

Heterocyclic *N*-Glycosyl Derivatives IX.
The Addition Reaction of 1-Chlorobenzotriazole to 2,3-Dihydro-4*H*-pyran.

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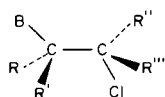
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Recently, Ross and Storr (1) reported the preparation of 1-chlorobenzotriazole, a new stable chemically versatile "positive halogen" reagent. They have also shown (2) that it readily adds to olefins in a stereospecifically *trans* way to give mixtures of 1- and 2-(2-chloroethyl)benzotriazoles in good yield.



B benzotriazol-1-yl, benzotriazol-2-yl

In an attempt to synthesize *N*-glycosyl benzotriazole derivatives with a halogen atom at C-2' of the sugar moiety, the reaction between 1-chlorobenzotriazole and 2,3-dihydro-4*H*-pyran, which can be considered as the simplest glycol, was studied.

When a methylene chloride solution of 1-chlorobenzotriazole was slowly added to an excess of 2,3-dihydro-4*H*-pyran in the same solvent, an instantaneous exothermic reaction took place. On work-up, a complex reaction mixture was obtained which could be resolved by the resulting on the separation of six compounds (I-VI, Chart 1). The structural and configurational assignment of these compounds is based on the following evidence.

The site of attachment of the tetrahydropyran ring to the benzotriazole was ascertained to be N-1 for compounds III, IV and V, and N-2 for compound I and II after comparing (Table I) their uv spectra with those of 1- and 2-alkylbenzotriazoles (3). Further, the nmr spectra of the N-1 compounds showed a complex aromatic pattern, while the nmr spectra of the N-2 derivatives was symmetrical (2).

Compound III was shown to be identical with a sample of 1-(tetrahydro-2-pyranyl)benzotriazole previously prepared from benzotriazole and 2,3-dihydro-4*H*-pyran (4) on the basis of a mixed melting point.

TABLE I

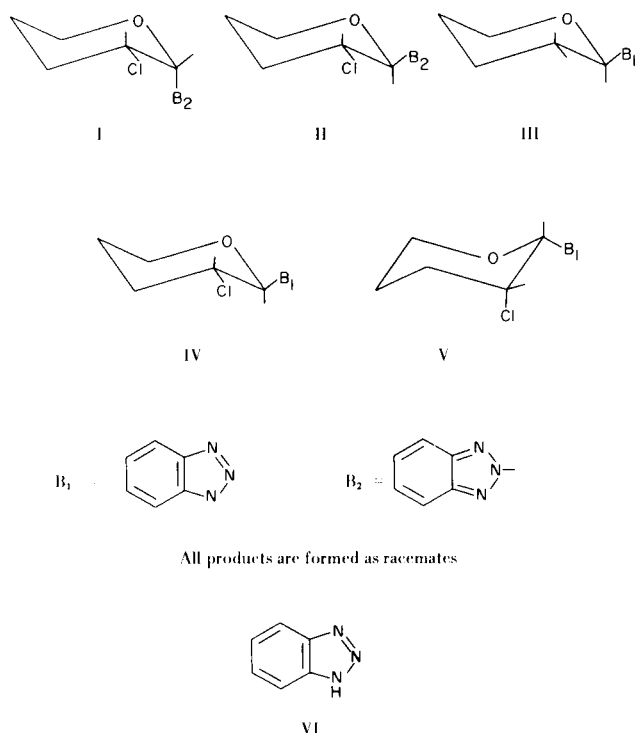
Ultraviolet Absorption Data of the Products Obtained
and Related 1- and 2-Alkylbenzotriazoles

Compound	EtOH λ max (m μ)	ϵ
I	275	10,425
	280	11,275
	287	9,750
II	275	12,078
	280	12,870
	287	11,286
III	255	6,780
	260 (sh)	6,390
	280	4,355
IV	255	7,075
	259 (sh)	6,615
	284	4,300
V	256	7,625
	261	7,235
	283	4,800
1-Alkylbenzotriazole (3)	255	6,460
	283	4,790
2-Alkylbenzotriazole (3)	275	7,950

The nmr spectra of the *trans* compounds II and IV consisted of a doublet for the H-2 proton at 4.08 and 4.01 τ , respectively. The large *vicinal* couplings (Table II) between H-2 and H-3 (8.9 and 9.1 Hz, respectively) indicated a *trans-diaxial* arrangement of these protons. Thus, II is the *trans*-2-(3-chlorotetrahydro-2-pyranyl)benzotriazole and IV is the *trans*-1-(3-chlorotetrahydro-2-pyranyl)benzotriazole.

The nmr spectra of compounds I and V exhibited a doublet for H-2 proton at 3.64 τ ($J_{2,3} = 3.9$ Hz) and 3.68 τ ($J_{2,3} = 2.7$ Hz), respectively. In both cases the magnitude of the coupling constants precluded the possibility

CHART I



of any definitive assignment of C-2 configuration. However, that compound I possessed the *cis* configuration was established utilizing the double-resonance technique to determine the values of the coupling constants $J_{3,4a}$ and $J_{3,4e}$. Irradiation of the doublet at 3.64 τ (H-2) resulted in a collapse of the signal centered at 5.41 τ (H-3) into a quartet (Fig. 1). The magnitudes of the coupling constants $J_{3,4a}$ and $J_{3,4e}$ were 9.1 and 4.4 Hz, respectively, which indicated that H-3 must be axially oriented with the chlorine atom assuming the equatorial position.

As for compound V, irradiation of the doublet at 2.68 τ (H-2) caused collapse of the multiplet centered at 5.31 τ (H-3) to a quartet (Fig. 1) showing splittings of 3.4 and 4.5 Hz corresponding to the couplings of H-3 with the protons in C-4. These values required the H-3 proton to be equatorial. Therefore, the benzotriazol-1-yl moiety must be equatorially oriented.

Noteworthy is the fact that in the *cis* compound V, the chlorine atom is axially oriented whereas in I, a *cis* benzotriazol-2-yl derivative, the chlorine atom is occupying an equatorial position. Although the reason for these stereochemistry preferences are not clear they can be attributed to the effect of the greater steric requirement of the benzotriazol-1-yl moiety in comparison with that of the benzotriazol-2-yl group, which forces the former system to assume an equatorial position.

TABLE II

Nmr Spectral Parameters of the Benzotriazole Derivatives

Compound	H-2	H-3	Chemical Shifts (deuteriochloroform, τ)				H-6a	H-6e	Benzotriazole	
			H-4a	H-4e	H-5a	H-5e				
I	3.64	5.41	7.5-8.5	7.13	7.5	8.5	5.72	6.25	2.11	2.66
II	4.08	5.13	7.8-8.4	7.5	7.8	8.4	6.28	5.93	2.10	2.67
III	4.04	←	7.0	8.7	→		6.20			
IV	4.01	5.16	7.8-8.4	7.5	7.8	8.4	6.27	6.02		
V	3.68	5.31					6.20	5.76		

Coupling Constants (Hz)

Compound	$J_{2,3}$	$J_{3,4a}$	$J_{3,4e}$
I	3.9	9.1	4.4
II	8.9	9.2	4.6
III	8.4-3.1		
IV	9.1		
V	2.7	3.4	and 4.5

The formation of the above compounds I, II, IV and V can be rationalized on the basis of the halonium and oxocarbenium mechanisms proposed by Lemieux and Fraser-Reid (5) for the halogenation and halogenomethoxylations of 2,3-dihydro-4H-pyran. On the other hand, benzotriazole and 1-(tetrahydro-2-pyranyl)benzotriazole (III) probably arose as a consequence of radical side reactions (2).

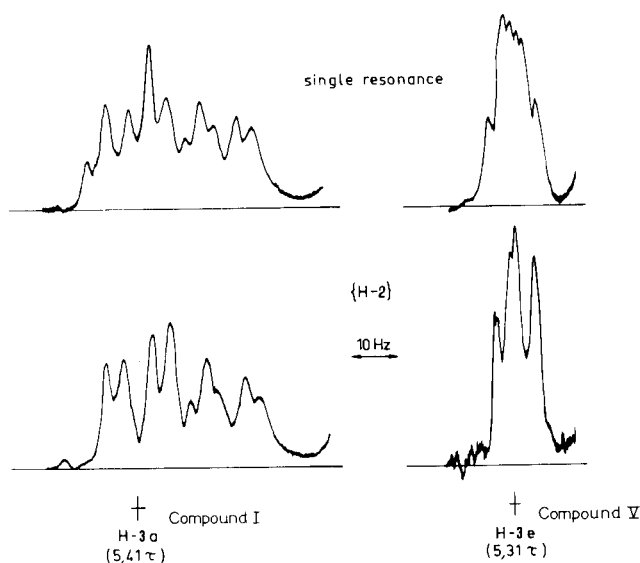


Figure 1

EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were recorded on Perkin-Elmer R-10 and Perkin-Elmer R-12 spectrometers using TMS as the internal standard. Silica gel GF₂₅₄ (Merck) was used for thin layer analyses. Spots were detected with uv light (254 mμ).

Reaction of 1-Chlorobenzotriazole with 2,3-Dihydro-4H-pyran.

A solution of 1.99 g. (0.013 mole) of 1-chlorobenzotriazole (1) in 30 ml. of dry methylene chloride was slowly added to a solution of 1.68 g. (0.02 mole) of freshly distilled 2,3-dihydro-4H-pyran in 25 ml. of methylene chloride and the resulting yellow mixture was set aside at room temperature overnight. It was evaporated *in vacuo*; the residue was dissolved in a small amount of chloroform and applied to 16 preparative tlc plates (20 x 20 cm and 2 mm thickness silica gel, Merck PF₂₅₄). The plates were developed eight times in a mixture of petroleum ether-ether (4:1) resulting in the separation of six bands which were detected by a uv lamp (254 mμ). In all the cases the products were extracted with ethyl acetate.

cis-2-(3-Chlorotetrahydro-2-pyranyl)benzotriazole (1).

The faster moving band afforded 0.46 g. of a syrup which was again chromatographed to give a pure material, which could not be crystallized.

Anal. Calcd. for C₁₁H₁₂ClN₃O: C, 55.57; H, 5.05; N, 17.68. Found: C, 55.51; H, 5.10; N, 17.82.

trans-2-(3-Chlorotetrahydro-2-pyranyl)benzotriazole (II).

The next band gave 0.62 g. of a solid. Recrystallization of this crude product from methanol furnished pure II, m.p. 107-108°.

Anal. Calcd. for C₁₁H₁₂ClN₃O: C, 55.57; H, 5.05; N, 17.68. Found: C, 55.48; H, 5.08; N, 17.63.

1-(Tetrahydro-2-pyranyl)benzotriazole (III).

The following band gave 0.07 g. of a thick oil which crystallized on scratching, m.p. 53-54° (petroleum ether). The melting point of this compound was not depressed when mixed with a sample of III prepared by another method (4).

trans-1-(3-Chlorotetrahydro-2-pyranyl)benzotriazole (IV) and *cis*-1-(3-Chlorotetrahydro-2-pyranyl)benzotriazole (V).

The next band gave 1.45 g. of a thick oil which was shown to be a mixture of compounds IV and V. These two products were separated by thick layer chromatography (20 x 20 cm and 2 mm thickness silica gel PF₂₅₄, Merck). The plates were developed 35 times in a mixture of petroleum ether-ether (4:1). From the faster moving band was obtained 1.02 g. of IV, m.p. 68-69° (ethyl acetate-petroleum ether).

Anal. Calcd. for C₁₁H₁₂ClN₃O: C, 55.57; H, 5.05; N, 17.68. Found: C, 55.68; H, 5.13; N, 17.71.

From the other band isolated 0.35 g. of a syrup which was rechromatographed to give pure V.

Anal. Calcd. for C₁₁H₁₂ClN₃O: C, 55.57; H, 5.05; N, 17.68. Found: C, 55.43; H, 5.27; N, 17.62.

Benzotriazole (VI).

Finally, the slower moving band gave 0.16 g. of a solid which was shown to be benzotriazole by comparison with an authentic sample.

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