Study of the Orientation of Lithiation of 1- and 2-Alkylbenzotriazoles

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Lithiation of 1-isopropylbenzotriazole (**1**) and subsequent reactions with iodine, with methyl iodide, and with D_2O each gave complex mixtures of products indicating that the lithiation of **1** occurs at mainly three positions in the benzene ring. By contrast, lithiation of 2-isopropylbenzotriazole (**11**) occurs only at the α-CH of the isopropyl group. 1-Methyl- (**14**) and 1-ethylbenzotriazole (**20**) show lithiation both at the α-CH and to a lesser extent in the benzene ring. The products of the reactions are isolated or are characterized by GC/MS. Reaction mechanisms are suggested.

Introduction

1-*n*-Alkylbenzotriazoles are lithiated mainly at the CH_2 group adjacent to N, and the lithiated derivatives subsequently react normally with electrophiles.[1] 2-*n*-Alkylbenzotriazoles undergo similar reactions but can also give dimerization products probably *via* radical intermediates.[2]

We have now examined the lithiation and subsequent reactions with electrophiles of 1- (**1**) and 2-isopropylbenzotriazole (**11**), as examples of *N*-secondary-alkyl benzotriazoles. As the 1-isomer (**1**) surprisingly afforded considerable quantities of ring-substitution products, we also reexamined the reactions of 1-methyl- (**14**) and 1-ethylbenzotriazole (**20**) under the same conditions.

Results

Products isolated and/or detected by GC/MS are listed in Table 1. Table 2 gives details of the CHN and MS characterization, and Tables 3 and 4 list NMR assignments.

Reaction of Lithiated 1-Isopropylbenzotriazole (1) with Iodine. 1-Isopropylbenzotriazole (**1**) was reacted with *n*-BuLi for 8 h at −78 °C and then with an equimolar amount of iodine for 3 days. Repeated flash column chromatography on silica gel allowed separation into seven fractions listed in increasing order of polarity (cf. Scheme 1): (i) recovered 1-isopropylbenzotriazole (**1**) (40%), (ii) 4-iodo-1-isopropylbenzotriazole (**3a**) (32%), (iii) 7-iodo-1-isopropylbenzotriazole (**4a**) (8%), (iv) 5(or 6)-iodo-1-isopropylbenzotriazole (**5a**) (1%), (v) 2-(benzotriazol-1-yl)-5-*n*-propyl-6,6−dimethyl-3-isopropyl-5-iodo[2.2.2]-bicyclooctadiene (**9a**) (2%), (vi) 2-(4-iodobenzotriazol-1−yl)-5-*n*-propyl-6,6-dimethyl-3-isopropyl-5-iodo[2.2.2]-bicyclooctadiene (**9b**) (0.5%), and (vii) 2,3-bis(benzotriazol-1-yl)-2,3-dimethylbutane (**6**) (1%). The material balance was 84% based on compounds isolated. We also analyzed the crude reaction mixture by GC/MS: the values given in Table 1 are calculated assuming all response factors are equal and are in reasonable agreement with the isolated yields.

Two of the products, **3a** and **4a**, were indicated by CHN analysis to be monoiodo derivatives of 1-isopropylbenzotriazole. The precise structures of the isomers **3a** and **4a** are defined unambiguously by their ^1H and ^{13}C NMR spectra (Figure 1 and Tables 3 and 4). Their proton spectra show three adjacent aromatic protons, giving rise to the d-t-d coupling pattern with all coupling constants (7.8 Hz) typical for *ortho*-coupling. This suggests one isomer contains the iodo substituent at the 4- and the other at the 7-position. When the two methyl moieties of the isopropyl group are irradiated, **3a** shows a positive NOE on the doublet at 7.57 ppm, while no positive NOE was found for **4a**, indicating that position 7 in the benzotriazole ring is occupied by a hydrogen atom in **3a**, while in **4a** it must be occupied by an iodine atom. Direct proton−carbon coupling was demonstrated by a HETCOR experiment. The *meta*-relationship between the hydrogen atoms presenting a t coupling pattern and the quaternary carbons was evidenced by INAPT experiments. In 1-substituted benzotriazoles, the carbon atoms present characteristic chemical shifts.[3] As shown in Figure 1, the t proton (7.20 ppm) in **3a** is *meta* to the carbons at 131.4 ppm (a δ value characteristic for position 7a of a 1−substituted benzotriazole) and 85.3 ppm; hence, it is in position 6. The t proton (7.08 ppm) in **4a** is *meta* to the carbons at 146.6 ppm (a δ value characteristic for position 3a) and 71.2 ppm and is therefore in position 5. Furthermore, **3a** shows a signal at 109.7 ppm, typical for a CH in position 7, while no signal near 120 ppm, usual for a CH in position 4, is found. The signal expected for a CH in position 4 (120.3 ppm) is present in **4a**, while the signal for a CH in position 7 is missing. The strong shielding effect of the iodine atom on the direct bound quaternary carbon (30−35 ppm) and the deshielding effect on the CH in the *ortho* position (ca. 10 ppm) are also noticeable.

Compound **5a** could not be isolated pure in sufficient quantity to run NMR experiments but was tentatively assigned as 5- or 6-iodo-1-isopropylbenzotriazole on the basis of its HRMS and the ^1H and ^{13}C NMR spectra of its mixture with **3a** and **4a** that showed only isopropyl signals in the aliphatic region.

The structure assigned to compound **9a** was suggested by NMR experiments. Direct proton−carbon couplings were demonstrated by HETCOR. Assignments of the chemical shifts are given in Figure 2. A COSY experiment revealed the proton−proton couplings in the isopropyl group, the couplings of the methyl triplet at 0.80

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[1] Katritzky, A. R.; Wu, J.; Kuzmierkiewicz, W.; Rachwal, S. *Liebigs Ann. Chem.* **1994**, 1.

[2] Katritzky, A. R.; Wu, J.; Kuzmierkiewicz, W.; Rachwal, S.; Balasubramanian, M.; Steel, J. P. *Liebigs Ann. Chem.* **1994**, 7.

[3] Katritzky, A. R.; Ghiviriga, I.; Cundy, D.; Steel, P. J. *Heterocycles* **1994**, *38*, 1041.

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Table 1. Isolated Yields of the Products of the Reactions of Lithiated Alkylbenzotriazoles (SM) with Electrophiles (E)

				product and isolated yield[b] (%)						recovered	
SM	E	prep proc[a]	overall yield (%)	1-subst.	4-subst.	5(6)-subst.	7-subst.	dimers	others	BtH	Alk-Bt
1	I_2	A	84 (99)		**3a** 32, (38)	**5a**, 1 (2)	**4a**, 8 (10)	**6**, 1 (1)	**9a**, 2 (5) **9b**, 0.5 (1)	(1)	40 (42)
	MeI	B	(100)	**2b**,[c] (2)	**3b** (32)	**5b** (3)	**4b** (8)	**6** (1)	**9a**, 1 (1) **10**, 5 (13)		(40)
	D_2O	C	(98)		**3c**	**5c** (25)[d]	**4c**	**8** (2) **7** (1)			(70)
11	I_2	A	84 (96)					**12**, 74 (78)	**13a** (4)		10 (14)
	MeI	B	75 (100)					**12**, 35 (40)	**13b** (13)		40 (47)
	D_2O	C	45 (97)					**12** 45 (54)	**13c** (20)		(23)
14	I_2	A	63 (94)		**17a** (6)	**19a** (5)	**18a** (3)	**16**, 8 (12)		20 (27)	35 (41)
	MeI	B	88	**15b**, 80[e]							8
	D_2O	C	(93)		**17c**	**19c** (25)[d]	**18c**	**16** (15)			(53)
20	I_2	A	61 (96)		**23a** (4)	**25a** (13)	**24a** (2)	**22**, 46 (54)			15 (23)
	MeI	B	76	**21b**, 15[e]							61
	D_2O	C	(90)		**23c**	**25c** (10)[d]	**24c**	**22** (16)		(3)	(61)

[a] Defined in Experimental section. [b] The percentage of the compound in the reaction mixture, as measured by GC, is given in parentheses. [c] Lit.[9] [d] Overall yield of 4-, 5(6)- , and 7-deuterated compounds. [e] Lit.[1]

Table 2. Melting Points and CHN and/or MS of the Products of the Reactions of Lithiated Alkylbenzotriazoles with Electrophiles (E_nX)

compd	E_nX	prep proc	mol formula	yield (%)	mp (°C)	Anal. Calcd (Found)
1			$C_9H_{11}N_3$	35	oil[a]	
3a	I_2	A	$C_9H_{10}IN_3$	32	oil	C, 37.65 (37.78); H, 3.51 (3.60); N, 14.64 (14.37)
4a	I_2	A	$C_9H_{10}IN_3$	8	oil	M^+-1: 286.994 (286.999)[b]
5a	I_2	A	$C_9H_{10}IN_3$	1	oil	M^+: 287.999 (287.999)[c]
9a	I_2	A	$C_{18}H_{30}IN_3$	2	320–334	
9b	I_2	A	$C_{18}H_{29}I_2N_3$	0.5	324–326	
10	MeI	B	$C_{16}H_{27}N_3$	5	286–290	
11			$C_9H_{11}N_3$	34	oil[a]	
12	I_2 MeI D_2O	A B C	$C_{18}H_{20}N_6$	74 35 45	212	C 67.48 (67.67); H 6.29(6.28); N 26.23 (26.39)
14			$C_7H_7N_3$	52	65[d]	
16	I_2	A	$C_{14}H_{12}N_6$	8	162[e]	
20			$C_8H_9N_3$	35	oil[f]	
22	I_2	A	$C_{16}H_{16}N_6$	46	114–115	$M^+ - 1$: 292.142 (292.144)[b]

[a] Oil (lit.[6]). [b] Mass weight calculated by the EI + VE + LMR method. [c] Mass weight calculated by the POS FAB MAGIC method. [d] Lit.[7] mp 65 °C. [e] Lit.[8] mp 162 °C. [f] Oil (lit.[7]).

Table 3. ^1H NMR Assignments of Alkylbenzotriazoles[a]

	position in alkyl chain						position in benzotriazole ring											
	α			β			4			5			6			7		
compd	δ	*m*	*J*	δ	*m*	*J*	δ	*m*	*J*	δ	*m*	*J*	δ	*m*	*J*	δ	*m*	*J*
1	5.08	h	6.1	1.72	d	6.1	8.05	d	6.8	7.32	t	6.8	7.45	t	6.8	7.55	d	6.8
3a	5.06	h	5.9	1.72	d	5.9				7.76	d	7.8	7.20	t	7.8	7.57	d	7.8
4a	5.87	h	5.9	1.76	d	5.9	8.06	d	7.8	7.08	t	7.8	7.93	d	7.8			
11	5.12	h	6.1	1.72	d	6.1	7.87	m		7.35	m		7.35	m		7.87	m	
12				1.95	s		7.77	m		7.34	m		7.34	m		7.77	m	
14	4.33	s					8.00	d	7.5	7.33	t	7.5	7.44	t	7.5	7.47	d	7.5
16	5.24	s					7.16	m		7.16	m		7.16	m		7.16	m	
20	4.68	q	6.9	1.61	t	6.9	8.04	d	6.9	7.34	t	6.9	7.45	t	6.9	7.53	d	6.9

[a] δ (ppm); *J* (Hz); *m* = multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, h = septet, m = multiplet.

ppm with the protons at 1.19 and 1.20 ppm, and the vicinal and allylic couplings around the CH=CH double bond. Irradiation of the signal at 5.68 ppm in a NOEDIF experiment produced a positive NOE at 3.42 ppm; this allowed assignment of the protons in the CHCH=CHCH fragment as 3.42, 5.68 , 4.97, 4.45 ppm, respectively. The proton–carbon long-range couplings for **9a**, evidenced by INAPT experiments, provided further structural information. Transfer of polarization from the proton at 5.68 ppm to carbons at 32.1, 42.9, and 132.7 ppm enabled assignment of the cyclohexadiene pattern. The position of the quaternary carbon at 66.6 ppm was assigned on the basis of its signal in the INAPT spectra, when the protons at 4.45, 4.97, 3.42, 2.32, and 1.77 ppm were irradiated. The polarization transfer from the protons at 2.32 and 1.77 ppm to the carbon at 42.9 ppm proved that these methyl groups are bonded to the carbon at 66.6 ppm. The other quaternary aliphatic carbon (26.1 ppm) was assigned to the two-carbon bridge on the basis of polarization transfer from the proton at 3.42 ppm. The strong deshielding of the 26.1 ppm signal (ca. 40 ppm) suggested that it is bonded to an iodine atom. The isopropyl group must be bonded to the carbon atom at

Table 4. ^{13}C NMR Assignments in Alkylbenzotriazoles

	position in alkyl		position in benzotriazole					
compd	α	β	3a	4	5	6	7	7a
1	51.2	21.8	145.8	119.6	123.4	126.5	109.4	131.7
3a	52.1	22.0	147.4	85.3	133.1	127.9	109.7	131.4
4a	51.1	23.1	146.6	120.3	125.3	138.7	71.2	133.0
11	58.6	22.4	143.6	117.7	125.7	125.7	117.7	143.6
12	72.1	24.4	143.6	118.2	126.1	126.1	118.2	143.6
14	34.1		145.8	119.6	123.8	127.2	109.2	133.4
16	47.5	47.5	143.5	118.1	126.1	126.1	118.4	143.8
20	43.1	14.8	146.0	119.8	123.6	127.0	109.2	132.5

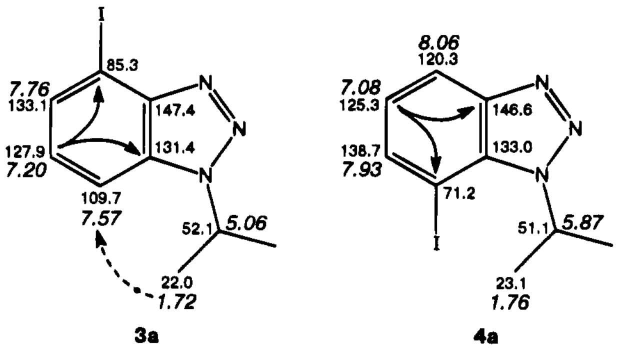
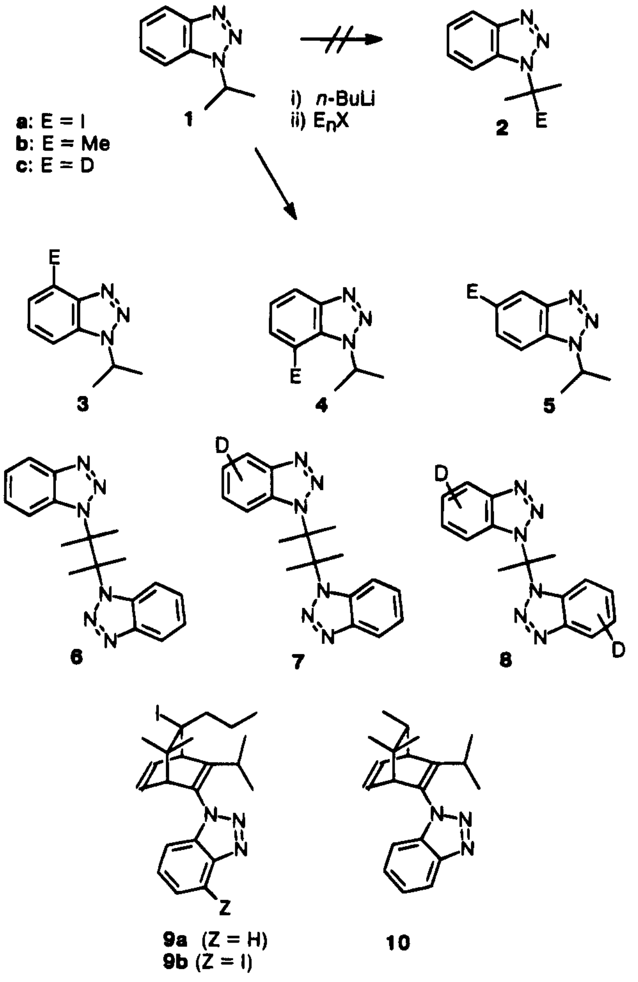


Figure 1. Structures of **3a** and **4a** as evidenced by NMR: hashed arrow, NOE effects; ↷, transfer of polarization from ^{1}H to ^{13}C in INAPT.

Scheme 1



132.7 ppm, because this carbon showed a signal in the INAPT spectrum when the proton at 1.67 ppm was irradiated. The chemical shifts of the remaining aliphatic signals (one methyl and two methylene groups), for which one substitution position remained, were assigned to an *n*-propyl group, bonded to the carbon at 26.1 ppm, on the basis of the polarization transfer from the proton at 3.42 ppm to the carbon at 33.0 ppm. The chemical shifts of the remaining aromatic signals were consistent with a benzotriazol-1-yl group that was attached to the carbon with a chemical shift of 140.2 ppm. The positions of the two methyl groups at 1.77 and 2.32 ppm were assigned on the basis of NOEDIF experiments: when the signal at 1.77 ppm was irradiated, a positive NOE at 4.97 ppm occurred, and a positive NOE from 2.32 to 7.71 ppm was also observed.

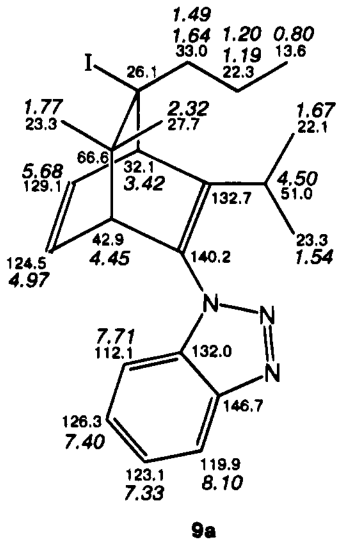
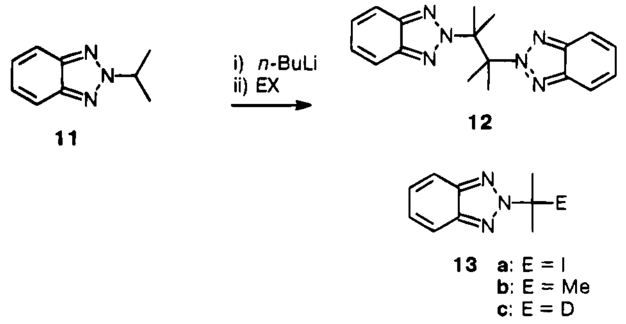


Figure 2. ^{1}H and ^{13}C NMR chemical shift assignments of compound **9a**.

Scheme 2



The proton spectrum of **9b** was similar to that of **9a**, except that the benzotriazole moiety showed three signals (7.75 d, 7.64 d, and 7.12 t). The chemical shifts and multiplicity of these signals were similar to those of 4-iodo-1-isopropylbenzotriazole (**3a**). Hence, **9b** was assigned the structure presented in Scheme 1. Compounds **9a** and **9b** were not obtained in sufficient quantity for elemental analysis and did not show molecular ions in the HRMS spectra, which is not unusual for highly polar structures, e.g., **15a**.[4]

The dimer **6** was characterized by GC/MS and its structure assigned from the molecular ion (M^+ = 320) and fragmentation pattern showing an M/2 ion with 93% relative intensity.

Reaction of Lithiated 2-Isopropylbenzotriazole (11) with Iodine. Lithiation of 2-isopropylbenzotriazole (**11**) and reaction with an equimolar amount of iodine gave, as a single isolated product, dimer **12** (74%) (Scheme 2), which was characterized by CHN analysis and ^{1}H and ^{13}C NMR spectroscopy (Tables 2–4). The proton spectrum of dimer **12** shows the characteristic phenylene pattern of the benzotriazol-2-yl ring: signals at 7.77 (m, 4H) and 7.34 (m, 4H) ppm and a singlet for the methyl groups at 1.95 ppm (12H). The carbon spectrum shows signals for the benzotriazol-2-yl ring (118.2, 126.1, and 143.6 ppm) and signals for methyl (24.4

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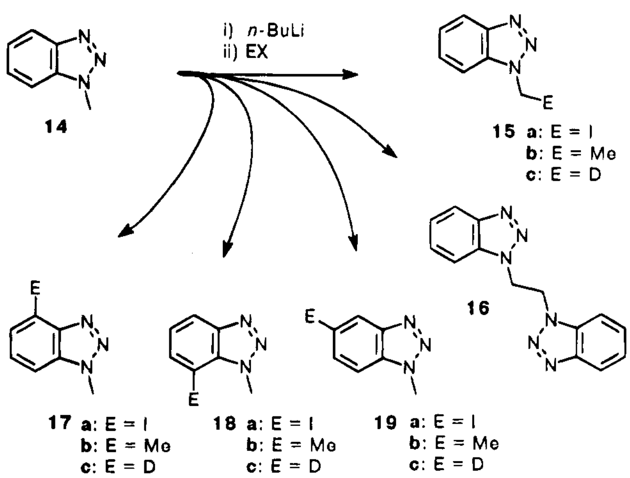
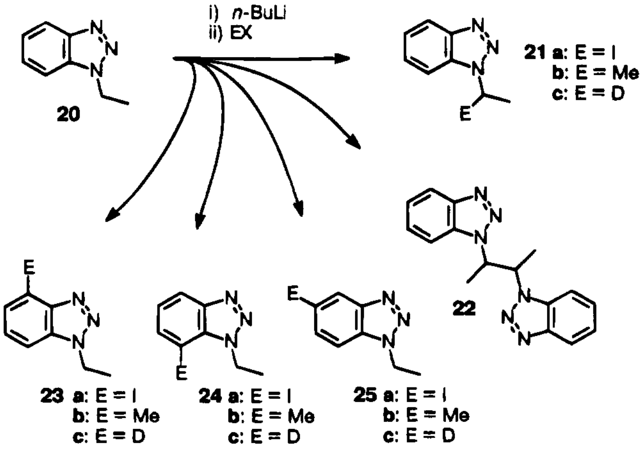
(4) Katritzky, A. R.; Wu, J.; Wrobel, L.; Rachwal, S.; Steel, J. P. *Acta Chem. Scand.* **1993**, *47*, 167.

Scheme 3



Scheme 4



ppm) and quaternary carbons (72.1 ppm), as demonstrated by an APT experiment.

Reaction of Lithiated 1-Methylbenzotriazole (14) and 1-Ethylbenzotriazole (20) with Iodine. Reaction of 1-methylbenzotriazole (**14**) with *n*-butyllithium and subsequently with iodine gave a complex mixture (Table 1), (Scheme 3). Separation by chromatography gave the known[2] dimer **16** (8%), benzotriazole (20%), recovered **14** (35%), and a mixture of iodination products **17a**, **18a**, and **19a** (14%). The mixture of **17a**, **18a**, and **19a** was analyzed by GC/MS, and the structures were assigned on the basis of the fragmentation patterns, as discussed later.

Similar treatment of 1-ethylbenzotriazole (**20**) gave a similar mixture, as shown in Table 1 and Scheme 4); the major compound is the novel dimer **22** (46%). Dimer **22** was characterized by HRMS and its fragmentation pattern (M/2 = 146 (80% relative intensity)).

Reaction of Lithiated 1-Isopropylbenzotriazole (1) with Methyl Iodide. When 1-isopropylbenzotriazole (**1**) was lithiated and then reacted with methyl iodide, a complex reaction mixture was again obtained. As shown in Table 1, GC/MS analysis of this reaction mixture indicated products similar to those obtained in the reaction of **1** with iodine. The composition of the crude product, listed in order of increasing polarity, was shown by GC/MS analysis to be: (i) recovered 1-isopropylbenzotriazole (**1**) (40%), (ii) 4-methyl-1-isopropylbenzotriazole (**3b**) (32%), (iii) 7-methyl-1-isopropylbenzotriazole (**4b**) (8%), (iv) 5(or 6)-methyl-1-isopropylbenzotriazole (**5b**) (3%), (v) 1-*tert*-butylbenzotriazole (**2b**) (2%), (vi) 2-(benzotriazol-1-yl)-5-*n*-butyl-6,6-dimethyl-3-isopropyl-5-iodo-[2.2.2]bicyclooctadiene (**9a**) (1%), (vii) 2-(benzotriazol-1-yl)-3-isopropyl-5,6,6-trimethyl[2.2.2]bicyclooctadiene (**10**) (13%), and (viii) 2,3-bis(benzotriazol-1-yl)-2,3-dimethylbutane (**6**) (1%).

Assignments of the structures of the methylated products were made by comparison of their retention time and relative intensity in the GC trace with those of the similar iodinated compounds **3a-5a** and 1−*tert*-butylbenzotriazole (**2b**), as discussed later.

Products **6** and **9a** were identical to those obtained in the reaction with iodine, as evidenced by their GC/MS behavior.

Compound **10** was isolated as described in the Experimental Section. The structure of product **10** has not been elucidated unambiguously because it could not be isolated pure in sufficient amount. However, the proton spectrum suggests that **10** is 2(benzotriazol-1-yl)-3-isopropyl-5,6,6-trimethyl[2.2.2]bicyclooctadiene. The signals at 5.27 (ddd, 1H), 5.19 (ddd, 1H), 4.36 (m, 1H), and 3.35 ppm (m, 1H) indicate that **10** has the bicyclooctadiene skeleton of **9a**. Two methyl signals (3H, s) are found at 2.26 and 1.92 ppm. The signals at 8.05 (d, 1H), 7.50 (d, 1H), and 7.35−7.45 ppm (m, 2H) are assigned to a benzotriazol-1-yl nucleus. The signal at 1.60 ppm (t, 6H) is assigned to two overlapping doublets of an isopropyl group in the proximity of a chiral moiety, rather than to methyl groups in alkyl chains, due to the absence of other aliphatic multiplets. The triplet at ca. 0.80 ppm in the propyl chain of **9a** is also missing. The doublet at 0.89 ppm (3H) is assigned to a methyl group vicinal to a single hydrogen, which corresponds to position 5 of the bicyclooctadiene skeleton. The shift to lower field of the signals at 1.92, 5.72, and 5.19 ppm and to higher field of the signal at 2.26 ppm, compared with the corresponding signals in **9a**, suggest that the methyl group in position 5 of **10** occupies the same region in space as the iodine atom in **9a**.

Reaction of Lithiated 2-Isopropylbenzotriazole (11) with Methyl Iodide. Lithiation of 2-isopropylbenzotriazole (**11**) and reaction with an equimolar amount of methyl iodide gave dimer **12** (40% by GC, isolated 35%) and 2-*tert*-butylbenzotriazole (**13b**). The structures of these compounds were proven by comparison of their GC/MS behavior with that of standard compounds.

Reactions of Lithiated (Benzotriazol-1-yl)alkanes 1, 14, and 20 and (Benzotriazol-2-yl)alkanes 11 with Deuterium Oxide. Product mixtures derived from lithiated (benzotriazol-1-yl) and (benzotriazol-2-yl)alkanes and deuterium oxide were analyzed by GC/MS.

The products from 1-isopropylbenzotriazole (**1**) were resolved by GC into four peaks, in increasing order of polarity: (i) ring-substituted monodeutero-1−isopropylbenzotriazoles **3c-5c** (25%), (ii) compound of $M^+ = 278$, $C_{15}H_{12}N_6D_2$, which may have a structure of type **8** (2%), (iii) compound of $M^+ = 320$ which might be represented by the monodeuterated dimer **7** (1%), and (iv) recovered **1**, without any deuterium incorporation (70%).

The structure of **7** as monodeuterated **6** is also supported by the fact that these compounds have similar GC retention times. Incorporation of one deuterium atom into one benzotriazole nucleus in **3c**, **4c**, **5c**, and **7** and two atoms in **8** (into different benzotriazole nuclei) was evidenced by simulation of their mass spectra.

The products from 2-isopropylbenzotriazole (**11**) were separated by GC into three peaks in order of increasing polarity: (i) 1-(α-D-isopropyl)benzotriazole (**13c**) (20%),

Table 5. Mass Fragmentations in Ring-Iodinated 1-Alkylbenzotriazoles (*m/z*, Relative Intensity in Parentheses)

compd	M^+	$M^+ - I$	$M^+ - R$	$M^+ - N_2$	$M^+ - NR$	$M^+ - N_2R$	$M^+ - C_2N_3R$	$M^+ - (C - I)$	C_6H_3I	C_2HI	I	other
3a	287 (100)			259 (4)		217 (51)			203 (8)	152 (1)	127 (11)	204 (3), 104 (5), 176 (5), 104 (10)
4a	287 (100)	160 (15)	245 (7)	259 (30)	230 (8)	217 (36)	206 (16)	146 (10)	203 (17)		127 (5)	204 (20), 104 (5)
5a	287 (25)	160 (15)	245 (20)	259 (100)	230 (8)	217 (4)	206 (2)	146 (2)	203 (5)			204 (20), 104 (5)
15a[a]		132 (70)		104 (25)	91 (2)	77 (100)					127 (26)	
17a	259 (100)			231 (23)	230 (5)	216 (23)		120 (100)	203 (10)	152 (1)	127 (11)	204 (9), 104 (28)
18a	259 (100)	132 (10)	244 (10)	231 (20)	230 (40)	216 (30)	206 (3)	120 (100)	203 (12)		127 (3)	204 (30), 176 (5) 104 (28)
19a	259 (2)	132 (10)	244 (10)	231 (60)	230 (8)	216 (4)	206 (3)	120 (100)	203 (5)			204 (50), 247 (50) 174 (20), 104 (65)
23a	273 (100)			244 (2)	230 (8)	217 (40)			203 (15)	152 (1)	127 (23)	204 (5), 104 (10)
24a	273 (50)	147 (7)	245 (4)	244 (2)	230 (8)	217 (40)	206 (5)	146 (25)	203 (15)		127 (20)	176 (5), 104 (10)
25a	273 (25)	147 (2)	245 (15)	244 (5)	230 (20)	217 (20)	206 (1)	146 (2)	203 (15)		127 (6)	204 (20), 104 (5)

[a] Lit.[4]

Table 6. Mass Fragmentations in Ring-Methylated 1-Alkyllbenzotriazoles (m/z, relative intensity in parentheses)

compd	M^+	$M^+ - Me$	$M^+ - R$	$M^+ - N_2$	$M^+ - NR$	$M^+ - N_2R$	$M^+ - C_2N_3R$	$M^+ - (C\text{-}Me)$	C_6H_3Me	other
3b	175 (60)			147 (2)	106 (3)	104 (100)		146 (3)	90 (2)	
4b	175 (75)	160 (2)	132 (20)	147 (2)	106 (3)	104 (100)	66 (20)	146 (2)	90 (5)	132 (15), 117 (12). 105 (35)
5b	175 (11)	160 (1)	132 (20)		106 (5)	104 (100)			90 (5)	132 (15), 117 (10), 105 (60)
2b[a]	175 (80)	160 (1)	132 (50)		106 (5)	104 (100)			90 (5)	

(ii) dimer **12** (54%, isolated 45%), and (iii) recovered 2-isopropylbenzotriazole (**11**) (23%).

The products from 1-methylbenzotriazole (**14**) were separated by GC into three peaks in order of increasing polarity: (i) ring-substituted 1-methylbenzotriazoles **17c**, **18c**, and **19c** (25%), (ii) dimer **16** (15%), and (iii) recovered starting material (53%).

The products from 1-ethylbenzotriazole (**20**) were separated by GC into three peaks in order of increasing polarity: (i) ring-substituted 1-ethylbenzotriazoles **23c**, **24c**, and **25c** (10%), (ii) dimer **22** (16%), and (iii) recovered starting material (61%).

The deuteration ratio revealed by GC/MS for the reactions of lithiated alkylbenzotriazoles **1**, **11**, **14**, and **20** with deuterium oxide is in agreement with the intensities of the signals in the proton spectra of these reaction mixtures.

Assignment of the Structures of Ring-Substituted 1-Alkylbenzotriazoles. The structures of the products obtained in the reaction of **1** with methyl iodide (**3b**, **4b**, and **5b**) and of **14** and **20** with I_2 (**17a**, **18a**, and **19a** and **23a**, **24a**, and **25a**, respectively) were assigned on an empirical basis by comparison of their GC and MS behavior with that of the similar compounds **3a**, **4a**, and **5a**, whose structures had been elucidated by NMR and HMRS and by comparison with the side-chain substituted standards **2b** and **15a**. The retention times of compounds **3a**, **4a**, and **5a** are in the order **4a** < **3a** < **5a**. It was assumed that the retention times are dependent on the nature of ring substitution, and the retention time relationship of these isomers was extrapolated to the other mixtures to be **4b** < **3b** < **5b**, **18a** < **17a** < **19a**, and **24a** < **23a** < **25a**. The relative ratios of isomers in these mixtures were about the same (**3a**:**4a**:**5a** = 4.6:1.0:0.2, **3b**:**4b**:**5b** = 4.4:1.0:0.2, **17a**:**18a**:**19a** = 1.8:1.0:0.5 and **23a**:**24a**:**25a** = 2.0:1.0:0.2), which is also consistent with the structural assignments, provided that the nature of the 1-alkyl group has little influence on the relative reactivity of the positions in the aromatic ring.

Further support for these assignments was provided by analysis of the mass spectral fragmentation patterns. Data for ring-iodinated and ring-methylated 1-alkylbenzotriazoles are presented in Tables 5 and 6, respectively. In all compounds substituted in position 4 (**3a**, **17a**, **23a**, and **3b**), the lines corresponding to $M^+ - I$ ($M^+ - Me$) and $M^+ - R$ fragmentations are missing, while they are present in the other isomers. All compounds substituted in position 5(6) (**5a**, **19a**, **25a**, and **5b**) show a much lower intensity for the molecular ion than the other isomers. Compounds substituted in the α position of the alkyl chain, **15a** and **2b**, display different retention times and fragmentation patterns than their ring-substituted counterparts (**17a**, **18a**, and **19a** and **3b**, **4b**, and **5b** correspondingly).

Discussion

The results in Table 1 include data for the outcome of reactions of lithiated 1-methylbenzotriazole (**14**) and 1-ethylbenzotriazole (**20**) with methyl iodide taken from the literature[1] and demonstrate that the lithiation of 1-isopropylbenzotriazole occurs at the benzene ring much more readily than at the α-CH of the isopropyl group. Thus, only 2% of 1-*tert*-butylbenzotriazole (**2b**) was indicated in the reaction quenched with methyl iodide, and only ca. 1% of dimer **6** was formed. The GC/MS and isolation results for the iodine quenched products and the GC/MS results for the methyl iodide quenched products are in good agreement, showing that this ring lithiation occurs predominantly in the 4–position (leading to **3a** and **3b** ca. 32%) followed by the 7-position (leading to **4a** and **4b** ca 8%) with a small amount occurring in the 5- or 6-position.

The extraordinary formation of bicyclo[2.2.2]octadiene compounds **9a**, **9b**, and **10** cannot yet be understood. Compounds **9a** and **9b** are constructed from four isopropyl and one *n*-butyl blocks. The formation and reactions of these propene synthons may be related to the formation of alkenes in the decomposition of lithiated 2-alkylbenzotriazoles.[5] We plan further investigations.

For 2-isopropylbenzotriazole the product slates are much simpler: no benzene ring lithiation and predomi-

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nant formation of a dimeric product, presumably by a mechanism similar to that proposed earlier for the formation of dimers from 2-ethyl- and 2-methylbenzotriazole.[2] The only other significant products (**13a**, **13b**, and **13c**) result from the quenching of α-CH lithiation intermediates, all pointing to exclusive α-CH lithiation.

α-CH lithiation is again predominant for 1-ethylbenzotriazole as previously reported[1] and leads to a high proportion of dimer on reaction with iodine. However, the experiments employing I_2 and D_2O indicate some 20% of ring lithiation does occur, apparently mainly in the 5- or 6- position.

For 1-methylbenzotriazole some 14% of ring lithiation is found, with an isomer distribution indicating much more even lithiation at the various ring positions.

Experimental Section

Melting points were determined on a hot-plate microscope and are uncorrected. ^1H and ^{13}C NMR spectra were obtained at 300 and 75 MHz correspondingly, with tetramethylsilane as internal standard. *J* values are given in Hz. Low-resolution mass spectra were recorded on a Hewlett-Packard 5890 gas chromatograph, equipped with a flame ionization detector and a Hewlett-Packard 5972 mass selective detector. Mass spectra simulations were performed using Window Chem software. Thin layer chromatography (TLC) was carried out on precoated TLC plates (silica gel G60). *n*-Butyllithium (*n*-BuLi) was purchased as a 2.5 M solution in hexane. Tetrahydrofuran, toluene, and diethyl ether were distilled from sodium benzophenone ketyl under nitrogen prior to use.

The syntheses of 1- and 2-alkylbenzotriazoles **1**, **11**, **14**, and **20** were carried out according to the literature procedures mentioned in Table 2.

Elemental analysis or HRMS data, melting points, yields and reference to the preparative procedures for the products of the reactions of alkylbenzotriazoles with electrophiles are given in Table 2. ^1H and ^{13}C chemical shifts are presented in Tables 3 and 4, respectively.

General Procedure A for the Reaction of 1- and 2-Alkylbenzotriazoles 1, 11, 14, and 20 with Iodine. To a solution of the benzotriazole derivative (2 mmol) in dry THF at −78 °C was added an equimolar amount of *n*-BuLi. The solution was stirred at −78 °C for 8 h, and then an equimolar amount of iodine (as a solution in THF) was added and the reaction mixture allowed to warm to room temperature. The reaction mixture was quenched with cold water after 3 days. The phases were separated, and the aqueous phase was extracted with diethyl ether. The combined organic phase was washed with a saturated aqueous solution of sodium thiosulfate (50 mL) and then with water (2 × 50 mL) and dried over anhydrous Na_2SO_4. The solvent was removed at 70 °C/50 mmHg to give a residual mixture which was analyzed by GC/MS.

The mixture resulting from the reaction of lithiated 1-isopropylbenzotriazole (**1**) with iodine was separated by flash column chromatography on silica gel, using chloroform:hexane, 1:2 as eluant. The products thus isolated are given in Table 1.

2-(Benzotriazol-1-yl)-5*n*-propyl-6,6-dimethyl-3-isopropyl-5-iodo[2.2.2]bicyclooctadiene (9a). Crude **9a** was purified by preparative TLC, eluting with chloroform:diethyl ether, 96:4.

General Procedure B for the Reaction of 1- and 2-Alkylbenzotriazoles 1, 11, 14, and 20 with Methyl Iodide. To a solution of the corresponding benzotriazole derivative (2 mmol) in dry THF at −78 °C was added an equimolar quantity of *n*-BuLi. The solution was stirred at −78 °C for 8 h, and then an equimolar amount of methyl iodide (as a solution in THF) was added and the reaction mixture allowed to warm to room temperature. Stirring was continued for 20 h, and the reaction mixture was quenched with cold water. The phases were separated, and the aqueous phase was extracted with diethyl ether. The combined organic layer was washed with water (2 × 50 mL) and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* to give a residual mixture with the composition indicated in Table 1.

2-(Benzotriazol-1-yl)-3-isopropyl-5,6,6-trimethyl[2.2.2]-bicyclooctadiene (10). A mixture containing starting material and methyl ring-substituted 1-isopropylbenzotriazoles **9a** and **10** was dissolved in methylene chloride and washed with 20% HCl (30 mL). The organic extract contained a mixture of starting material, methyl ring substituted 1-isopropylbenzotriazoles, and **9a**. The acidic phase was extracted with diethyl ether (50 mL), washed with water (20 mL), and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* and the residue purified by preparative TLC, eluting with chloroform:diethyl ether, 96:4.

General Procedure C for the Reaction of 1- and 2-Alkylbenzotriazoles 1, 11, 14, and 20 with Deuterium Oxide. To a solution of the corresponding benzotriazole derivative (2 mmol) in dry THF at −78 °C was added an equimolar amount of *n*-BuLi. The solution was stirred at −78 °C for 8 h, and then a 2-fold excess of deuterium oxide was added and the reaction mixture allowed to warm to room temperature. The stirring was continued for 20 additional h. The phases were separated, and the aqueous phase was extracted with diethyl ether. The combined organic layer was washed with water (2 × 50 mL) and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* to give a residual mixture the composition of which was determined by GC/MS (Table 1).

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