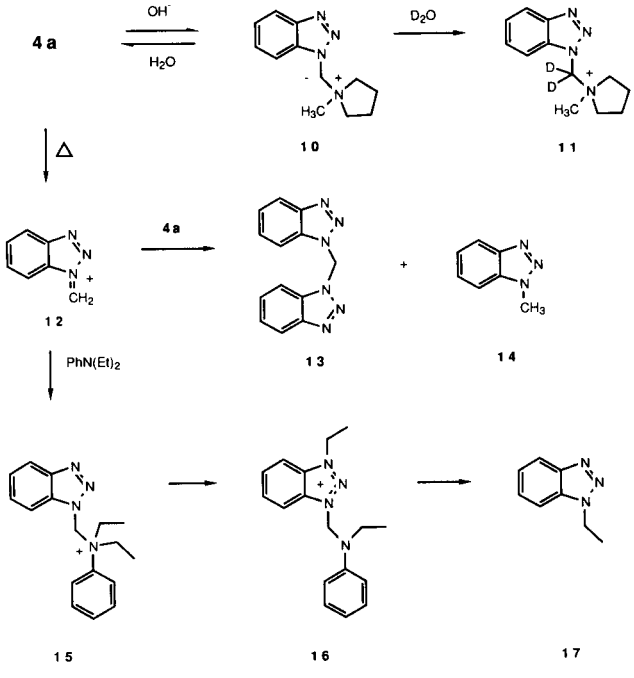
Compound No.	C-7a	C-7	C-6	C-5	C-4	C-3a	$BtCH_2$	Other
4a	133.3	109.6	128.6	124.2	119.0	144.2	68.0	61.5, 46.6, 20.4
4b	134.2	110.4	129.4	125.2	119.9	144.7	65.8	59.7, 54.2, 21.5, 8.5
4c	134.8	111.0	129.4	125.2	119.9	144.9	66.7	58.4, 21.8
4d	134.6	110.6	129.4	125.1	119.8	144.9	71.1	59.5, 57.1, 43.8
4e	134.3	110.5	129.3	125.0	119.8	144.9	68.7	145.5, 137.7, 128.0, 125.4, 61.9, 46.9, 21.0, 20.7
4f	134.5	110.7	129.3	125.1	119.8	144.9	70.6	50.6
4g	134.7	110.7	129.3	125.0	119.8	144.9	70.2	58.2, 44.5, 20.4, 19.0
4h	134.4	110.8	129.4	125.1	119.8	145.0	69.2	50.2, 44.5
4i	133.8	109.9	128.9	124.9	119.6	144.4	74.5	142.9, 130.5, 130.0, 121.9, 51.7
4j	134.4	110.6	129.3	125.1	119.9	144.7	64.7	52.1, 7.7
4k	134.7	111.5	130.5 [a]	125.7	120.2	145.3	67.4	133.2, 131.2, 129.6 [a], 126.4, 62.5, 58.6, 21.9
4l	134.2	110.4	129.5 [a]	125.3	120.0	144.8	66.2	135.9, 129.0 [a], 128.6, 127.0, 60.6, 59.2, 28.6, 21.6

[a] Interchangeable assignments.

yl)-4-(dimethylamino)pyridinium cation was reported as stable in alcohol, and to readily react with alkylating agents [34].

Salts **4** appeared to be quite stable in water; no change in their nmr spectra was observed after storage in deuterium oxide for several days. However, when the salt **4a** was treated with two equivalents of potassium hydroxide in a deuterium oxide/DMSO-d_6 mixture, the methylene protons adjacent to benzotriazole readily exchanged with deuterium to give **11** (Scheme 2) as shown by the absence of a strong singlet at δ 6.45 in the ^{1}H nmr spectrum (see Table 2). Treatment of this salt with base thus may form an intermediate *N*-ylide species **10** which could further react with an electrophile to afford an α-substituted adduct. However, when salt **4a** and 2 equivalents of potassium hydroxide were dissolved in deuterium oxide/DMSO-d_6 and 1 equivalent of electrophile added (methyl iodide, benzyl bromide, benzoyl chloride or benzaldehyde), no such reactions were found.

Scheme 2

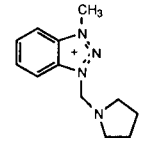


Reactions of **4a** at Elevated Temperatures.

Compound **4a** was heated at 200° in diphenyl ether under argon for 2 hours whereupon chromatography afforded bis(benzotriazol-1-yl)methane **13** and methylbenzotriazole **14**. Reaction seems to occur *via* cation **12** which attacks a molecule of benzotriazole formed by decomposition of **4** or a molecule of **4a** to give **13**. No electrophilic attack on the diphenyl ether was observed. Dissociation of salts **4** to cation **12** is required to explain all reactions with **4a**. Bis(benzotriazol-1-yl)methane **13** appeared to be the main or one of the side-products from many reactions of **4a**, especially at elevated temperatures.

1-Methylbenzotriazole **14** which was also formed by thermal decomposition of **4a** appeared to be a frequent contaminant in the reaction mixtures. It may be formed from cation **12** *via* a reductive pathway (*e.g.* with hydrogen iodide). More probable, however, seems to be the route *via* rearrangement of **4a** to a thermally more stable salt **18** which then decomposes to give **14**. Support for such a reaction mechanism was obtained from decomposition of **4a** in the presence of *N,N*-diethylaniline leading to 1-ethylbenzotriazole **17**. In this case, electrophilic attack of **12** on the aniline nitrogen afforded the ammonium cation **15** which subsequently rearranges to benzotriazolium cation **16** and undergoes further decomposition to **17** (Scheme 2).

Chart 2



The formation of bis(benzotriazol-1-yl)methane (**13**) from **4a** at elevated temperatures was observed *via* high-resolution ms. A relatively strong peak at m/z 250 was found to have composition $C_{13}H_{10}N_6$ and was assigned to **13**. Fragment ions at m/z 222 (loss of one molecule of nitrogen) and 193 (loss of two molecules of nitrogen and one proton) support this conclusion. Benzotriazole derivatives substituted at the 1-position have been shown to undergo facile loss of nitrogen in this manner [35]. Another major ion was also seen at m/z 132 which is likely to be the cationic intermediate **12** (Scheme 2).

Reactions of Benzotriazol-1-ylmethylammonium Salts with Grignard Reagents.

Salt **4a** reacted with benzylmagnesium chloride under mild conditions to give 1-phenethylbenzotriazole in a moderately good yield. This indicates that cation **12**, a possible intermediate in this reaction, may form from **4a** at relatively low temperature. Only a trace amount of methylbenzotriazole was detected by nmr spectroscopy in the crude reaction mixture indicating that rearrangement of **4a** to **14** requires higher temperatures.

Careful investigation of the reaction of **4a** with ethylmagnesium iodide revealed that the reaction with benzylmagnesium chloride was rather unique. The expected 1-propylbenzotriazole was formed in low yield in a complex product mixture. Some products were isolated, others were identified by their spectral features, and still others

remained unidentified. The crude reaction mixture obtained from **4a** with 10 equivalents of ethylmagnesium iodide in ether (45°) for 15 hours, showed by ^{1}H nmr spectroscopy three products: *n*-propylbenzotriazole (10%), methylbenzotriazole (40%), and various ring-opened ortho-phenylenediamine derivatives (50%). The propylbenzotriazole was identified by a triplet at δ 4.6 (BtCH_2) whereas methylbenzotriazole gives a distinct singlet at δ 4.2. The aryl protons of the ring-opened products resonate in the range of δ 6.5-7.0, which is further upfield than the signal due to the benzotriazole moiety.

Reaction of 10 equivalents of freshly prepared ethylmagnesium iodide with **4a** for 44 hours, gave, on column chromatography (as identified by ^{1}H, ^{13}C nmr spectroscopy and gc/ms) the unsymmetrically substituted ortho-phenylenediamines **21-23** (Scheme 3, R = Et) together with a mixture of methylbenzotriazole, ethylbenzotriazole and *n*-propylbenzotriaole. Using a Grignard reagent having and β-H may act as a reducing agent *via* β-hydride elimination.

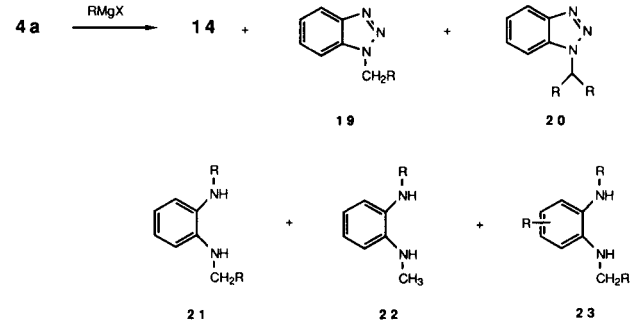
Low resolution gc/ms of **21** (R = Et) showed an M + 1 ion at 207, and a molecular ion at 206. The major fragment peaks at m/z 177 (M-C_2H_5) and 119 ($EtC_6H_3NH\cdot$)$^+$ are characteristic of *N*-alkylated phenylenediamines [36,37]. High resolution ms with molecular fragment analysis showed the molecular ion to be $C_{13}H_{22}N_2$. We can also observe fragments which can be assigned to an aryliminium species (ArN = CH_2^+). These species typically lose 14 (CH_2) or 28 (NCH_2) mass units to give aryl radical cations. After one amino group is lost, the fragmentation pattern of the resulting cation is very similar to that observed for *N*-substituted anilines. A minor impurity (M = 204) is likely due to the ortho-benzodiimine analog, which is the product of oxidation.

Further support for our suggested ring-opened product comes from the ^{13}C nmr of these components. Comparison with literature values [38] for chemical shifts of unsubstituted, *N*-substituted and *N,N'*-disubstituted phenylenediamines is in agreement with our structure. Six aryl resonances can be seen in the nmr spectrum, which may indicate an unsymmetrically *N,N'*-disubstited product, however, the presence of an ethyl group in the 4- or 5-position on the ring also destroys the symmetry of the compound.

We wished to determine if β-hydride elimination was the operative mechanism for formation of the reduced product, methylbenzotriazole. We repeated the experiment with 10 equivalents of methylmagnesium iodide, a Grignard reagent which does not contain β-H. The major products were ethylbenzotriazole and isopropylbenzotriazole, with a small amount of methylbenzotriazole. The mixture of these three compounds was characterized by nmr spectroscopy and gc/ms.

Structures of the recognized products from several Grignard reactions on **4a** are given in Scheme 3. Formation of orthophenylenediamine derivatives **21** and **22** is not unexpected after our recent finding that such products are formed upon treatment of 1-alkylbenzotriazoles with Grignard reagents [39]. Quite new and unexpected, however, is the finding that Grignard reagents can attack the benzene ring of the benzotriazole system to give **23**. The reaction seems to be similar to a nucleophilic attack of Grignard reagents on the aryl ring of nitroarenes [40] and indicates that an ammoniomethyl group at nitrogen-1 of the benzotriazole ring possess an effective electron-withdrawing effect on the benzotriazole system. Even more unexpected is formation of **20** which was identified in the reaction of **4a** with methylmagnesim iodide giving 1-isopropylbenzotriazole. This product may arise by deprotonation of 1-ethylbenzotriazole at the α-position followed by transfer of a methyl group from **4a** to give 1-isopropylbenzotriazole.

Scheme 3



EXPERIMENTAL

Melting points were determined on a Fisher hot-stage apparatus and are uncorrected. The ^{1}H and ^{13}C nmr chemical shifts were measured in ppm on the δ scale using tetramethylsilane as an internal standard. All nmr spectra were recorded on either a Varian XL-200 or Varian VXR-300 nmr spectrometer. Elemental analyses were performed in house under the supervision of Mr. M. Courtney. Gas chromatography/mass spectrometry data was obtained using a Varian 3400 gas chromatograph and Finigan-Mart Model 700 Ion Trap Detector. High resolution ms were obtained on a Kratos/AEI-MS30 mass spectrometer. Diethyl ether and tetrahydrofuran were distilled from sodium/benzophenone prior to use.

1-Benzylpyrrolidine.

1-Benzylpyrrolidine was prepared by the method of Shapiro *et al* [41] and distilled *in vacuo* to afford 54% of the product as an oil, bp 90-94°/10 mm (lit bp 111°/13 mm); ^{1}H nmr (deuteriochloroform): δ 1.75-1.85 (m, 4H), 2.45-2.55 (m, 4H), 3.60 (s, 2H), 7.20-7.35 (m, 5H); ^{13}C nmr: δ 23.4, 54.1, 60.7, 126.8, 128.2, 128.9, 139.4.

1-Phenethylpyrrolidine.

Benzylmagnesium chloride was prepared from benzyl chloride (7.6 g, 60 mmoles) and magnesium turnings (2 g, 82 mmoles) in

ether (40 ml) and heated to 45° for 3 hours. After this time, 1-(benzotriazol-1'-yl)methylpyrrolidine (6.07 g, 30 mmoles) was added and heating was continued for 10 hours. Excess Grignard reagent was quenched with saturated ammonium chloride solution and the organic and aqueous layers were separated. The aqueous layer was extracted with 4 × 25 ml of ether and the combined organic layers were washed with 40 ml of water, 40 ml of 3 *M* sodium hydroxide and 40 ml of water. The organic phase was dried over magnesium sulfate and concentrated *in vacuo* to afford 5.2 g (100%) of 1-phenethylpyrrolidine. An analytical sample was obtained by vacuum distillation, bp 101-103°/9 mm (lit bp 98-100°/10 mm [42]); ^{1}H nmr (deuteriochloroform): δ 1.76-1.86 (m, 4H), 2.56-2.62 (m, 4H), 2.63-2.74 (m, 2H), 2.77-2.94 (m, 2H), 7.15-7.40 (m, 5H); ^{13}C nmr: δ 23.4, 35.8, 54.2, 58.4, 126.0, 128.3, 128.6, 140.5.

Synthesis of Benzotriazol-1-ylmethylamines (**1**).

2-(Benzotriazol-1'-yl)methylaminopyridine:

This compound was prepared by the method previously published by our group [23a] in 71% yield after recrystallization from toluene; ^{1}H nmr (deuteriochloroform): δ 6.25-6.40 (m, 3H), 6.57 (d, 1H, J = 8.3 Hz), 6.66 (dd, 1H, J = 7.2 Hz), 7.26-7.49 (m, 3H), 7.99 (dd, 2H, J = 8.4 Hz), 8.20 (d, 1H, J = 5.0 Hz); ^{13}C nmr: δ 54.2, 108.8, 111.3, 114.9, 119.4, 123.9, 127.2, 132.8, 137.8, 146.0, 147.7, 156.2; mp 143-146° (lit mp 137-138°).

Anal. Calcd. for $C_{12}H_{11}N_5$: C, 63.99; H, 4.92; N, 31.09. Found: C, 63.74; H, 4.92; N, 31.31.

1-(Benzotriazol-1'-yl)methylpyrrolidine.

This compound was prepared by a previously reported method [25] in 95% yield after recrystallization from ether; ^{1}H nmr (deuteriochloroform): δ 1.55-1.75 (m, 4H), 2.60-2.80 (m, 4H), 5.60 (s, 2H), 7.20-8.05 (m, 4H); ^{13}C nmr: [43] δ 23.6, 23.8, 49.2, 50.0, 64.9, 72.4, 109.7, 118.0, 119.4, 123.5, 126.0, 127.1, 133.9, 143.9, 145.6; mp 75-78° (lit mp 79-81°).

Anal. Calcd. for $C_{11}H_{14}N$: C, 65.54; H, 7.02; N, 28.05. Found: C, 65.32; H, 6.98; N, 27.70.

4-(Benzotriazol-1'-yl)methylmorpholine.

This compound was prepared by the same procedure as the pyrrolidine adduct and was graciously supplied to us by our colleague, Konstantina Yannakopoulou.

N-(Benzotriazol-1-ylmethyl)-*N*-methyl-4-pyridylamine.

A mixture of benzotriazole (4.76 g, 40 mmoles), 37% formaldehyde (1.20 g, 40 mmoles), *N*-methyl-4-aminopyridine (4.32 g, 40 mmoles) and 60 ml of benzene were reacted under Dean-Stark conditions until the theoretical amount of water was observed to be removed by azeotropic distillation (10 hours). The contents were concentrated *in vacuo* and subjected to vaccum sublimation (0.8 torr/80°) to remove unreacted *N*-methyl-4-aminopyridine (mp 129-131°). The crude residue was purified by chromatography (39:1 chloroform:ethanol on silica) and the eluted fractions were concentrated. Trituration with dry acetonitrile afforded *N*-(benzotriazol-1-ylmethyl)-*N*-methyl-4-pyridylamine as colorless microcrystals (6.02 g, 63%), mp 146-149°; ^{1}H nmr (deuteriochloroform): δ 3.10 (s, 3H), 6.15 (s, 2H), 6.85 (d, 2H, J = 4.8 Hz), 7.25-7.45 (m, 3H), 8.05 (d, 1H, J = 7.8 Hz), 8.30 (d, 2H, J = 4.8 Hz); ^{13}C nmr: δ 37.1, 63.6, 107.9, 109.4, 120.2, 124.2, 128.0, 132.2, 146.2, 150.5, 152.5.

Anal. Calcd. for $C_{13}H_{13}N_5$: C, 65.26; H, 5.48; N, 29.27. Found: C, 65.24; H, 5.45; N, 29.46.

General Procedure for Quaternization of Benzotriazol-1-ylmethylamines - Method A.

Benzotriazole-Amine adducts **1** (Scheme 1) were dissolved in a minimal amount of acetonitrile with stirring at room temperature. To the solution was added 1.5 equivalents of electrophile (Table 1) and stirring was continued for 48 hours. The crude precipitate was removed by filtration, and to the filtrate was added 10 ml of ether. Stirring was continued for an additional 24 hours, and any further precipitate was isolated and combined with the initial crop. The crude product **4** was dried, recrystallized and characterized (Table 1).

2-(Benzotriazol-1'-yl)methylaminopyridinium Methiodide (**7**).

This compound was prepared by the general method described for quaternization of benzotriazol-1-ylmethylamines. Quaternization occurs on the pyridyl ring rather than the amine *N*-atom (23% from methanol:petroleum ether); ^{1}H nmr (DMSO-d_6): δ 3.95 (s, 3H), 6.50 (d, 2H, J = 6.1 Hz), 7.19 (t, 1H, J = 6.8 Hz), 7.48 (t, 1H, J = 7.7 Hz), 7.67 (t, 1H, J = 7.7 Hz), 7.87 (d, 1H, J = 8.8 Hz), 8.09 (d, 1H, J = 8.4 Hz), 8.18-8.31 (m, 2H), 8.42 (d, 1H, J = 6.0 Hz), 9.40 (t, 1H, J = 6.0 Hz); ^{13}C nmr: δ 42.6, 54.1, 111.1, 111.5, 114.7, 119.2, 124.4, 127.8, 132.2, 142.6, 143.9, 145.2, 152.4; mp 216-219°.

Anal. Calcd. for $C_{13}H_{14}IN_5$: C, 42.52; H, 3.84; N, 19.07. Found: C, 42.41; H, 3.81; N, 19.13.

4-*N*-(Benzotriazol-1'-yl)methyl-*N*-methylaminopyridinium Methiodide (**8**).

This salt was prepared *via* the method described for quaternization of benzotriazol-1-ylmethylamines where quaternization occurs on the *N*-atom of the pyridyl ring (16% from methanol:petroleum ether); ^{1}H nmr (DMSO-d_6): δ 3.32 (s, 3H), 4.02 (s, 3H), 6.70 (s, 2H), 7.44 (t, 2H, J = 7.6 Hz), 7.62 (t, 2H, J = 7.6 Hz), 8.00-8.10 (dd, 2H, J = 8.2 Hz), 8.50 (d, 2H, J = 7.5 Hz); ^{13}C nmr: δ 38.4, 44.7, 62.0, 109.1, 110.6, 119.3, 124.5, 128.2, 132.5, 143.9, 144.9, 156.0; mp 193-196°.

Anal. Calcd. for $C_{14}H_{16}IN_5$: C, 44.11; H, 4.23; N, 18.37. Found: C, 44.15; H, 4.19; N, 18.41.

1,3-Dibenzylbenzotriazolium Bromide.

Benzyl bromide (1.71 g, 10 mmoles) and 1-(benzotriazol-1'-yl)-methylpyrrolidine (1.01 g, 5 mmoles) were heated together in a sealed tube at 60° for 16 hours, and then at 80° for an additional 8 hours. The crude solid was recrystallized from 2:1 ethyl acetate:methanol to give 1.24 g (65%) 1,3-dibenzylbenzotriazolium bromide, mp 187-188°; ^{1}H nmr (DMSO-d_6): δ 6.35 (s, 4H), 7.35-7.50 (m, 6H), 7.50-7.65 (m, 4H), 7.90-8.05 (m, 2H), 8.40-8.55 (m, 2H); ^{13}C nmr: δ 54.6, 114.1, 128.7, 128.9, 129.1, 131.3, 132.5, 134.5; ms: fragment ions at m/z 300 (dibenzylbenzotriazolium), 210 (benzylbenzotriazolim) and 91 ($C_6H_5CH_2^+$).

Anal. Calcd. for $C_{20}H_{18}BrN_3$: C, 63.17; H, 4.77; N, 11.05. Found: C, 62.91; H, 5.15; N, 11.03.

Attempted Preparation of *N*-(Benzotriazol-1'-yl)methyl-*N,N*-dioctyl-*N*-methylammonium Tosylate.

1-(Benzotriazol-1'-yl)methyl-*N,N*-dioctylamine (1.86 g, 5 mmoles) and methyl tosylate (0.93 g, 5 mmoles) were heated as a neat mixture at 60° for 16 hours. The solid residue was triturated with ether and the insoluble matter (0.81 g) was filtered. Recrystallization from 1:1 ethyl acetate:ethanol gave 0.55 g of colorless prisms, mp 174-179° and >210° (mixture); ^{1}H nmr (deuteriochloroform): δ 0.88 (t, 6H), 1.10-1.34 (m, 20H), 1.50-1.70 (m, 4H),

2.05-2.18 (m, 2H), 2.32 (s, 6H), 2.70-2.84 (m, 2H), 4.61 (s, 6H), 7.11 (d, 4H, J = 8.0 Hz), 7.61 (d, 4H, J = 8.0 Hz), 7.77-7.83 (m, 2H), 8.14-8.20 (m, 2H); ^{13}C nmr: δ 14.0, 21.2, 22.6, 25.7, 26.7, 29.04, 29.11, 31.7, 38.2, 47.7, 113.8, 125.7, 128.6, 131.0, 135.4, 139.6, 142.9.

Based upon the nmr spectra we believe the product is a 1:1 mixture of 1,3-dimethylbenzotriazolium tosylate (**6**, R^3 = Me) and *N,N*-dioctylammonium tosylate. The molar ratio of protons of benzotriazolyl:tosylate:*n*-octyl is 1:2:2, and the simplicity of the splitting pattern in the aryl region of the ^{1}H nmr spectrum suggests a highly symmetrical structure. Low resolution gc/ms shows two components. The first component shows a peak at m/z 241 (dioctylamine). The second component shows major fragments at m/z 186 (methyl tosylate), 155 (p-$MeC_6H_4SO_2^+$), 133 (methylbenzotriazole), 105 (*N*-methylbenziminium) and 91 ($MeC_6H_4^+$).

General Procedure for Reaction of Iodomethylbenzotriazole with Tertiary Amines - Method B.

Chloromethylbenzotriazole was dissolved was dissolved in dry acetone with stirring at room temperature. One equivalent of sodium iodide was added and the mixture was stirred for 4 hours. Sodium chloride was removed by filtration and to the filtrate was added 1 equivalent of tertiary amine. The reaction mixture was stirred for 24-48 hours and the crude material was removed by filtration. The product **4** as recrystallized and characterized (Table 1).

1-(Benzotriazol-1'-yl)methyl-4-*N,N*-dimethylaminopyridinium Iodide (**9**).

This compound was prepared by the method described for the reaction of iodomethylbenzotriazole with tertiary amines and was obtained as prisms from methanol (75%); ^{1}H nmr (DMSO-d_6): δ 3.15 (s, 6H), 7.10 (d, 2H, J = 7.7 Hz), 7.25 (s, 2H), 7.45 (t, 1H, J = 7.1 Hz), 7.70 (t, 1H, J = 8.3 Hz), 8.10 (d, 1H, J = 8.9 Hz), 8.60 (d, 2H, J = 7.7 Hz); ^{13}C nmr: δ 30.7, 40.1, 64.6, 108.2, 110.5, 119.6, 125.0, 128.8, 132.1, 141.3, 145.2, 156.3; mp 201-203 °.

Anal. Calcd. for $C_{14}H_{16}IN_5$: C, 44.11; H, 4.23; N, 18.37. Found: C, 44.08; H, 4.19; N, 18.47.

Treatment of Quaternary Salt with Potassium Hydroxide.

The quaternary salt **4a** (0.34 g, 1 mmole) was dissolved in 1 ml of DMSO-d_6. To this solution was added 0.11 g (2 mmoles) of potassium hydroxide dissolved in a minimal amount of deuterium oxide. The mixture was stirred for 5 minuts, and 1 equivalent of electrophile (methyl iodide, benzaldehyde, benzoyl chloride or benzyl bromide) was added. The mixture was stirred at room temperature and periodically monotored by ^{1}H nmr to observe product formation. After stirring at room temperature for 72 hours, the reaction mixture (benzyl bromide) was heated at 90° for 2 hours.

Thermal Decomposition of **4a**.

A mixture of **4a** (3.40 g, 10 mmoles) and diphenyl ether was stirred at 200° under argon for 2 hours. According to ^{1}H and ^{13}C nmr, the only products present in the mixture were starting diphenyl ether, methylbenzotriazoles (characteristic resonances at δ 4.26 in ^{1}H nmr and 34.1 in ^{13}C nmr) and bis(benzotriazol-1-yl)-methane (characteristic resonances at δ 7.43 in ^{1}H nmr and 58.0 in ^{13}C nmr). Column chromatography (silica gel, methylene chloride) of the mixture allowed separation of diphenyl ether from the other two components. Trituration with ether afforded bis(benzotriazol-1-yl)methane (0.45 g, 38%) as colorless prisms, mp 191° (lit mp 192° [43]); ^{1}H nmr (deuteriochloroform): δ 7.38 (m, 1H), 7.43 (s, 2H), 7.52 (m, 1H), 7.87 (d, 1H, J = 8.3 Hz), 8.02 (d, 1H, J = 8.4 Hz); ^{13}C nmr: δ 58.0, 109.8, 120.2, 124.8, 128.7, 132.2 and 146.3. 1-Methylbenzotriazole (0.20 g, 15%) was recovered from the ether solution.

Reaction of *N*-(Benzotriazol-1-ylmethyl)-*N*-methylpyrrolidinium Iodide with *N,N*-Diethylaniline.

A mixture of salt **4a** (3.40 g, 10 mmoles) and *N,N*-diethylaniline (2.40 g, 15 mmoles) was heated together at 200° for 4 hours under an argon atmosphere. After cooling to room temperature, the reaction mixture was dissolved in chloroform (15 ml), filtered and separated by flash chromatography using silica gel (100 g) with methylene chloride as an eluent.

The first fraction appeared to be unreacted *N,N*-diethylaniline. The second fraction gave 1-ethylbenzotriazole (0.55 g, 37%) as a colorless oil; ^{1}H nmr (deuteriochloroform): δ 1.58 (3H, t, J = 7.3 Hz), 4.63 (2H, q, J = 7.3 Hz), 7.32 (1H, t, J = 8.2 Hz), 7.43 (1H, t, J = 7.8 Hz), 7.49 (1H, d, J = 8.3 Hz), 8.01 (1H, d, J = 8.3 Hz); ^{13}C nmr: δ 14.9, 43.1, 109.4, 119.7, 123.8, 127.1, 132.5 and 146.0. The product was further characterized as the picrate: orange prisms, mp 111°.

Anal. Calcd. for $C_{14}H_{12}N_6O_7$: C, 44.69; H, 3.21; N, 22.33. Found: C, 44.31; H, 3.01; N, 21.99.

The third fraction appeared to be a mixture of bis(benzotriazol-1-yl)methane and 1-methylbenzotriazole. Trituration of the mixture with ether gave pure bis(benzotriazol-1-yl)methane as colorless prisms (0.33 g, 28%); mp 191° (lit mp 192° [43]).

The ethereal filtrate was concentrated to 5 ml and upon storage at −5° for 24 hours afforded 1-methylbenzotriazole as colorless prisms (0.10 g, 8%).

Reaction of **4a** with Benzylmagnesium Chloride.

To a solution of benzylmagnesium chloride prepared from magnesium turnings (0.72 g, 30 mmoles) and benzyl chloride (2.30 ml, 20 mmoles) in ether (20 ml) was added THF (15 ml) and salt **4a**. The salt dissolved quickly and after a short time a new precipitate was observed. The resulting mixture was stirred at 45° for 3 hours under argon.

Methanol (1.0 ml) was carefully added to destroy excess Grignard reagent (exothermic reaction occurred) followed by 1.0 ml of water and 5 g of anhydrous potassium carbonate. The mixture was stirred at room temperature for 30 minutes, filtered and the solid material was washed with chloroform (2 × 30 ml). The combined filtrate and washings were concentrated to give 2.30 g of an oil which according to proton and carbon-13 nmr consisted of 1-phenethylbenzotriazole (52 mole %), bibenzyl (19 mole %), THF (22 mole %) and *N*-methylpyrrolidine (6 mole %).

Column chromatography of the mixture (silica gel, methylene chloride) afforded pure 1-phenethylbenzotriazole (1.42 g 64%) as an oil; ^{1}H nmr (deuteriochloroform): δ 3.28 (t, 2H, J = 7.4 Hz), 4.83 (t, 2H, J = 7.4 Hz), 7.05-7.38 (m, 8H), 8.03 (d, 1H, J = 8.2 Hz); ^{13}C nmr: δ 36.2, 49.6, 109.1, 119.8, 123.7, 126.9, 127.1, 127.4, 128.4, 128.6, 137.3, 141.0. The product was further characterized as its picrate, dark-orange prisms from methanol, mp 115-117°.

Anal. Calcd. for $C_{20}H_{16}N_6O_7$: C, 53.10; H, 3.56; N, 18.50. Found: C, 53.08; H, 3.53; N, 18.54.

Reaction of Quaternary Salt with Ethylmagnesium Iodide/Methylmagnesium Iodide.

The reaction vessel was charged with 2.92 g (120 mmoles) magnesium turnings and 35 ml of ether. The reaction apparatus was

purged with argon, 0.5 g (2.0 mmoles) of iodide was addd and the solution was stirred until it became colorless. Ethyl iodide (8.0 ml, 100 mmoles) was added dropwise at a rate sufficient to maintain reflux. Upon completion of addition, **4a** (3.44 g, 10 mmoles) was added in one portion and the reaction mixture was heated to reflux for 44 hours. Upon cooling the reaction mixture was slowly added to 150 ml of ice with vigorous stirring. Approximately 50 ml of chloroform was added to the mixture and stirred for 15 minutes. The *p*H of the aqueous layer was adjusted to 8 with concentrated acetic acid and the organic and aqueous phases were separated. The aqueous layer was extraced with 3 × 25 ml of chloroform and the combined organic layers were washed with 2 × 40 ml water. Drying over sodium sulfate and concentration *in vacuo* afforded the crude mixture.

Attempted purification by chromatography afforded three fractions which were analyzed by nmr spectroscopy and gc/ms. The first fraction was 85% pure with the main product being **23** (R = Et); ^{1}H nmr (deuteriochloroform): δ 0.80-1.00 (m, 7H), 1.15-1.33 (m, 6H), 1.46-1.70 (m, 3H), 3.02-3.22 (m, 3H), 6.60-6.80 (m, 3H); ^{13}C nmr: δ 10.1, 15.1, 26.4, 29.7, 39.0, 55.3, 112.15, 112.29, 118.4, 119.1, 136.8 and 137.5; ms: m/z 206 (molecular ion, $C_{13}H_{22}N_6$).

The second fraction from chromatography was comprised of 3 compounds. The first compound, *N*-methyl-*N'*-ethylorthophenylenediamine (**22**, 16%) gave a molecular ion at m/z 150 and major fragment peaks at m/z 135 (loss of CH_3) and 119 ($C_7H_7N_2$). The second (26%) and third (58%) compounds each gave molecular ions at m/z 178 and major fragment ions at m/z 149 (loss of C_2H_5) and 119 ($C_7H_7N_2$). One of these compounds is likely to be *N*-ethyl-*N'*-propylorthophenylenediamine (**21**, R = Et) and the other is isomeric with this product. The last fraction from chromatography was a mixture of 1-ethylbenzotriazole (71%, m/z 147, 119) and 1-propylbenzotriazole (29%, m/z 161).

The same procedure was used for the reaction of methylmagnesium iodide using the following quantities: methyl iodide (6.2 ml, 100 mmoles), magnesium turnings (2.92 g, 120 mmoles) and salt **4a** (3.44 g, 10 mmoles). The gc/ms of the crude product mixture indicated six compounds were present. The two major components were 1-ethylbenzotriazole (59%, m/z 147) and 1-isopropylbenzotriazole (24%, m/z 161). The ^{1}H nmr spectrum contains a quartet at δ 4.62 (CH_2, J = 7.1 Hz) and a triplet at δ 1.59 (CH_3, J = 7.1 Hz) which are characteristic of 1-ethylbenzotriazole. The isopropyl group is defined by a multiplet at δ 5.05 (CH) and two doublets at 1.68 (CH_3) and 1.18 (CH_3).

REFERENCES AND NOTES

[1] This paper is a part of our series on Chemistry of Benaotriazoles.

[2a] G. Dressaire and Y. Langlois, *Tetrahedron Letters*, **21**, 67 (1980); [b] Y. Langlois, N. Van Bac and Y. Fall, *Tetrahedron Letters*, **26**, 1009 (1985).

[3] M. S. Kharasch, G. H. Williams and W. Nudenberg, *J. Org. Chem.*, **20**, 937 (1955).

[4] H. R. Snyder, E. L. Eliel and R. E. Carnahan, *J. Am. Chem. Soc.*, **73**, 970 (1951).

[5] J. H. Brewster and M. W. Kline, *J. Am. Chem. Soc.*, **74**, 5179 (1952).

[6] S. Grethe, H. L. Lee and M. R. Uskoković, *Tetrahedron Letters*, 1937 (1969).

[7] S. H. Pine, *Org. React.*, **18**, 403 (1970).

[8] N. Shirai and Y. Sato, *J. Org. Chem.*, **53**, 194 (1988).

[9] C. R. Hauser and D. N. Van Eenam, *J. Am. Chem. Soc.*, **79**, 5512 (1957).

[10] S. W. Kantor and C. R. Hauser, *J. Am. Chem. Soc.*, **73**, 4122 (1951).

[11] A. C. Cope and E. R. Trumball, *Org. React.*, **11**, 317 (1960).

[12a] U. Burger, A. O. Bringhen, P. J. Wirthner and J.-C. Schärer, *Helv. Chim. Acta*, **68**, 2275 (1985); [b] U. Burger and A. O. Bringhen, *Tetrahedron Letters*, **29**, 4415 (1988).

[13] A. Tzschach and K. Kellner, *J. Prakt. Chem.*, **316**, 851 (1974); *Chem. Abstr.*, **82**, 16908f (1975).

[14] V. Kalcheva, *God. Soffi. Univ., Khim. Fak.*, **62**, 501 (1970); *Chem. Abstr.*, **73**, 130917x (1970).

[15] H. Hellman, I. Löschmann and F. Lingens, *Chem. Ber.*, **87**, 1690 (1954).

[16] L. Cekuoliene, *Liet. TSR Mokslu Akad. Darb., Ser. B*, 41 (1986); *Chem. Abstr.*, **107**, 198247e (1987).

[17] [a] H. Möhrle and P. Spillmann, *Tetrahedron*, **25**, 5595 (1969); [b] *ibid.*, **26**, 4895 (1970).

[18] D. Pancechowska-Ksepko, H. Foks, E. Landowska, M. Janowiec and Z. Zwolska-Kwiek, *Acta. Pol. Pharm.*, **43**, 116 (1986); *Chem. Abstr.*, **107**, 198246d (1987).

[19] N. D. Vinogradova, S. G. Kuznetsov and S. M. Chigareva, *Khim.-Farm. Zh.*, **15**, 44 (1981); *Chem. Abstr.*, **96**, 34995a (1982).

[20] D. Svikle, A. Prikule, J. Susters and I. A. Veselov, *Khim.-Farm. Zh.*, **12**, 70 (1978); *Chem. Abstr.*, **89**, 100047b (1978).

[21a] H. Böhme and M. Haake, *Chem. Ber.*, **105**, 2233 (1972); [b] H. Böhme, U. Bomke and J. P. Denis, *Arch. Pharm. (Weinheim)*, **315**, 40 (1982); *Chem. Abstr.*, **96**, 217356n (1982).

[22] H. Böhme and M. Haake, *Ann. Chem.*, **705**, 147 (1967).

[23a] A. R. Katritzky, S. Rachwal and B. Rachwal, *J. Chem. Soc., Perkin Trans. 1*, 799 (1987); [b] *ibid.*, 805 (1987).

[24] A. R. Katritzky, B. Pilarksi and L. Urogdi, *Org. Prep. Proced. Int.*, **21**, 139 (1989).

[25] A. R. Katritzky, K. Yannakopoulou, W. Kuzmierkiewicz, J. M. Aurreecoechea, G. J. Palenik, A. E. Koziol, M. Szczesniak and R. Skarjune, *J. Chem. Soc., Perkin Trans. 1*, 2673 (1987).

[26] A. R. Katritzky and M. Drewniak, *J. Chem. Soc., Perkin Trans. 1*, 2339 (1988).

[27] A. R. Katritzky, M. Drewniak and P. Lue, *J. Org. Chem.*, **53**, 5854 (1988).

[28] A. R. Katritzky and M. Drewniak, *Tetrahedron Letters*, **29**, 1755 (1988).

[29] A. R. Katritzky and C. V. Hughes, *Chem. Scripta*, **29**, 27 (1989).

[30] J. Elguero, C. Marzin, A. R. Katritzky and P. Linda, "The Tautomerism of Heterocyclic", A. R. Katritzky and A. J. Boulton, eds, Academic Press, New York, NY, 1976, p 154.

[31] G. Barbieri, R. Benassi, R. Grandi, U. M. Pagnoni and F. Taddei, *Org. Magn. Reson.*, **12**, 159 (1979).

[32] A. R. Katritzky, W. Kuzmierkiewicz, B. Rachwal, S. Rachwal and J. Thomson, *J. Chem. Soc., Perkin Trans. 1*, 811 (1987).

[33] S. T. Kocharyan, T. L. Razina, S. M. Ogandzhanyan and A. T. Babayan, *J. Org. Chem. USSR, Engl. Trans.*, **17**, 1256 (1981).

[34] S. Takimoto, Y. Kodera and H. Ohta, *Fukuoka Daigaku Rigaku Shuho*, **15**, 23 (1985); *Chem. Abstr.*, **104**, 50762m (1986).

[35] R. Lawrence and E. S. Waight, *Org. Mass Spectrom.*, **3**, 367 (1970).

[36] K. Henrick, D. L. Kepert, E. Shewchuk, K. R. Trigwell and S. B. Wild, *Aust. J. Chem.*, **27**, 727 (1974).

[37] P. Vouros and K. Biemann, *Org. Mass Spectrom.*, **2**, 375 (1969).

[38] A. Bulbarela, H. Tlahuext, H. R. Morales, L. Cuéllar, G. Uribe and R. Contreras, *Magn. Reson. Chem.*, **24**, 1093 (1986).

[39] A. R. Katritzky, S. Rachwal and B. Rachwal, *J. Org. Chem.*, in press.

[40] G. Bartoli, M. Bosco, R. Dal Pozzo and M. Petrini, *Tetrahedron*, **43**, 4221 (1987).

[41] S. L. Shapiro, H. Soloway and L. Freedman, *J. Am. Chem. Soc.*, **80**, 6060 (1958).

[42] J. H. Paden and H. Adkins, *J. Am. Chem. Soc.*, **58**, 2487 (1936).
[43] Chemical shifts for the 2-positional isomer are also given, see ref [25].
[44] J. H. Burckhalter, V. C. Stephens and L. A. R. Hall, *J. Am. Chem. Soc.*, **74**, 3868 (1952).