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Benzotriazole-assisted β-Lithiation of Vinyl Ethers

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Keywords : vinyl ether; benzotriazole; β-lithiation; calculation; PM3; MNDO.

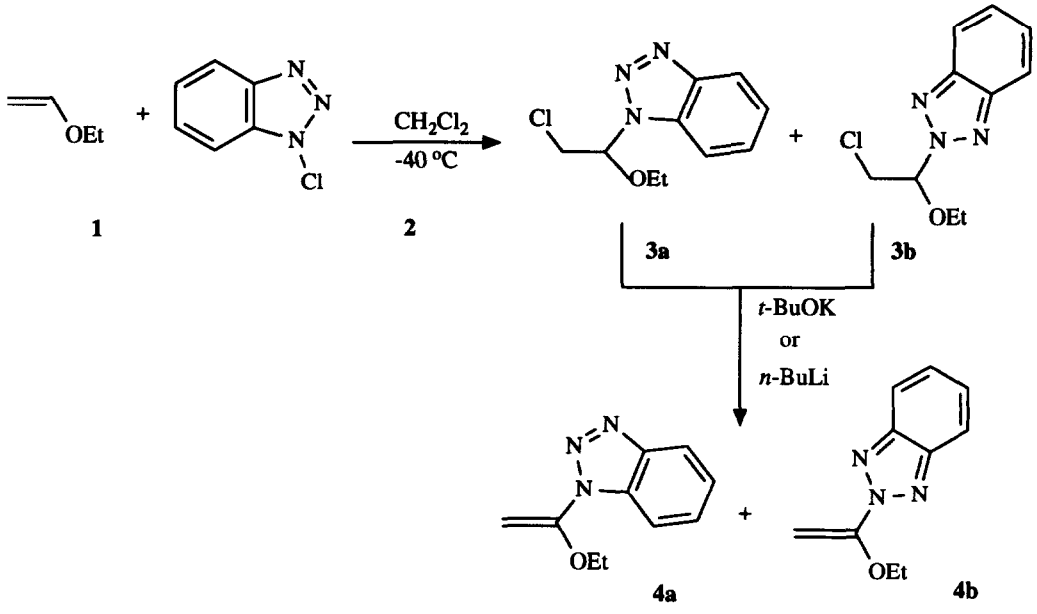
Abstract: *Benzotriazole-assisted β-deprotonation of (α-benzotriazolylvinyl) ethers occurs stereoselectively at the* cis *position as shown by quenching with a variety of electrophiles. Semiempirical calculations of the lithiated enol ethers by PM3 and MNDO methods disclosed a higher stabilization for the* cis*-isomers over the corresponding* trans*-isomers.*

INTRODUCTION

Heteroatom-assisted metallation has been very useful in synthesis for the functionalization of a great variety of compounds.[1] Considerable effort has been devoted to the regiospecific metallation of vinyl ethers. α-Lithiation of vinyl ethers is known to proceed smoothly upon treatment with organolithium compounds at low temperature.[2,3] Direct β-lithiation of vinyl ethers however has been far less documented. Recently, McDougal and Rico reported the smooth β-lithiation by *sec*-butyllithium of methoxymethyl vinyl ether which was then reacted with a variety of electrophiles.[4,5] *cis*-2-Ethoxyvinyl lithium has been synthesized by transmetallation from the corresponding tin derivative[6] or by metal halogen exchange from *cis*-2-ethoxyvinyl bromide.[7] However, β-lithiation is generally assisted by additional directing groups such as halogens[8] or thioaryl groups.[9] The nitrogen assisted β-lithiation of vinyl ethers has not been reported previously, although the nitrogen assistance for β-lithiation is known e.g. for enamines.[10]

RESULTS AND DISCUSSION

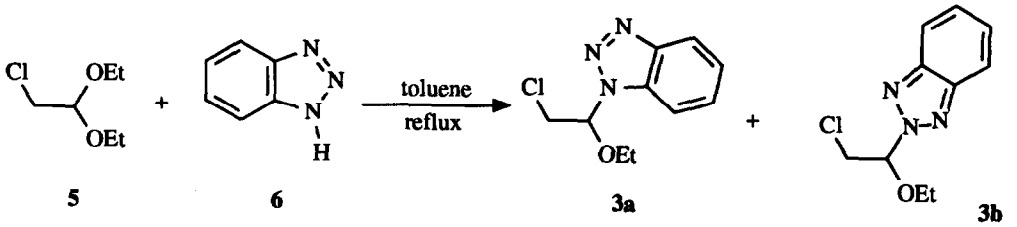
Benzotriazole has been shown to be a good activating group for various α-lithiations.[11,12,13,14] It serves as both a strong electron-withdrawing group and coordinative group during the lithiation. These two properties both can facilitate smooth metallation. In this paper, we wish to report the successful β-lithiation of 1-(benzotriazol-1-yl)-1-ethoxyethene **4a** and 1-(benzotriazol-2-yl)-1-ethoxyethene **4b** and their subsequent reactions with a variety of electrophiles.



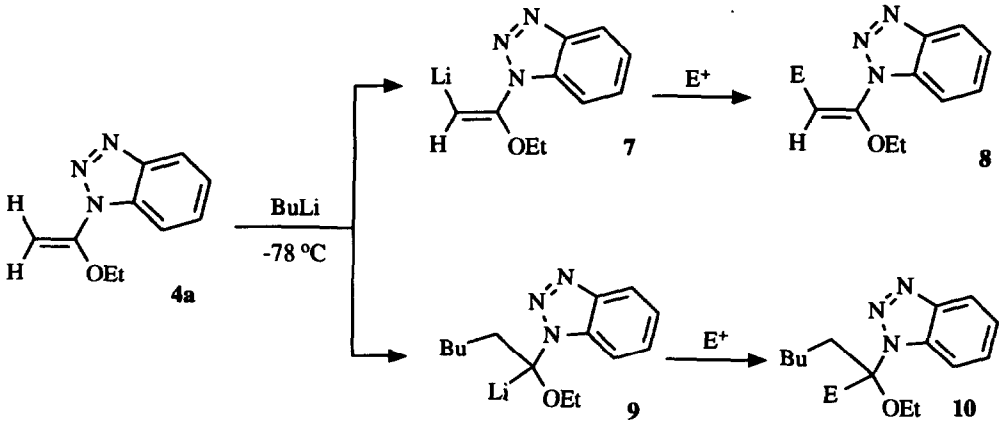
1-(Benzotriazol-1-yl)-1-ethoxyethene **4a** and 1-(benzotriazol-2-yl)-1-ethoxyethene **4b** were prepared by two distinct pathways. The first method consisted of the addition of 1-chlorobenzotriazole **2** to ethyl vinyl ether **1** yielding a mixture of 1-benzotriazolyl-2-chloro-1-ethoxyethane **3** (total yield 90%).[15] Treatment of the adducts **3a** and **3b** with one equivalent of strong base (e.g. butyllithium or potassium *t*-butoxide) at low temperature led to the isolation of the corresponding benzotriazole substituted vinyl ethers **4a** and **4b** in good yields. The separation of the two isomers **3a** and **3b** was accomplished by column chromatography on silica gel. Such separation was deemed necessary because the lithiation of 1-(benzotriazol-2-yl)-1-ethoxyethene **4b** was slow and incomplete and use of the mixture of **4a** and **4b** resulted in lower yields after reaction with an electrophile. The lability of the vinyl ethers **4** obtained after elimination of hydrochloride by treatment of **3** with a strong base, made it preferable to separate the benzotriazole isomers as the adducts **3**, rather than as **4**.

Variation of the reaction conditions (*e.g.* reaction temperature, solvent) for the addition of 1-chlorobenzotriazole to the vinyl ether **1** did not lead to a significant change of the 1-/2-isomer ratio. Although lowering the temperature (-78°C) could slightly increase the proportion of the benzotriazol-1-yl derivative, this isomer always predominated which conflicts with contradictorious literature data.[15]

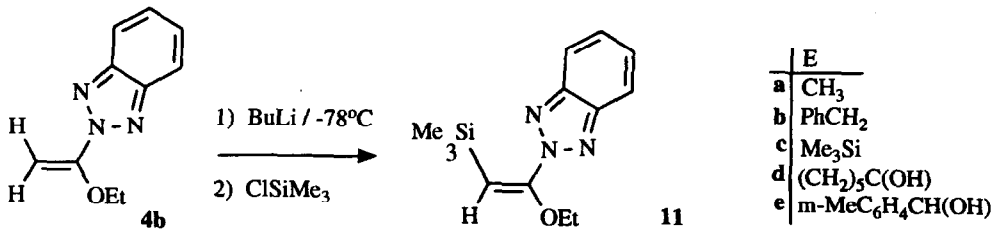
An alternative route for the synthesis of **3** (method 2) was found by treatment of chloroacetaldehyde diethyl acetal with benzotriazole in refluxing toluene. Benzotriazole reacted here as an acid protonating the oxygen with consequent displacement of the alkoxonium group leading to the same products. An advantage of this approach was the higher 1-/2-isomer ratio (82% benzotriazol-1-yl isomer) of the reaction mixture from which it was possible to crystallize the pure benzotriazol-1-yl isomer, discarding the need for column chromatography.



5 **6** **3a** **3b**



4a **7** **8** **9** **10**



4b **11**

	E
a	CH_3
b	$PhCH_2$
c	Me_3Si
d	$(CH_2)_5C(OH)$
e	m-$MeC_6H_4CH(OH)$

Compounds **4a** and **4b** were used to study the effect of the nitrogen atom in the assisted β-lithiation of vinyl ethers. Treatment of compound **4a** with butyllithium at -78 °C followed by quenching with a variety of electrophiles such as several alkyl halides, an aldehyde, a ketone, and trimethylsilyl chloride gave the corresponding *cis*- alkylated derivatives **8** in good yields (58% - 77%). None of the *trans* isomer was detected but in the cases of methyl iodide and trimethylsilyl chloride, small amounts of addition products of butyllithium to the alkene **10a** and **10c** (3.7% - 5.7%) were found. The benzotriazol-2-yl isomer **4b** behaved similarly, but the yields of the alkylated products were much lower (18 - 21%). Reaction of the benzotriazol-2-yl isomer **4b** with butyllithium at -78°C followed by reaction with trimethylsilyl chloride led to the silylated product **11** in 21 % yield whereas the benzotriazol-1-yl isomer gave the silylated product in 77% yield.

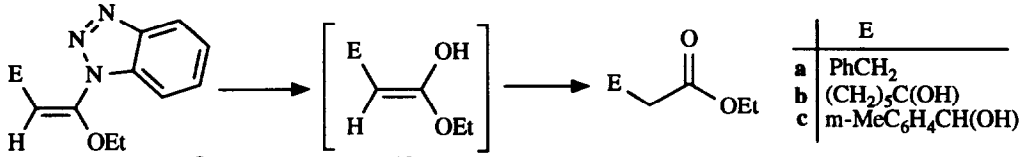
The alkylated products **8** were subsequently hydrolyzed in THF to the corresponding esters **13** in good yields. Spectroscopic data are summarized in Tables 1 and 2. The *cis*-orientations of the electrophile and the benzotriazole group in compounds **8** were confirmed by the NMR data, including Nuclear Overhauser Effect (NOE) experiments. Irradiation of the -O-CH_2- signal of the ethoxy group (at 3.83 ppm for **8a** and at 4.21 ppm for **8c**), showed an enhanced signal of the *cis* olefin proton (7 and 11% NOE respectively compared to a 2 and 4% NOE for the *cis* protons in the starting compounds **4a** and **4b**), which supported the presence of a *cis*-olefin proton relative to the ethoxy group.

Table 1 : ^{1}H NMR Data of Benzotriazolyl Substituted Vinyl Ethers.

Compd.	Benzotriazole ring				R	=C-H	O-CH_2	CH_3
	H - 4	H - 5	H - 6	H - 7				
4a	8.05 dd (8.3, 1.0)	7.80 dd (8.3, 1.0)	7.50 dt (8.3, 1.0)	7.36 dt (8.3, 1.0)	4.97 d (3.8)	4.25 d (3.8)	4.17 q (7.0)	1.53 t (7.0)
8a	8.00 dd (8.3, 1.0)	7.45 m	7.45 m	7.30 m	1.43 d (7.0)	5.03 q (7.0)	3.83 q (7.0)	1.25 t (7.0)
8b	8.03 dt (8.3, 1.0)	7.5 m	7.5 m	7.34 dt (8.2, 1.4)	3.19 d (7.6) 7.1 m	5.16 t (7.6)	3.91 q (7.0)	1.30 t (7.0)
8c	8.16 d (8.3)	7.68 d (8.3)	7.61 t (8.3)	7.48 t (8.3)	0.0 s	4.73 s	4.21 q (7.0)	1.54 t (7.0)
8d	8.11 dd (8.3, 0.9)	7.70 dd (8.3, 0.9)	7.58 dt (8.3, 0.9)	7.45 dt (8.3, 0.9)	1.4 m 3.39 br.s	5.20 s	4.00 q (7.0)	1.40 m
8e	8.07 d (8.3)	7.68 d (8.3)	7.53 dt (8.3, 0.8)	7.41 dt (8.3, 0.8)	2.30 (s, 3H), 3.45 (s,1H), 5.14 (d,9.1, 1H), 7.03 (m, 1 H), 7.18 (m, 3H)	5.26 d (9.1)	4.03 q (7.0)	1.39 t (7.1)

Table 2 : ^{13}C NMR Spectral Shifts (ppm) of Benzotriazolyl Substituted Vinyl Ethers.

Compd	Benzotriazole ring						O-C=	=C-H	O-CH_2	R	CH_3
	C-3A	C-4	C-5	C-6	C-7	C-7A					
4a	145.6	119.5	124.0	128.0	112.2	131.3	151.5	76.2	64.8	-	13.9
8a	144.4	119.8	124.2	128.1	110.6	132.8	145.1	96.8	64.9	11.2	14.3
8b	144.4	120.0	124.3	128.3	110.6	132.9	145.3	101.1	65.1	32.1, 126.3, 128.4 128.5, 139.9	14.3
8c	145.5	119.7	124.2	128.0	111.4	132.4	152.5	90.6	64.5	-0.1	14.1
8d	144.7	120.1	124.8	128.7	111.4	132.7	145.4	108.3	65.1	22.5, 25.4, 38.8, 69.6	14.3
8e	145.3	119.9	124.7	128.1	111.4	132.4	146.5	102.6	65.1	21.3, 68.8, 122.8, 126.4, 128.2, 128.5 137.9, 142.8	14.1



8 **12** **13**

	E
a	$PhCH_2$
b	$(CH_2)_5C(OH)$
c	m-$MeC_6H_4CH(OH)$

As already mentioned, McDougal and Rico observed stereoselective β-lithiation of methoxymethyl vinyl ethers[4,5] assuming the formation of a six-membered complex **14** leading to direct β-lithiation. In the current case, the benzotriazole group in **4a** could coordinate with the lithium atom via a five-membered intermediate **15** facilitating β-lithiation. Furthermore, the electron withdrawing effect of the benzotriazole group increases the acidity of the β-proton which dynamically favors the deprotonation. In contrast, the *trans*-lithiated products, if formed, would produce a more strained four-membered ring complex with the ethoxy group in **19**.

In order to evaluate this hypothesis, semiempirical calculations[16] were carried out for compounds **15** - **21** (**15**, **17**, **19**, **21** are uncomplexed, and **16**, **18**, **20**, **22** are complexed with two THF solvent molecules) with the PM3[17,18] and MNDO[19] methods. These results revealed a lower heat of formation (ΔH_f) for **15** than for **19** (see Table 3), which supports the five-membered ring complex structure of the lithiated intermediate. In all cases the corresponding benzotriazol-2-yl derivatives are less stable than their benzotriazol-1-yl analogs (See Table 3). The energy difference of the 1-/2-isomers varies between 5 to 9 kcal/mol (PM3) or 4 to 11 kcal/mol (MNDO) in favour of the benzotriazol-1-yl compounds. Further, in the structures **19** - **22**, which are 4 to 9 kcal/mol (PM3; or 1 to 7 kcal/mol, MNDO) less stable than their analogs **15** - **18** (last column of Table 3), there is almost no bonding interaction between the lithium cation and the oxygen atom of the ethoxy moiety

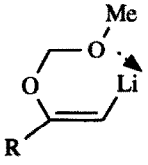
(See Table 4). Therefore, the "directing" influence of the heteroatoms (O vs. N) is only expressed in the case of the five-membered ring systems with the geometrically favoured Li-N interaction as found for **15** and **17**. This is further supported by the PM3 calculation of the transistion states for the reaction of **4a** with MeLi to give **15** or **19** (See equation 1).

Equation 1

MeLi + **4a** ⟶ Adduct ⟶ TS(N) or TS(O) ⟶ **15** or **19** + CH_4

Energies (kcal / mol) :

25.6 63.3 69.9 83.3 or 87.2 83.8 92.4 -13.0



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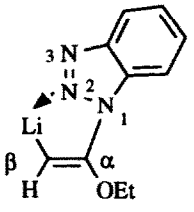
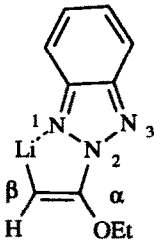


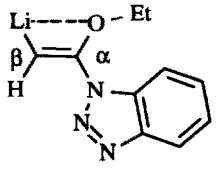
15

16 (2 THF)



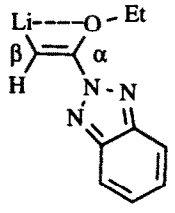
17

18 (2THF)



19

20 (2 THF)



21

22 (2 THF)

Relative to the adduct, the kinetic controlled process via TS(N) [Transition State with coordination to Nitrogen] to give the *cis*-product **15** is favoured by 3.9 kcal/mol, compared with the pathway via TS(O) [Transition State with coordination to Oxygen] to the *trans* product **19**. The relative preference for the benzotriazol-1-yl intermediates in the five-membered ring conformation thus accounted for the high degree of stereoselectivity for the *cis*-alkylation.

In summary, 1-(benzotriazol-1-yl)-1-ethoxyethene and 1-(benzotriazol-2-yl)-1-ethoxyethene underwent facile stereoselective β-lithiation, most likely due to coordination of nitrogen of the benzotriazole moiety towards lithium via a five-membered ring complex. Semiempirical calculations also indicated the preferential formation of *cis*-oriented products. Subsequent hydrolysis of the alkylated products provided the corresponding esters.

Table 3 : Heats of formation [in kcal / mol] and energy differences, PM3 and [MNDO] results.

Benzotriazol-1-yl Species		Benzotriazol-2-yl Species		Energy difference			
4a	63.3	**4b**	72.1	**4a-4b**	- 8.8		
	[37.7]		[48.5]		[-11.2]		
15	83.8	**17**	90.2	**15 - 17**	-6.4	**15 - 19**	-8.6
	[29.6]		[36.1]		[-6.5]		[-1.2]
16	-36.8	**18**	-30.1	**16 - 18**	-6.7	**16 - 20**	-6.8
	[-108.3]		[-101.0]		[-7.3]		[-1.6]
19	92.4	**21**	97.5	**19 - 21**	-5.1	**17 - 21**	-7.3
	[30.8]		[39.9]		[-9.1]		[-3.8]
20	-30.0	**22**	-25.7	**20 - 22**	-4.3	**18 - 22**	-4.4
	[-106.7]		[-97.8]		[-8.9]		[-3.2]
TS(N) [a]	83.3 (1) [c]					**TS(N) - TS(O)**	-3.9
TS(O) [b]	87.2 (1) [c]					**TS(N) - Adduct**	14.4
Adduct	69.9					**TS(O) - Adduct**	18.3

[a]For the lithiation of **4a** with MeLi (ΔH_f = 25.6 kcal / mol)[18] to give **15** and CH_4 (ΔH_f = - 13.0 kcal/mol)[17]. [b]For the lithiation of **4a** with MeLi to give **19** and CH_4.
[c] Number of imaginary frequencies

EXPERIMENTAL

General: Melting points were determined with a Kofler hot stage apparatus and are uncorrected. ^1H and ^{13}NMR spectra were recorded on a Varian VXR 300 MHz spectrometer in $CDCl_3$ using TMS as an internal reference for ^1H spectra and $CDCl_3$ for ^{13}C NMR spectra (abbreviations used: s singlet; d doublet; t triplet; q quartet; and dd doublet of doublets). Elemental analyses were performed on a Carlo Erba-1106 instrument under the supervision of Dr.D. Powell. High resolution mass measurements were recorded on an AEI MS-30 mass spectrometer. Column chromatography was carried out on MCB silica gel (230-400 mesh).

1-Benzotriazolyl-2-chloro-1-ethoxyethane 3a and 3b[15]

Method A. 1-Chlorobenzotriazole (7.7 g, 50 mmol) dissolved in dichloromethane (50 ml) was added dropwise to a solution of ethyl vinyl ether (4.5 g, 63 mmol) in dichloromethane (50 ml) at -40 °C. The mixture was then allowed to warm up to 25°C and stirred overnight. The solvent was evaporated and the crude product separated by column chromatography with a graduent eluent (hexane : ethylacetate = 40 : 1, then 10 : 1) to give the product **3a** (5.1 g) and **3b** (3.9g) in 45% and 35% yield, respectively.

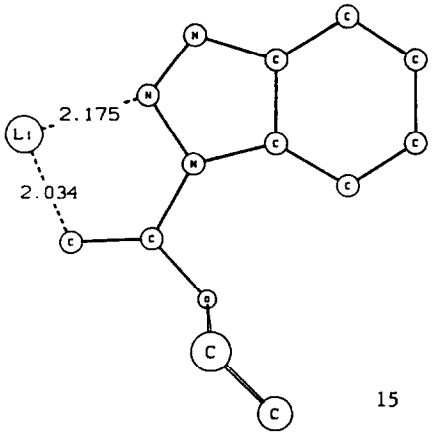
Table 4 : Bond Lengths (Å) , PM3 and [MNDO] Results.

Benzotriazol-1-yl derivatives							
Species	N2 - Li	Cβ - Li	O - Li	O(THF) - Li	N1 - N2	N2 -N3	N1 - Cα
15	2.175	2.034	-	-	1.394	1.279	1.477
	[2.273]	[1.874]	-	-	[1.351]	[1.271]	[1.476]
16	2.207	2.065	-	1.998	1.386	1.279	1.472
	[2.481]	[1.929]	-	[2.191]	[1.348]	[1.271]	[1.469]
19	-	1.975	3.366	-	1.381	1.264	1.453
	-	[1.869]	[2.497]	-	[1.351]	[1.260]	[1.443]
20	-	2.091	3.503	1.993	1.380	1.266	1.462
	-	[1.903]	[3.434]	[2.162]	[1.346]	[1.263]	[1.461]
TS(N)[a]	2.099	2.412	-	-	1.400	1.273	1.468
TS(O)[b]	-	2.343	2.111	-	1.256	1.396	1.451
Adduct[c]	-	-	-	-	1.385	1.271	1.444
Benzotriazol-2-yl derivatives							
Species	N1 - Li	Cβ - Li	O - Li	O(THF) - Li	N1 -N2	N2 -N3	N2 - Cα
17	2.129	2.044	-	-	1.374	1.316	1.484
	[2.198]	[1.879]	-	-	[1.341]	[1.315]	[1.494]
18	2.156	2.072	-	1.995	1.363	1.321	1.480
	[2.341]	[1.934]	-	[2.194]	[1.335]	[1.318]	[1.484]
21	-	1.995	3.120	-	1.337	1.332	1.474
	-	[1.866]	[2.596]	-	[1.330]	[1.328]	[1.462]
22	-	2.034	3.378	2.015	1.334	1.332	1.478
	-	[1.905]	[3.510]	[2.160]	[1.326]	[1.324]	[1.482]

[a] For the lithiation of **4a** with MeLi to give **15** and CH_4 : further bond lengths : Li-CH_3 2.034, Li - H 1.712, H - CH_3 1.580, H - Cβ 1.352

[b] For the lithiation of **4a** with MeLi to give **19** and CH_4 : further bond lengths : Li-CH_3 2.052, Li - H 1.727, H - CH_3 1.541, H - Cβ 1.303, Li - O 2.111

[c] With MeLi coordinated to N_3. Further bond lengths : N_3 - Li 2.027, Li - CH_3 1.940



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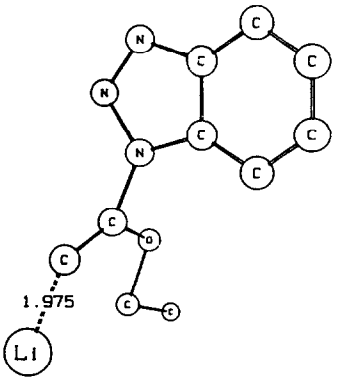

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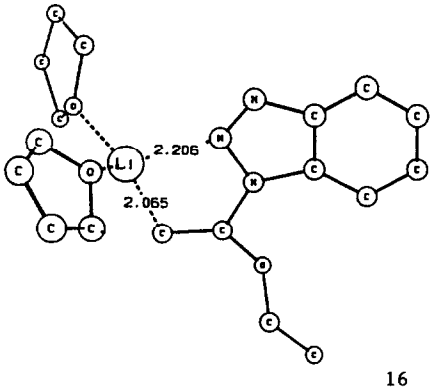

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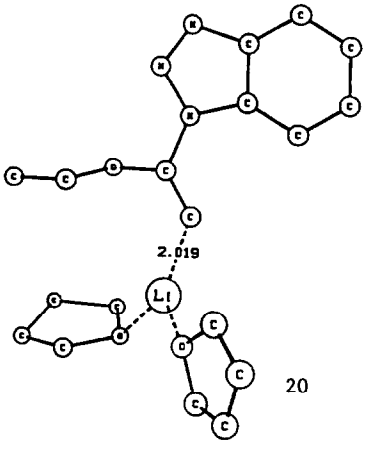

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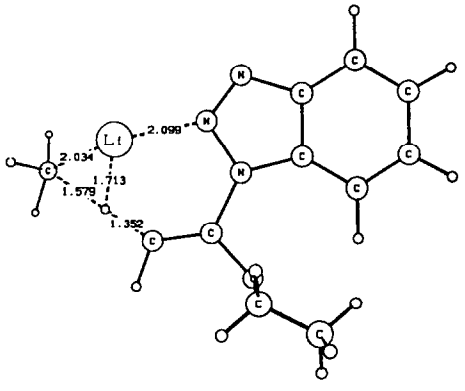
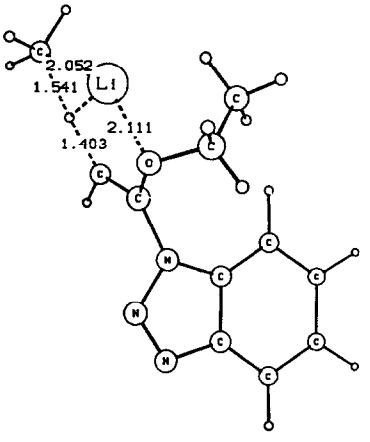


TS(N)



TS(O)

3a Cubic crystals, mp. 49 - 51 °C, ^{1}H NMR: 1.19 (t, *J* 7.0, 3H), 3.43 (m, 1H), 3.63 (m, 1H), 4.06 (dd, *J* 9.0 and 6.0, 1H), 4.08 (dd, *J* 9.0 and 6.0, 1H), 6.23 (t, *J* 6, 1H), 7.41 (t, *J* 8, 1H), 7.52 (t, *J* 7, 1H), 7.75 (d, *J* 8, 1H), 8.11 (d, *J* 8, 1H), ^{13}C NMR: 14.6, 43.8, 65.5, 89.1, 110.5, 120.3, 124.4, 128.0, 131.6, 146.6.

3b, oil, ^{1}H NMR: 1.18 (t, *J* 7, 3H), 3.45 (m, 1H), 3.67 (m, 1H), 4.14 (dd, *J* 11.5 and 5.5, 1H), 4.26 (dd, *J* 11.6 and 7.2, 1H), 6.07 (dd, *J* 7.2 and 5.5, 1H), 7.4 (m, 2H), 7.95 (m, 2H), ^{13}C NMR: 14.4, 43.7, 66.0, 93.4, 118.5, 127.0, 144.3.

Method B. Chloroacetaldehyde diethylacetal (15.2 g, 0.10 mol) in toluene (20 ml) was added dropwise to a stirred solution of benzotriazole (16.7 g, 0.14 mol) in toluene (200 ml). The reaction mixture was refluxed overnight under a nitrogen atmosphere. The mixture was then poured into an aqueous solution of sodium hydroxide (1 N), extracted with toluene (3 x 50 ml) and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave a mixture of **3a** and **3b** from which the 1-benzotriazol-1-yl-2-chloro-1-ethoxyethane **3a** was isolated by crystallization. Further separation of the mother liquor by column chromatography afforded the pure isomers **3a** (total 67%) and **3b** (10%).

1-Benzotriazolyl-1-ethoxy-ethenes 4a and 4b[15]

Method A. To a vigorously stirred solution of **3a** or **3b** (2.65 g, 11.7 mmol) in *tert*-butanol (20 ml) at -10°C, potassium *tert*-butoxide (1 M in THF, 13 ml, 13 mmol) was added. After addition the mixture was allowed to warm up to 25°C and was stirred for 3 h. The mixture was then poured into water (50 ml) and extracted with diethyl ether (3 x 80 ml). The combined extracts were washed with water (20 ml), dried ($MgSO_4$) and the solvent evaporated to give the desired products **4a** and **4b**. The spectral data are summarized in Tables 1 and 2 for **4a**. **4a** Yield : 92% ; Calcd C 63.48, H 5.86, N 22.21, Found C 63.23, H 5.90, N 22.10; **4b** Yield : 95% ; Calcd C 63.48, H 5.86, N 22.21, Found C 63.50, H 5.91, N 22.14; ^{1}H-NMR 1.52 (t, *J* 7.1, 3H), 4.18 (q, *J* 7.0, 2H), 4.34 (d, *J* 3.8, 1H), 5.33 (d, *J* 3.8, 1H), 7.35 (m,2H), 7.88 (m,2H), ^{13}C-NMR 14.0, 65.9, 78.4, 118.4, 127.3, 144.3, 153.3.

Method B. To a stirred solution of **3a** (3.4 g, 15 mmol) in dry THF (40 ml) at 0 °C under a nitrogen atmosphere, 1.2 equivalent of butyllithium (2 M in cyclohexane, 9 ml, 18 mmol) was added dropwise. The mixture was allowed to warm up to 25°C and was stirred overnight. It was then poured into an aqueous solution of sodium hydroxide (1 N) and extracted with diethyl ether (3x30 ml). After drying ($MgSO_4$) and evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography (eluant CH_2Cl_2), yielding 2.4 g (84%) of **4a**.

General procedures for lithiation of 1-Benzotriazolyl-1-ethoxy-ethenes 4

Preparation of **8a,b,c,11.** To a solution of **4a** (5 mmol) in dry THF (20 ml), 1.5 equivalent of butyllithium (2.5 M in pentane, 7.5 mmol) was added at -78 °C. The solution was stirred at -78 °C for 2 h, and a solution of the electrophile (8 mmol, 1.6 equivalent) in 5 ml of THF was added. The reaction mixture was then stirred at -78 °C for 4 h and further 12 h at 25°C. The mixture was then poured into a saturated ammonium chloride solution (50 ml) and extracted with diethyl ether (3 x 30 ml). The combined organic layers were washed with water (25 ml), dried ($MgSO_4$) and concentrated in vacuo. The products were isolated by column chromatography (graduent eluant ethyl acetate / hexane = 1 : 40 then 1 : 10). The spectral data are

summarized in Tables 1 and 2. **7a** Yield : 58% ; Calcd C 64.99, H 6.45, N 20.68, Found C 64.96, H 6.41, N 20.71. **7b** Yield : 64% ; Calcd C 73.08, H 6.14, N 15.05, Found C 73.00, H 6.25, N 14.88. **7c** Yield : 77% ; M/z$^+$ Calcd 261.130, Found 261.131. **11** Yield : 21% ; M/z$^+$ Calcd 261.130, Found 261.128 ; ^{1}H-NMR : 0.0 (s,9H), 1.49 (t, 3H, *J* 7.1), 4.16 (q, 2H, *J* 7.1), 4.65 (s,1H), 7.41 (m, 2H), 7.93 (m, 2H), ^{13}C-NMR 0.0, 14.1, 65.3, 90.5, 118.6, 127.3, 144.0, 155.2.

Preparation of **8d,e**. To a solution of **3a** (2.3 g, 10 mmol) in THF (60 ml), 1.1 equivalent of butyllithium (2.5 M in pentanes; 11 mmol, 4.4 ml) was added dropwise at 0 °C. The solution was stirred at 0 °C for 2 h and further at 25°C for 3 h. The reaction mixture was then cooled to -78 °C and the second equivalent of butyllithium was added. After stirring for 2 h at -78 °C a solution of the carbonyl compound (11 mmol, 1.1 equivalent) was added. The reaction mixture was stirred at -78 °C for 4 h and for a further 12 h at 25°C. The mixture was then treated as in method A. The spectral data are summarized in Tables 1 and 2. **7d** Yield : 35% (m.p. 108 -109°C) ; Calcd C 66.88, H 7.37, N 14.62, Found C 66.79, H 7.41, N 14.68. **7e** : Yield 43% ; Calcd C 69.87, H 6.19, N 13.59, Found C 69.82, H 6.51, N 13.50.

Procedure for the displacement of benzotriazole.

Method A. (Preparation of **13a**). Water (10 ml) and concentrated HCl (1 ml) were added to a solution of **8b** (0.7 g, 2.5 mmol) in 20 ml of ethanol at 25°C. After stirring for 2 days the reaction mixture was poured into water (100 ml), and the aqueous layer was extracted with diethyl ether (3 x 30 ml). The combined organic layers were washed with water (1 x 25 ml), dried ($MgSO_4$), and concentrated in vacuo. The ethyl hydrocinnamate[20] **13a** was distilled under reduced pressure yielding the pure product in 77% yield (0.3 g). ^{1}H NMR: 1.11 (t, *J* 7.1, 3H), 2.50 (t, *J* 8.1, 2H), 2.83 (t, *J* 8.1, 2H), 4.00 (q, *J* 7.1, 2H), 7.15 (m, 5H), ^{13}C NMR: 14.1, 30.9, 35.9, 60.3, 126.1, 128.2, 128.4, 140.5, 172.8.

Method B. (Preparation of **13b, 13c**). The synthesis of **13b** and **13c** can also be performed via a one-pot procedure starting from **4a** using the same procedures as described above. The products were isolated by column chromatography (ethyl acetate / hexane = 1 : 20) to give:

Ethyl cyclohexylideneacetate[21] **13b** (from cyclohexanone, 0.26 g, 34%), ^{1}H NMR: 1.27 (t, *J* 7.2, 3H) 1.63 (m, 6H), 2.2 (m, 2H), 2.83 (m, 2H), 4.14 (q, *J* 7.2, 2H), 5.60 (s, 1H), ^{13}C NMR: 14.2, 26.2, 27.7, 28.5, 29.7, 37.9, 59.3, 112.9, 163.4, 166.7;

Ethyl *trans*-m-methyl-cinnamate[22] **13c** (from m-tolualdehyde, 0.3 g, 31%), ^{1}H NMR: 1.32 (t, *J* 7.1, 3H), 2.33 (s, 3H), 4.25 (q, *J* 7.1, 2H), 6.41 (d, *J* 16.0, 1H), 7.2 (m, 4H), 7.65 (d, *J* 16.0, 1H), ^{13}C NMR: 14.3, 21.2, 60.3, 118.0, 125.2, 128.6, 128.7, 131.0, 134.4, 138.4, 144.7, 166.9.

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REFERENCES

1. Geschwend, H.W.; Rodriguez, H.R., Heteroatom Facilitated Lithiations. In *Organic Reactions*, Vol *26*, Dauben W.G. Ed., J.Wiley & Sons, New York, **1979**, pp 1.
2. Kraus, G.A.; Krolski, M.E., *Synth.Comm.* **1982**, *12*, 521.
3. Baldwin, J.E.; Höfle, G.A.; Lever, W.O.Jr., *J.Am.Chem.Soc.* **1974**, *96*, 7125.
4. McDougal, P.G.; Rico, J.G., *Tetrahedron Lett.* **1984**, *25*, 5977.
5. McDougal, P.G.; Rico, J.G.; VanDerveer, D., *J. Org. Chem.* **1986**, *51*, 4492.
6. Wollenberg, R.H.; Albizati, K.F.; Peries, R., *J. Am. Chem. Soc.* **1977**, *99*, 7365.
7. Lau, K.S.Y.; Schlosser, M., *J.Org.Chem.* **1978**, *43*, 1595.
8. Ficini, J.; Depezay, J.C., *Tetrahedron Lett.* **1968**, *25*, 937.
9. Vlattas, I.; Vecchia, L.D.; Lee, A.O., *J.Am.Chem.Soc.* **1976**, *98*, 2008.
10. Stork, G.; Shiner, C.S.; Cheng, C.W.; Polt, R.L., *J. Am. Chem. Soc.* **1986**, *108*, 304.
11. Katritzky, A.R.; Lang, H.; Lan, X., *Tetrahedron* **1993**, *49*, 2829.
12. Katritzky, A.R.; Lan, X.; Lam, J.N., *Chem Ber.* **1991**, *124*, 1809.
13. Katritzky, A.R.; Lan, X.; Lam, J.N., *Chem Ber.* **1991**, *124*, 1819.
14. Katritzky, A.R.; Yang, Z.; Lam, J.N., *J. Org. Chem.* **1991**, *56*, 6917.
15. Rees, C.W.; Storr, R.C., *J. Chem. Soc. (C)* **1969**, 1478.
16. MOPAC/6.0 : Stewart, J.J.P.; QCPE 455 **1990**.
17. Stewart, J.J.P., *J. Comput. Chem.* **1989**, *10*, 209.
18. Lithium parameters for PM3 : Anders, E.; Koch, R.; Freunscht, P., *J. Comput. Chem.* **1993**, in press.
19. Dewar, M.J.S.; Thiel, W., *J. Am. Chem. Soc.* **1977**, *99*, 4899.
20. Chatterjee, S.; Negishi, E.I., *J. Org. Chem.* **1985**, *50*, 3406.
21. Wadsworth, W.S.; Emmons W.D., *J. Am. Chem. Soc.* ***1961***, *83*, 1733.
22. Hixson, S.S.; Franke, L.A.; Gere, J.A.; Xing, Y., *J. Am. Chem. Soc.* **1988**, *110*, 3601.

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