1,3-Dipolar Cycloadditions of Electron-Rich Benzotriazol-1-ylpropenes

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The preparation of *trans*-3-benzotriazol-1-yl-1-(*N*-morpholino)prop-1-ene (**1**), *trans*-3-benzotriazol-1-yl-1-ethoxyprop-1-ene (**2**) and *trans*-1,3-bis-(benzotriazol-1-yl)propene (**3**) and their reactions with a benzonitrile oxide (**4**), *N*-(2,4-dibromophenyl)-1-phenylnitrilimine (**5**), and *p*-nitrophenyl azide (**6**) are described.

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Introduction.

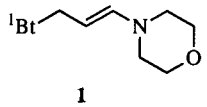
Pyrazoles [1], isoxazoles [2] and 1,2,3-triazoles [3] are three important classes of heterocycles that can each be synthesized through 1,3-dipolar reactions [4,5] of electron-rich alkenes, namely by their reactions with azides [6], nitrile oxides [7] and nitrile imines [8], respectively. The present contribution examines the 1,3-dipolar reactions of electron-rich benzotriazol-1-ylpropenes **1-3** with an azide **6**, a nitrile oxide **4** and a nitrile imine **5**.

Preparation of Bis-1,3-benzotriazol-1-yl-*trans*-propene (**3**) (Scheme 1).

Reaction of two equivalents of sodium benzotriazolate with epichlorohydrin (**7**) produced, after column chromatography, a mixture of 1,3-bis-benzotriazolyl-2-hydroxypropanes (**8**, 28%; **9**, 5%; **10**, 21%) along with small amounts of 1-(benzotriazol-2-yl)-3-chloropropan-2-ol (**11**, 18%) and 1-(benzotriazol-2-yl)propylene 2-oxide (**12**, 2%). Formation of **11** and **12** was virtually eliminated when two equivalents of benzotriazole were reacted with epichlorohydrin in the presence of triethylamine, to give a mixture from which compounds **8**, **9** and **10** were isolated in 38%, 6% and 29% yields, respectively, by column chromatography.

When **8** was reacted with thionyl chloride, the corresponding chloride **13** was isolated in 70% yield. Reaction of **10** with thionyl chloride formed chloride **14** in 38% isolated yield after a longer reaction time. Compound **9** failed

Diagram 1



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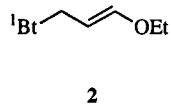

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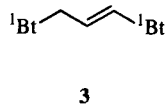

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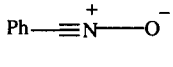

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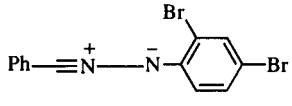

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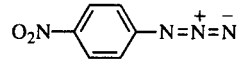

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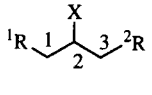
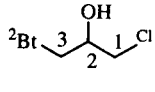
Diagram 2



8-10, 13 and 14



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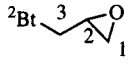

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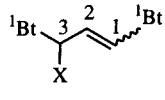
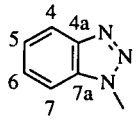
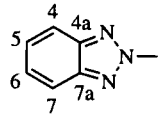
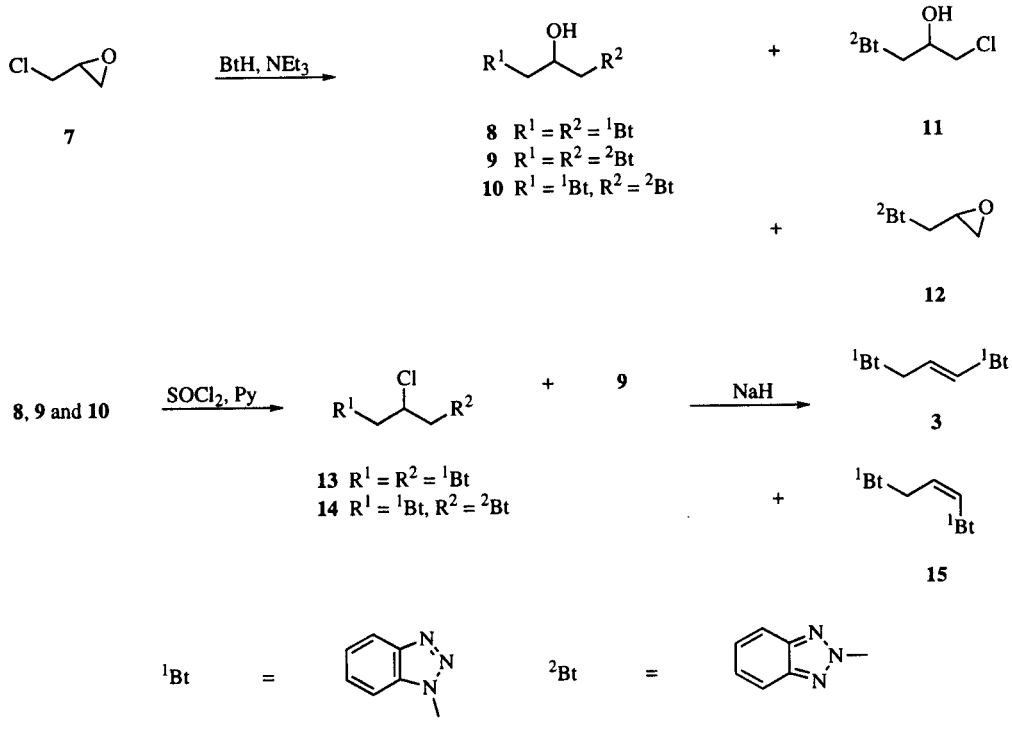


3, 15-21

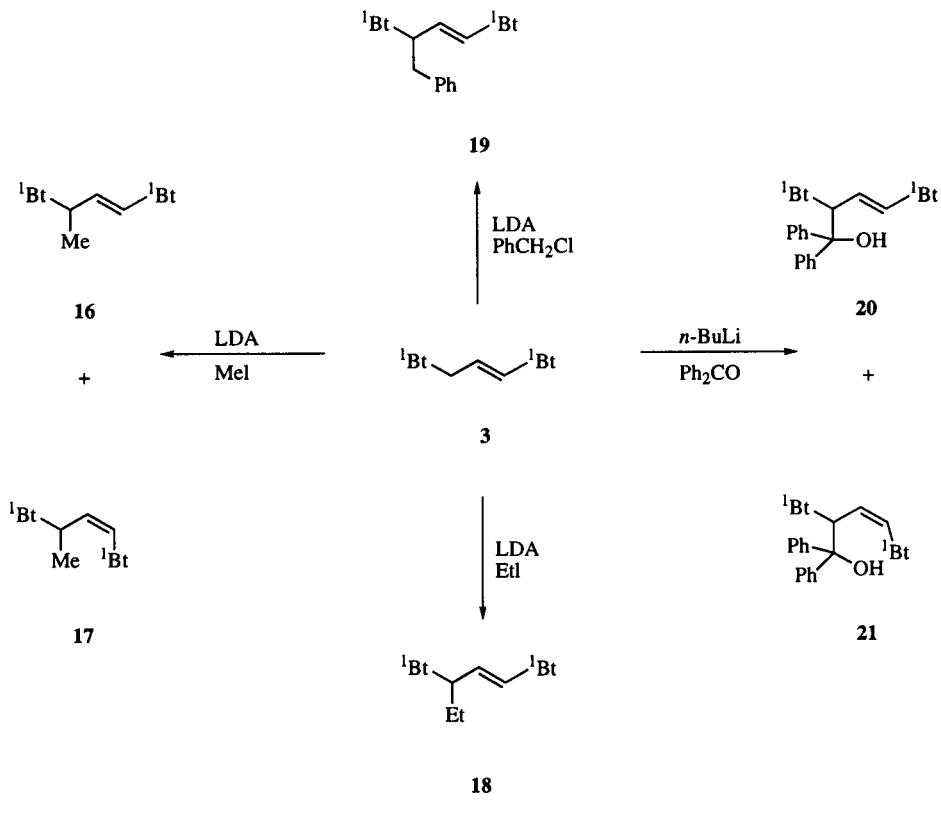
^1Bt = 

^2Bt = 

Scheme 1



Scheme 2



to react under similar conditions. Treatment of the above 6:1:5 mixture of **8**, **9** and **10** with thionyl chloride furnished 1,3-bis-benzotriazolyl-2-chloropropanes **13** and **14** in 44% and 9% isolated yields along with unreacted **9**.

Dehydrohalogenation of **13** or **14** with sodium hydride produced similar ratios of elimination products **3** and **15** (around 7:1 after column chromatography). However, the reaction of **14** required a longer time and concomitant conversion of **14** to **13** was observed by both tlc and ^{1}H nmr of the reaction mixture. Treatment of a 4:1 mixture of **13** and **14** with sodium hydride formed elimination products **3** and **15** isolated in 69% and 10% yields, respectively, after column chromatography.

Alkylation of Bis-1,3-benzotriazol-1-ylpropene (**3**).

Compound **3** was alkylated by treatment of a mixture of a 50% molar excess of the appropriate alkyl halide and **3** with a single equivalent of lithium diisopropylamide at -78° (Scheme 2). In all cases, alkylation occurred adjacent to the double bond. Alkylation of **3** with methyl iodide gave both the *trans* and *cis* isomers of bis-1,3-(benzotriazol-1-yl)but-1-ene (**16**) and (**17**) in 35% and 13% yields, respectively. When ethyl iodide or benzyl chloride were used, only the *trans* isomers **18** (81%) and **19** (55%) were isolated.

Successive treatment of **3** with *n*-butyllithium and benzophenone furnished the *trans*- and *cis*-hydroxyalkyl compounds **20** and **21** in 21% and 14% yields, respectively.

^{1}H and ^{13}C NMR Spectra.

The ^{1}H and ^{13}C nmr spectral data for compounds **3** and **8-21** are shown in Tables 1 and 2. Compounds **8**, **9** and **10** were unambiguously identified through analysis of their ^{1}H nmr spectra. As expected in all cases, the hydrogens attached to C-1 produced an AB type coupling pattern. The attachment sites on the benzotriazolyl rings were de-

Table 1

^{1}H NMR Chemical Shifts (in ppm) and Coupling Constants (in Hz) of Compounds **3** and **8-21** ($CDCl_3$)

No.	H1a/H1b	H2	H3a/H3b	Bt Resonances	Other
3	7.52-7.67 (m) [b]	6.81 (br dt, 14.1, 6.5)	5.60 (dd, 6.5, 1.4)	7.41-7.47 (m), 7.52-7.67 (m), 8.11 (d, 8.7), 8.13 (d, 8.3)	
8 [c]	4.76 (dd, 14.3, 7.8)/4.95 (dd, 14.2, 3.8)	4.54-4.58 (m)	4.76 (dd, 14.3, 7.8)/4.95 (dd, 14.2, 3.8)	7.38 (dd, 8.1, 7.0), 7.53 (dd, 8.0, 6.9), 7.84 (d, 7.8), 8.00 (d, 7.7)	
9 [c]		4.87-4.99 (m) [a]		7.40 (dd, 6.6, 3.0), 7.85 (dd, 6.6, 3.0)	4.42 (d, 4.5) (OH)
10		4.78-5.02 (m) [a]		7.36-7.44 (m), 7.55 (dt, 8.0, 1.0), 7.87-7.43 (m), 8.04 (d, 8.3)	5.63 (s) (OH)
11	3.58 (dd, 11.5, 6.0)/3.63 (dd, 11.5, 5.1)	4.49-4.51 (m)	4.88 (dd, 14.2, 6.0)/4.93 (dd, 4.6, 4.4)	7.37 (dd, 6.3, 3.0), 7.83 (dd, 6.3, 3.0)	
12	2.76 (dd, 4.8, 2.5)/2.95 (t, 4.2)	3.38-3.63 (m)	4.82 (dd, 14.1, 5.0)/4.92 (dd, 14.0, 4.3)	7.39 (dd, 6.5, 2.8), 7.88 (dd, 6.4, 3.0)	
13		4.95-5.20 (m) [a]		7.41 (t, 8.3), 7.50-7.56 (m), 7.61 (d, 8.4), 8.09 (d, 8.4)	
14		4.99-5.23 (m) [a]		7.24-7.41 (m), 7.45-7.51 (m), 7.58 (d, 8.4), 7.84 (dd, 6.8, 3.3), 8.04 (d, 8.3)	
15	7.29 (br d, 10.0)	5.95-6.02 (m)	6.06-6.09 (m)	7.36-7.42 (m), 7.45-7.53 (m), 7.57-7.64 (m), 8.09 (dd, 7.4, 1.0), 8.18 (dd, 7.4, 0.9)	
16	7.30-7.70 (m) [b]	6.95 (dd, 14.4, 6.9)	5.85-5.95 (m)	7.30-7.70 (m), 8.06 (br d, 8.3), 8.11 (br d, 8.3)	2.08 (d, 7.0) (Me)
17	7.15 (dd, 9.4, 1.0)	6.23 (t, 9.4)	6.82-6.89 (m)	7.32-7.63 (m), 8.06 (br d, 8.2), 8.16 (br d, 8.3)	2.07 (d, 6.8) (Me)
18	7.30-7.68 (m) [b]	6.95 (dd, 14.4, 7.6)	5.60 (br q, 7.5)	7.30-7.68 (m), 8.07 (br d, 8.3), 8.13 (br d, 8.3)	1.02 (t, 7.3), 2.39-2. (m), 2.48-2.61 (m) (CH_2)
19	7.07-7.58 (m) [b]	7.05 (dd,14.4, 7.5)	5.82 (dq, 7.4, 1.0)	7.07-7.58 (m), 8.05-8.09 (m)	3.66 (dd, 13.8, 6.8, CH_2a), 3.78 (dd, 13 8.4, CH_2b), 7.01-7.: (m, Ph)
20	7.07-7.78 (m) [b]	6.87 (dd, 14.6, 7.3)	6.52 (d, 7.4)	7.07-7.78 (m), 8.01 (t, 8.2)	7.07-7.78 (m) (Ph), 5.65 (s) (OH)
21	6.83-8.14 (m)[b]	6.42 (t, 9.5)	6.83-8.14 (m) [b]	6.83-8.14 (m)	6.83-8.14 (m) (Ph), 5.76 (s) (OH)

[a] The resonances for H1, H2 and H3 are overlapped. [b] Uncertain assignment. [c] In DMSO-d_6.

Table 2

^{13}C NMR Chemical Shifts (in ppm) of Compounds **3** and **8-21** (at 75 MHz, in $CDCl_3$)

No.	C1	C2	C3	Bt Resonances	Other
3	126.8	113.5	47.8	109.2, 109.8, 120.3, 120.5, 124.2, 124.9, 127.8, 128.7, 131.3, 123.8, 146.3 (2C)	
8 [a]	51.6	69.0	51.6	111.3, 119.2, 124.3, 127.5, 134.0, 145.3	
9 [a]	58.9	69.4	58.9	111.1, 117.8 (2C), 118.9, 123.8, 126.3 (2C), 127.1, 133.7, 143.7 (2C), 145.1	
10	51.3	68.9	59.5	118.0, 126.9, 144.4	
11	45.6	70.2	58.6	117.9, 126.8, 144.3	
12	46.0	49.9	58.4	118.1, 126.6, 144.7	
13	51.2	57.2	51.2	109.6, 120.1, 124.3, 128.1, 133.8, 145.7	
14	51.6	56.5 [b]	59.2 [b]	109.5, 118.1 (2C), 120.1, 124.2, 127.0 (2C), 127.9, 133.6, 144.6 (2C), 145.8	
15	121.4	117.0	46.1	109.2, 109.5, 120.1, 120.4, 124.1, 125.1, 127.5, 128.8, 132.5, 133.0, 145.3, 146.1	
16	124.6	119.2	55.0	109.6, 109.8, 120.1, 120.2, 124.0, 125.2, 127.4, 128.4, 131.2, 132.0, 146.1, 146.2	20.4 (Me)
17	122.5	119.8	52.3	109.2, 109.8, 119.8, 120.3, 123.9, 124.9, 127.2, 128.6, 132.6, 145.1, 145.9	20.8 (Me)
18	125.8	118.2	61.4	109.6, 109.9, 120.3, 120.4, 124.1, 124.7, 127.5, 128.5, 131.2, 132.4, 146.2 (2C)	10.7 (CH_3), 28.1 (CH_2)
19	125.9	117.7	61.1	109.3, 109.9, 120.1, 120.4, 124.0. 124.7, 127.2, 127.5, 131.2, 132.6, 145.9, 146.2	41.5 (CH_2), 128.5 (2C), 128.7, 129.0 (2C), 135.9 (Ph)
20	127.3 [b]	115.4	65.0	109.1, 110.2, 120.3, 120.5, 124.6, 124.7, 127.5 [b], 127.6 [b], 131.1, 133.3, 144.9, 146.2	81.0 (COH); 125.0 (2C), 125.9 (2C), 128.3 (2C), 128.5, 128.5, 128.6 (2C), 142.7, 144.1 (Ph)
21	121.9	118.3	61.3	109.3, 110.6, 119.7, 120.0, 124.4, 125.0, 126.9, 127.1, 132.5, 133.8, 144.6, 144.9	81.1 (COH); 124.9 (2C), 125.5 (2C), 127.6 (2C), 128.1 (2C), 128.2 (2C), 128.5, 142.4, 144.1 (Ph)

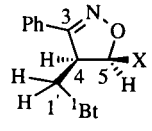
[a] In DMSO-d_6. [b] Uncertain assignment.

termined through the characteristic patterns produced by the benzotriazol-l-yl (two doublets and two triplets) and benzotriazol-2-yl (two doublets of doublets) systems.

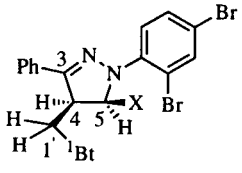
While compounds **13** and **14** produced more complicated ^1H nmr spectra than those of **8**, **9** and **10**, the attachment sites of the benzotriazolyl groups were ascertained in a similar way.

With regard to the alkenyl compounds, differentiation

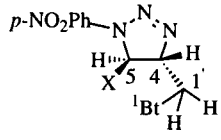
Diagram 3



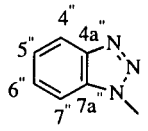
22-24



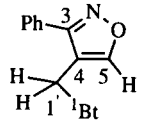
26 and **27**



29 and **30**



= ^1Bt



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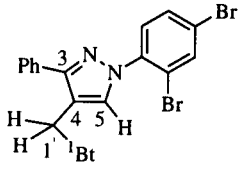

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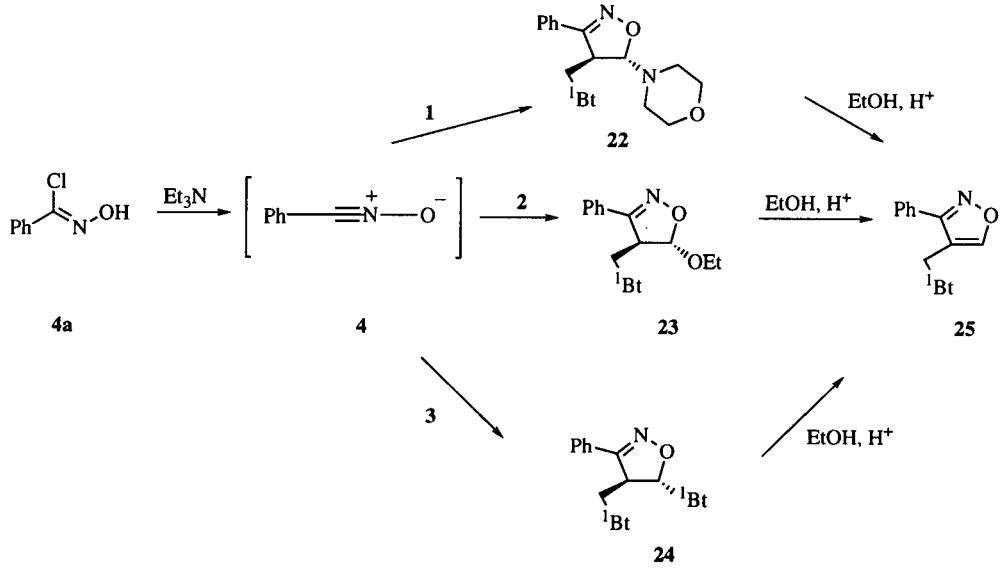
of *cis* and *trans* isomers was possible through examination of the vicinal coupling constants observed for H1 or H2 across the double bond. In the case of the *trans* isomers **3**, **16**, **18**, **19** and **20** the vicinal H1-H2 coupling is around 14 Hz. In the case of the *cis* isomers **15**, **17** and **21**, vicinal H1-H2 couplings are around 10 Hz. These figures are in agreement with known vicinal couplings across double bonds of unsaturated compounds [18]. NOE experiments confirmed these assignments.

Reactions of Benzotriazol-1-ylpropenes with 1,3-Dipoles.

The reactions of benzotriazol-1-ylpropenes (*trans*-3-benzotriazol-1-yl-1-(*N*-morpholino)prop-1-ene [17] (**1**), *trans*-3-benzotriazol-1-yl-1-ethoxyprop-1-ene [19] (**2**) and *trans*-1,3-bis-(benzotriazol-1-yl)propene (**3**)) each formed the expected isoxazoline when reacted with benzonitrile oxide (**4**), formed *in situ* from benzhydroxamoyl chloride (**4a**) and base [20], giving **22**, **23** and **24** in 70%, 80% and 65% yields, respectively. Treatment of **22**, **23** or

Scheme 3



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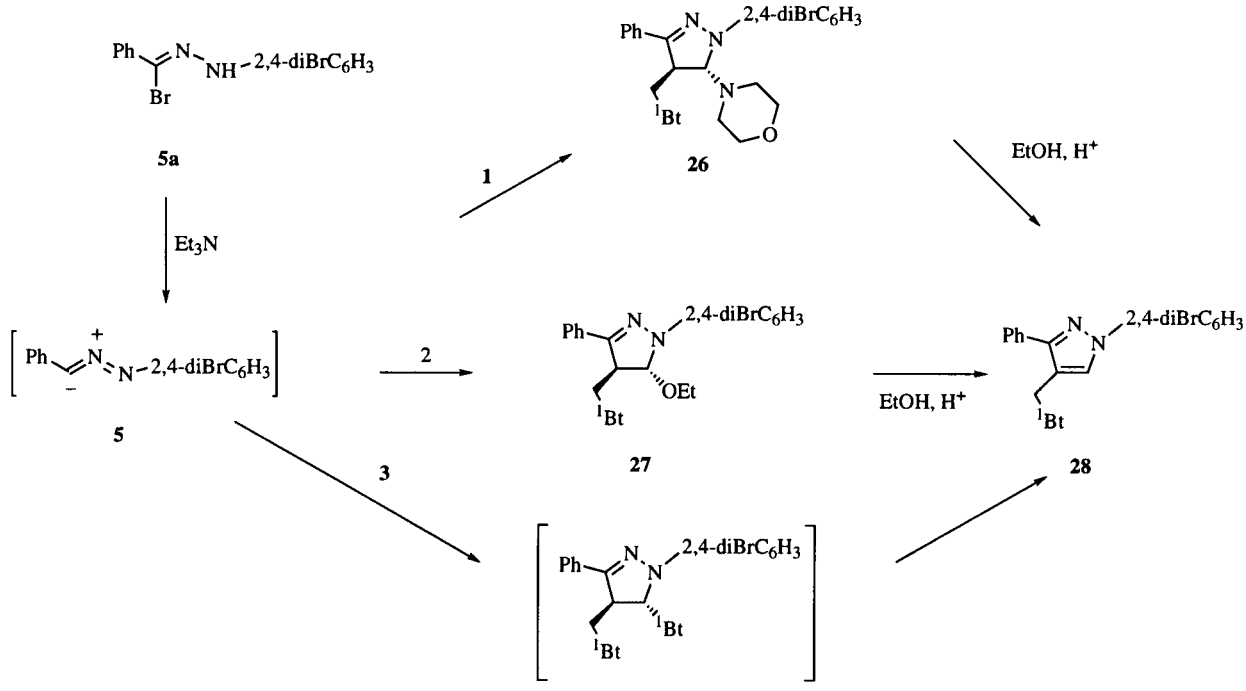

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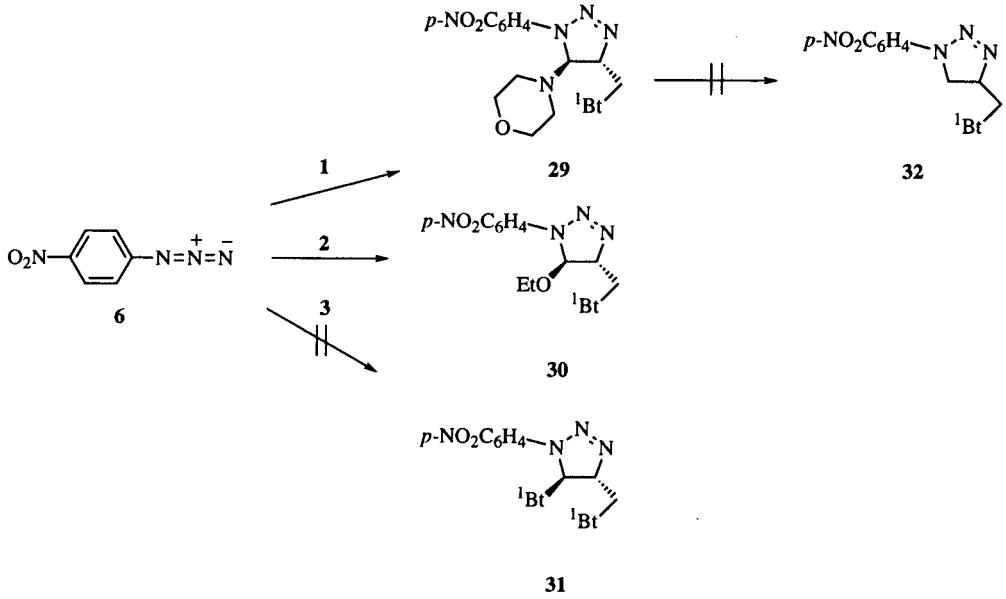

24 with refluxing ethanolic hydrochloric acid each gave the same expected isoxazole **25** in yields of around 90%.

Compounds **1** and **2** formed the expected pyrazolines **26** and **27**, in yields of 70% and 60%, respectively, when reacted with *N*-(2,4-dibromophenyl)phenylnitrilimine (**5**) (formed *in situ* from *N*-(2,4-dibromophenyl)phenylhydrazonyl bromide (**5a**) and base in refluxing benzene) [20], while **3** formed pyrazole **28** directly in 80% yield. Treatment of **26** or **27** with ethanolic hydrochloric acid at 20° also gave pyrazole **28** each in yields of 90%.

Compounds **1** and **2** formed 1,2,3-triazolines **29** and **30** when reacted with *p*-nitrophenyl azide **6** [21] in yields of 80% and 70%, respectively, while **3** failed to react. However, all attempts to eliminate morpholine from **29** with acid, base or heat to form 1,2,3-triazole **32** were unsuccessful.

^{1}H and ^{13}C NMR Spectra.

The ^{1}H and ^{13}C nmr spectral data for compounds **22-30** are shown in Tables 3 and 4.

Table 3

^{1}H NMR Chemical Shifts (in ppm) of Compounds **22-30**

No.	H4	H5	H1'a/H1'b	Bt, Aryl Resonances	Other
22	4.12 (ddd, 7.7, 5.4, 2.1)	5.38 (d, 2.1)	4.78 (dd, 14.5, 8.0)/4.88 (dd, 14.5, 5.4)	7.27-7.64 (m), 8.02 (d, 8.2)	2.45-2.65 (m), 3.57 (t, 4.8) morpholine
23	4.16-4.21 (m)	5.67 (s)	4.69 (dd, 14.6, 9.4)/4.81 (dd, 14.6, 4.8)	7.26-7.74 (m), 8.06 (d, 8.3)	1.12 (t, 7.0)/3.47-3.54 (m), 3.82-3.89 (m) EtO
24	5.55 (ddd, 8.1, 4.4, 1.7)	7.23-8.01 (m) [a]	5.04 (dd, 14.8, 8.1)/5.13 (dd, 14.8, 4.5)	7.23-8.01 (m)	7.23-8.01 (m) Bt
25	----	8.39 (s)	5.77 (s)	7.21-7.58 (m), 8.02 (dd, 7.9, 0.8)	----
26	4.26-4.31 (m)	5.66 (d, 1.1)	4.76 (dd, 14.2, 9.8)/4.87 (dd, 14.2, 5.2)	7.33-7.79 (m), 8.05 (d, 8.4)	2.01-2.20 (m)/3.19-3.34 (m) morpholine
27	4.31 (dd, 9.5, 5.5)	5.76 (s)	4.72-4.86 (m)	7.36-7.80 (m), 8.07 (d, 6.0)	0.74 (t, 7.0)/2.90-2.98 (m), 3.10-3.18 (m) EtO
28	----	7.64 (s)	5.86 (s)	7.14-7.73 (m), 7.96 (d, 8.0)	----
29	4.74 (dd, 8.6, 15.6)	5.20 (d, 3.0)	5.03-5.11 (m)	7.39-7.68 (m), 8.03 (d, 8.4), 8.19 (dd, 7.1, 2.1)	1.97-2.19 (m)/3.42-3.58 (m) morpholine
30	4.81 (dd, 15.7, 8.2)	5.79 (d, 2.0)	5.05-5.12 (m)	7.32 (dt, 9.2, 2.0), 7.37-7.65 (m), 8.00 (d, 8.4), 8.18 (dt, 9.2, 2.0)	1.06 (t, 7.0)/3.11-3.25 (m) EtO

[a] Uncertain assignment.

Table 4

^{13}C NMR Chemical Shifts (in ppm) of Compounds **22-30**

No.	C3	C4	C5	C1′	Bt Resonances	Other
22	155.5	50.0	100.4	47.2	108.5, 120.1, 124.0, 127.7, 133.1, 145.6	47.4, 66.4 (morpholine), 126.4 (2C), 127.7, 129.0 (2C), 130.4 (Ph)
23	157.7	54.6	106.0	45.5	108.6, 120.3, 124.2, 127.7, 133.1, 145.8	14.8, 64.2 (OEt), 127.0 (2C), 127.9, 129.1 (2C), 130.8 (Ph)
24	159.6	54.8	90.9	47.8	110.0, 1115, 121.7, 122.0, 126.0, 126.3, 129.7, 130.0, 133.8, 134.6, 147.4, 148.0	128.1, 129.0 (2C), 131.0 (2C), 133.1 (Ph)
25	160.7	113.2	158.4	40.7	108.9, 119.9, 124.0, 127.6, 132.2, 145.8	127.4, 128.1 (2C), 128.9 (2C), 130.0 (Ph)
26	147.6	46.9	84.4	46.5	108.9, 120.2, 124.1, 127.7, 133.3, 145.7	46.5, 66.3 (morpholine), 114.8, 116.4, 125.0, 125.5 (2C), 129.0 (2C), 129.3, 130.5, 130.9, 135.5, 142.7 (Ph)
27	150.5	53.5	93.9	45.1	109.0, 120.2, 124.2, 127.7, 133.3, 145.8	14.8, 64.6 (OEt), 116.5, 118.1, 126.0 (2C), 127.7, 128.9 (2C), 129.6 [a], 130.7, 131.1 [a], 135.1, 141.6 (Ph)
28	151.7	114.5	132.4	43.1	109.6, 120.0, 123.9, 128.6, 132.5, 146.1	118.6, 122.6, 127.3, 128.2 (2C), 128.8 (2C), 129.0, 131.5, 131.9, 136.1, 138.4 (Ph)
29	----	74.4 [a]	76.0 [a]	47.3	109.3, 120.3, 124.6, 128.3, 132.9, 145.8	45.6, 66.3 (morpholine), 115.2 (2C), 125.4 (2C), 143.2, 144.1 (Ph)
30	----	81.6	84.1	46.2	109.3, 120.1, 124.4, 128.2, 133.1, 145.7	14.7, 61.0 (OEt), 114.8 (2C), 125.5 (2C), 143.3, 143.6

[a] Interchangeable resonances.

The regioselectivity of the reactions of nitrile oxides [4], nitrilimines [4] and azides [5] with, β-substituted alkyl or aryl enamines and enol ethers have been well established and the products presented here possess the predicted regioselectivity. Evidence for the relative orientation of the substituents in **22-24**, **26**, **27**, **29** and **30** is furnished by their ^1H nmr spectra. In all cases, H5 may be identified by its multiplicity (a low-frequency doublet). It may be noted that in all instances this peak appears at lower field than the peak representing H4 (a multiplet), suggesting that C5 is attached to two heteroatoms, thus confirming the predicted regioselectivity.

The ^{13}C nmr spectra were assigned with the assistance of APT and fully-coupled ^{13}C spectra.

EXPERIMENTAL

All nmr spectra were recorded using a Varian VXR-300 spectrometer in deuteriochloroform as solvent, unless otherwise stated. Tetramethylsilane was used as the internal reference for ^1H nmr spectra recorded at 300 MHz. Deuteriochloroform was used as the internal reference for ^{13}C nmr spectra recorded at 75 MHz. Melting points were measured with a hot stage microscope and are uncorrected. Column chromatography was carried out on Merck Ceaseless 60 (5386) silica gel. All reagents were commercially available.

Thin layer chromatography (tlc) was carried out on pre-coated tlc plates (silica gel G60) obtained from Fisher. Sodium sulfate was used as a drying agent, unless otherwise stated. Lithium diisopropylamide was purchased from Aldrich as a 1.5 *M* solution in cyclohexane. Tetrahydrofuran, benzene and toluene were distilled from sodium benzophenone ketyl under nitrogen prior to use. All moisture-sensitive reactions were carried out in a dry argon atmosphere.

Preparation of Bis-1,3-(benzotriazolyl)propan-2-ols **8**, **9**, and **10**, 1-Chloro-3-benzotriazol-2-yl)propan-2-ol (**11**) and 3-Benzotriazol-2-yl-propylene 2-Oxide (**12**).

Method 1.

A stirred suspension of epichlorohydrin (**7**) (13.8 g, 0.15 mole) and sodium benzotriazolate (42.3 g, 0.30 mole) in 500 ml of dry tetrahydrofuran was heated at reflux for 4 hours. The mixture was cooled, diluted with water, acidified with 5% hydrochloric acid and extracted with three 250 ml portions of dichloromethane. The combined organic extracts were dried and the solvent evaporated to dryness to yield an oil that solidified on standing. Column chromatography (silica gel-benzene:acetone 4:1) gave **8**, **9**, **10**, **11** and **12** in 28%, 5%, 21%, 18% and 2% yields, respectively.

Bis-1,3-(benzotriazol-1-yl)propan-2-ol (**8**).

This compound was obtained as colorless needles (benzene), mp 170-171°.

Anal. Calcd. for $C_{15}H_{14}N_6O$: C, 61.22; H, 4.76; N, 28.57. Found: C, 61.11; H, 4.62; N, 28.72.

1-(Benzotriazol-1-yl)-3-(benzotriazol-2-yl)propan-2-ol (**9**).

This compound was obtained as colorless needles (dichloromethane), mp 139-140°.

Anal. Calcd. for $C_{15}H_{14}N_6O$: C, 61.22; H, 4.76; N, 28.57. Found: 61.14; H, 4.78; N, 28.85.

Bis-1,3-(benzotriazol-2-yl)propan-2-ol (**10**).

This compound was obtained as colorless needles (dichloromethane), mp 161-162°.

Anal. Calcd. for $C_{15}H_{14}N_6O$: C, 61.22; H, 4.76; N, 28.57. Found: C, 60.92; H, 4.76; N, 28.43.

1-Chloro-3-(benzotriazol-2-yl)propan-2-ol (**11**).

This compound was obtained as colorless needles (benzene), mp 83-85°.

Anal. Calcd. for $C_9H_{10}N_3OCl$: C, 51.06; H, 4.73; N, 19.86. Found: C, 50.91; H, 4.71; N, 19.90.

3-(Benzotriazol-2-yl)propylene-2-oxide (**12**).

This compound was obtained as colorless needles (chloroform), mp 51-52°.

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.41; H, 5.19; N 24.32.

Method 2.

A stirred mixture of epichlorohydrin (**7**) (13.8 g, 0.15 mole), benzotriazole (35.7 g, 0.30 mole) and triethylamine (15.1 g, 0.15 mole) in 500 ml of dry toluene was heated at reflux for 7 hours when an oily layer separated. The mixture was cooled, diluted with 200 ml of water and extracted with three 250 ml portions of dichloromethane. The combined organic extracts were dried and the solvent evaporated to dryness to yield an oil that solidified on standing and, after crystallization from methanol, was used in the next step. Column chromatography of a portion (silica gel-benzene:ethyl acetate 4:1) gave **8**, **9** and **10** in 38%, 6% and 29% yield, respectively, along with traces of **11** and **12**.

General Procedure for the Preparation of Bis-1,3-(benzotriazolyl)-2-chloropropanes **13** and **14**.

Method 1.

Thionyl chloride (0.238 g, 2 mmoles) in 5 ml of dry toluene was slowly added to a warm solution of **8** or **10** (0.294 g, 1 mmole) and pyridine (0.158 g, 2 mmoles) in 5 ml of dry toluene. After addition, the mixture was heated at reflux for 1-3 hours, cooled, diluted with water, and extracted with three 10 ml portions of dichloromethane. The combined organic extracts were dried and the solvent was evaporated to dryness to yield an oil which was chromatographed (silica gel-dichloromethane:ethyl acetate 4:1).

Bis-1,3-(benzotriazol-1-yl)-2-chloropropane (**13**).

This compound was prepared (70%) from **8** with 1 hour reaction time and was obtained as colorless needles (chloroform), mp 185-186°.

Anal. Calcd. for $C_{15}H_{13}N_6Cl$: C, 57.60; H, 4.16; N, 26.88. Found: C, 57.43; H, 4.13; N, 26.91.

1-(Benzotriazol-1-yl)-3-(benzotriazol-2-yl)-2-chloropropane (**14**).

This compound was prepared (38%) from **10** with heating for 3 hours and was obtained as colorless needles (dichloromethane, diethyl ether), mp 150-151°.

Anal. Calcd. for $C_{15}H_{13}N_6Cl$: C, 57.60; H, 4.16; N, 26.88. Found: C, 57.31; H, 4.19; N, 27.08.

Method 2.

Thionyl chloride (19.8 g, 167 mmoles) in 20 ml of dry toluene was slowly added to a warm solution of **8**, **9** and **10** (24.5 g, 83 mmoles) (obtained as above as an approximately 6:1:5 mixture) and pyridine (13.16 g, 167 mmoles) in 1500 ml of dry toluene. After addition, the mixture was heated at reflux for 3 hours, cooled, diluted with water, and extracted with three 250 ml portions of dichloromethane. The combined organic extracts were dried and the solvent evaporated to dryness to yield an oil which was chromatographed (silica gel-dichloromethane:ethyl acetate 4:1) to give **13** and **14** in 44% and 9% yield, respectively along with unreacted **9**.

Preparation of Bis-1,3-(benzotriazol-1-yl)-2-propenes **3** and **15**.

Method 1.

A suspension of sodium hydride (0.015 g, 0.64 mmole) in 2 ml of dry tetrahydrofuran was added drop by drop to a warm solution (40-50°) of **13** (0.1 g, 0.32 mmole) in 5 ml of dry tetrahydrofuran. After addition, the mixture was stirred for 1 hour at 50°, cooled, diluted with water, and extracted with three 10 ml portions of dichloromethane. The combined organic extracts were dried and the solvent evaporated to dryness to yield a solid which was chromatographed (silica gel-dichloromethane:ethyl acetate 4:1) to give **3** and **15** in 73% and 12% yields, respectively.

Bis-1,3-(benzotriazol-1-yl)-*trans*-propene (**3**).

This compound was obtained as colorless needles (dichloromethane), mp 147-148°.

Anal. Calcd. for $C_{15}H_{12}N_6$: C, 65.22; H, 4.35; N, 30.43. Found: C, 65.09; H, 4.32; N, 30.74.

Bis-1,3-(benzotriazol-1-yl)-*cis*-propene (**15**).

This compound was obtained as colorless needles (benzene), mp 175-176°.

Anal. Calcd. for $C_{15}H_{12}N_6$: C, 65.22; H, 4.35; N, 30.43. Found: C, 65.19; H, 4.33; N, 30.83.

Method 2.

A suspension of sodium hydride (0.84 g, 35 mmoles) in 10 ml of dry tetrahydrofuran was added drop by drop to a warm solution (40-50°) of **13** and **14** (10 g, 32 mmoles) (obtained as above as an approximately 4:1 mixture) in 500 ml of dry tetrahydrofuran. After addition, the mixture was stirred for 3 hours at 50°, cooled, diluted with water, and extracted with three 50 ml portions of dichloromethane. The combined organic extracts were dried and evaporated to dryness to yield a solid which was chromatographed (silica gel-dichloromethane:ethyl acetate 4:1) to give **3** and **15** in 69% and 10% yields, respectively.

General Procedure for the Preparation of 3-Alkyl-bis-1,3-(benzotriazol-1-yl)prop-1-enes **16-21.**

All of these reactions were carried out under a nitrogen atmosphere. A stirred solution of compound **3** (0.15 g, 0.54 mmole) and methyl iodide (0.767 g, 5.4 mmoles) in 10 ml of dry tetrahydrofuran was cooled to -78°. To the mixture was slowly added 0.36 ml of a 1.5 *M* solution of lithium diisopropylamide in cyclohexane. After addition was complete, the solution was stirred at -78° for 2 hours. The solution was allowed to warm to room temperature. The reaction was quenched with 10 ml of water. The organic products were isolated through extraction with dichloromethane. The dichloromethane was dried (magnesium sulfate) and the solvent evaporated to dryness to yield an oil. Separation by column chromatography (silica gel-dichloromethane:ethyl acetate 4:1) gave **16** and **17** in 35% and 13% yields, respectively.

Bis-1,3-(benzotriazol-1-yl)-*trans*-but-1-ene (**16**).

This compound was obtained as colorless needles (diethyl ether), mp 118-119°.

Anal. Calcd. for $C_{16}H_{14}N_6$: C, 66.21; H, 4.83; N, 28.97. Found: C, 65.91; H, 4.88; N, 29.25.

Bis-1,3-(benzotriazol-1-yl)-*cis*-but-1-ene (**17**).

This compound was obtained as a colorless oil; hrms: $M^{+\bullet}$ + 1 Calcd. for $C_{16}H_{15}N_6$: 291.1358. Found: 291.1318.

Bis-1,3-(benzotriazol-1-yl)-*trans*-pent-1-ene (**18**).

This compound was obtained (81%) from ethyl iodide as colorless needles (diethyl ether), mp 80-81°.

Anal. Calcd. for $C_{17}H_{16}N_6$: C, 67.11; H, 5.26; N, 27.63. Found: C, 66.85; H, 5.27; N, 27.43.

Bis-1,3-(benzotriazol-1-yl)-4-phenyl-*trans*-but-1-ene (**19**).

This compound was obtained (55%) from benzyl chloride as colorless needles (diethyl ether), mp 120-121°.

Anal. Calcd. for $C_{22}H_{18}N_6$: C, 72.13; H, 4.92; N, 22.95. Found: C, 72.27; H, 4.97; N, 22.97.

1,3-Bis-(benzotriazol-l-yl)-4,4-diphenyl-4-hydroxy-but-1-ene **20** and **21**.

A stirred solution of compound **3** (0.5 g, 1.8 mmoles) in 10 ml of dry tetrahydrofuran was cooled to -78° under a nitrogen atmosphere. To the solution was slowly added 0.9 ml of a 2 *M* solution of *n*-butyllithium in cyclohexane. After 15 minutes, benzophenone (0.189 g, 1.8 mmoles) was added in one portion and the solution stirred at -78° for 2 hours. The reaction mixture was allowed to warm to room temperature. The reaction was quenched with 10 ml of water. The organic products were isolated through extraction with dichloromethane. The dichloromethane was dried (magnesium sulfate) and evaporated to yield an oil. Separation by column chromatography (silica gel-chloroform) gave **20** and **21** in 21% and 14% yields, respectively.

1,3-Bis-(benzotriazol-1-yl)-4,4-diphenyl-4-hydroxy-*trans*-but-1-ene (**20**).

This compound was obtained as colorless needles (chloroform), mp 158-160°.

Anal. Calcd. for $C_{28}H_{22}N_6O$: C, 73.35; H, 4.86; N, 18.33. Found: C, 73.66; H, 4.94; N, 18.25.

1,3-Bis-(benzotriazol-1-yl)-4,4-diphenyl-4-hydroxy-*cis*-but-1-ene (**21**).

This compound was obtained as colorless needles (chloroform), mp 140-142°; hrms: $M^{+\bullet}$+1 Calcd. for $C_{28}H_{23}N_6O$: 459.1933. Found: 459.1912.

General Procedure for the Preparation of Isoxazolines **22**, **23** and **24**.

To a stirred solution of 1-benzotriazol-1-ylpropene **1** [17] (0.5 g, 1.9 mmoles) and benzhydroxamyl chloride [22] (0.3 g, 1.9 mmoles) in 20 ml of benzene was added triethylamine (0.3 ml, 2.1 mmoles) and the mixture stirred overnight. Water was added and the mixture was extracted with two 20 ml portions of chloroform. The combined organic extracts were dried over magnesium sulfate, filtered and evaporated to dryness under reduced pressure. Column chromatography (silica gel-chloroform) gave **22** in 70% yield.

4-Benzotriazol-l-ylmethyl-5-morpholino-3-phenyl-4,5-dihydroisoxazole (**22**).

This compound was obtained as colorless needles (diethyl ether), mp 165-166°.

Anal. Calcd. for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27. Found: C, 66.08; H, 5.84; N, 19.11.

4-Benzotriazol-1-ylmethyl-5-ethoxy-3-phenyl-4,5-dihydroisoxazole (**23**).

This compound was obtained (80%) from **2** [19] as colorless needles (diethyl ether), mp 126-127°.

Anal. Calcd. for $C_{18}H_{18}N_4O_2$: C, 67.07; H, 5.63; N, 17.38. Found: C, 67.03; H, 5.69; N, 17.60.

4-Benzotriazol-1-ylmethyl-5-(benzotriazol-1-yl)-3-phenyl-4,5-dihydroisoxazole (**24**).

This compound was obtained (65%) from **3** as colorless needles (diethyl ether), mp 165-166°.

Anal. Calcd. for $C_{22}H_{17}N_7O$: C, 66.83; H, 4.33; N, 24.80. Found: C, 66.63; H, 4.33; N, 25.03.

4-Benzotriazol-1-ylmethyl-3-phenyloxazole (**25**).

To a solution of **22**, **23** or **24** (1 mmole) in 5 ml of ethanol was added concentrated hydrochloric acid (2 ml). The reaction mixture was heated at reflux for 4 hours and cooled. The solution was neutralized with a saturated solution of sodium bicarbonate and extracted with two 20 ml portions of chloroform. Column chromatography gave **25** in 85-90% yield from **22**, **23** or **24**, mp 89-90°.

Anal. Calcd. for $C_{16}H_{12}N_4O$: C, 69.54; H, 4.38; N, 20.29. Found: C, 69.26; H, 4.41; N, 20.58.

General Procedure for the Preparation of Pyrazolines **26** and **27**.

To a stirred solution of 1-benzotriazol-1-ylpropene **1** [17] (0.5 g, 1.9 mmoles) and *N*-(2,4-dibromophenyl)phenylhydrazonyl bromide [23] (0.86 g, 1.9 mmoles) in 20 ml of benzene was added triethylamine (1.2 ml, 8.4 mmoles) and the mixture heated at reflux overnight. Water was added and the mixture was extracted with two 20 ml portions of chloroform. The combined organic extracts were dried over magnesium sulfate, filtered and evaporated to dryness under reduced pressure. Column chromatography (silica gel-chloroform) gave **26** in 70% yield.

1-(2,4-Dibromophenyl)-4-methylbenzotriazol-1-yl-5-morpholino-3-phenyl-4,5-dihydropyrazole hydrate (**26**).

This compound was obtained as colorless needles (diethyl ether), mp 100-103°.

Anal. Calcd. for $C_{26}H_{24}Br_2N_6O{\cdot}H_2O$: C, 50.83; H, 4.27; N, 13.68. Found: C, 50.79; H, 3.95; N, 13.53.

1-(2,4-Dibromophenyl)-4-methylbenzotriazol-1-yl-5-ethoxy-3-phenyl-4,5-dihydropyrazole (**27**).

This compound was obtained from **2** [19] (60%) as colorless needles (diethyl ether), mp 75-76°.

Anal. Calcd. for $C_{24}H_{21}Br_2N_5O$: C, 51.91; H, 3.81; N, 12.61. Found: C, 52.11; H, 3.81; N, 12.56.

1-(2,4-Dibromophenyl)-4-methylbenzotriazol-1-yl-3-phenylpyrazole (**28**).

Method 1.

To a solution of **26** or **27** (1 mmole) in 5 ml of ethanol was added concentrated hydrochloric acid (2 ml). The solution was neutralized with a saturated solution of sodium bicarbonate and extracted with two 20 ml portions of chloroform. The combined

organic extracts were dried over magnesium sulfate, filtered and evaporated to dryness under reduced pressure. Compound **28** was obtained in 90% yield from **26** or **27**.

Method 2.

To a stirred solution of *trans*-bis-1,3-benzotriazol-1-ylpropene **3** (0.52 g, 1.9 mmoles) and *N*-(2,4-dibromophenyl)phenylhydrazonyl bromide [23] (0.86 g, 1.9 mmoles) in 20 ml of benzene was added triethylamine (1.2 ml, 8.4 mmoles) and the mixture heated at reflux overnight. Sodium bicarbonate solution was added and the mixture was extracted with two 20 rnl portions of chloroform. The combined organic extracts were dried with magnesium sulfate, filtered and evaporated to dryness under reduced pressure. Column chromatography (silica gel-chloroform) gave **28** in 80% yield, mp 95-97°.

Anal. Calcd. for $C_{22}H_{15}Br_2N_5$: C, 51.89; H, 2.97; N, 13.75. Found: C, 51.86; H, 2.98; N, 13.73.

General Procedure for the Preparation of 1,2,3-Triazolines **29** and **30**.

A stirred solution of 1-benzotriazol-1-ylpropene **1** [17] (1.9 mmoles) and *p*-nitrophenyl azide [24] (0.32 g, 1.9 mmoles) in 20 ml of benzene was heated at reflux overnight. Water was added and the mixture was extracted with two 20 ml portions of chloroform. The combined organic extracts were dried over magnesium sulfate, filtered and evaporated to dryness under reduced pressure. Column chromatography (silica gel-chloroform) gave **29** in 80% yield.

4-Benzotriazol-1-ylmethyl-5-morpholino-1-(4-nitrophenyl)-4,5-dihydro-1,2,3-triazole (**29**).

This compound was obtained as colorless needles (diethyl ether), mp 195-197°.

Anal. Calcd. for $C_{19}H_{20}N_8O_3$: C, 55.88; H, 4.94; N, 27.44. Found: C, 55.80; H, 4.88; N, 27.49.

4-Benzotriazol-1-ylmethyl-5-ethoxy-1-(4-nitrophenyl)-4,5-dihydro-1,2,3-triazole (**30**).

This compound was obtained from **2** [18] (70%) as colorless needles (diethyl ether), mp 164-165°.

Anal. Calcd. for $C_{17}H_{17}N_7O_3$: C, 55.58; H, 4.66; N, 26.69. Found: C, 55.24; H, 4.62; N, 26.64.

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