N-POLYAZOLYLMETHANES. IV. REACTION OF BENZOTRIAZOLE WITH METHYLENE CHLORIDE AND CHLOROFORM UNDER PHASE TRANSFER CONDITIONS

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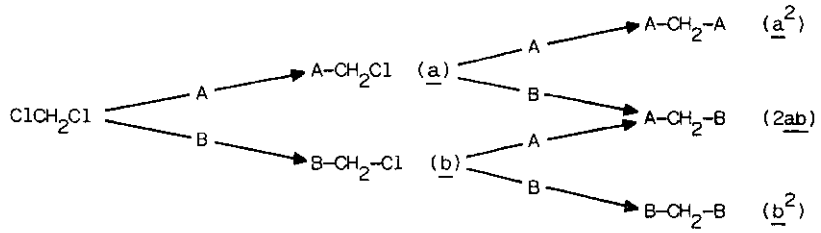
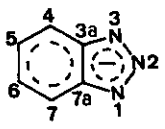
Abstract - Six out of seven possible products obtained from benzotriazole and methylene chloride or chloroform have been isolated and characterized. An intermediate, 2-dichloromethylbenzotriazole, has been isolated for the first time. The relative amounts of the different isomers follow an $(a+b)^n$ relationship (n = 2 or 3). Proton and carbon-13 nmr spectroscopy and mass spectrometry have been used to identify the N,N'-bis-and N,N',N''-trisbenzotriazole derivatives.

In the preceding publications of this series[1-3] it has been shown that methylene chloride reacts with a variety of azoles under PTC conditions to afford N,N'-diazolylmethanes (1,1'-methylenediazoles). When an azole exists as an equilibrium of two tautomers, three isomers are obtained, whose relative amounts follow a relationship of the form $a^2 + 2ab + b^2$, a and b being the amounts of the intermediate, non isolated, $N-CH_2Cl$ derivatives (Scheme 1). [1,2] Since the reaction under PTC conditions takes place on the azole anion, A and B do not represent the individual tautomers but the two nucleophilic centers of a "dissymetric" azole.



Scheme 1

In order to know if this simple rule is always followed, we have studied the reaction of benzotriazole with methylene chloride. Benzotriazole anion 1 presents two different nucleophilic centers, the nitrogen atoms $N_{1(3)}$ and N_2, and according to scheme 1, can give rise to three isomers, the 1,1'-(2), the 1,2'-(3), and the 2,2'-disubstituted derivative (4).



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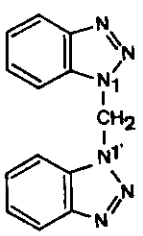

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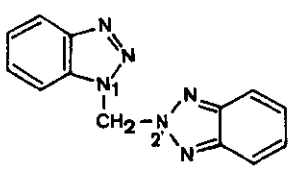

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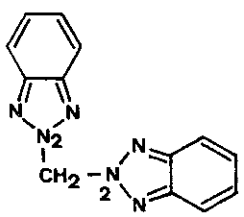

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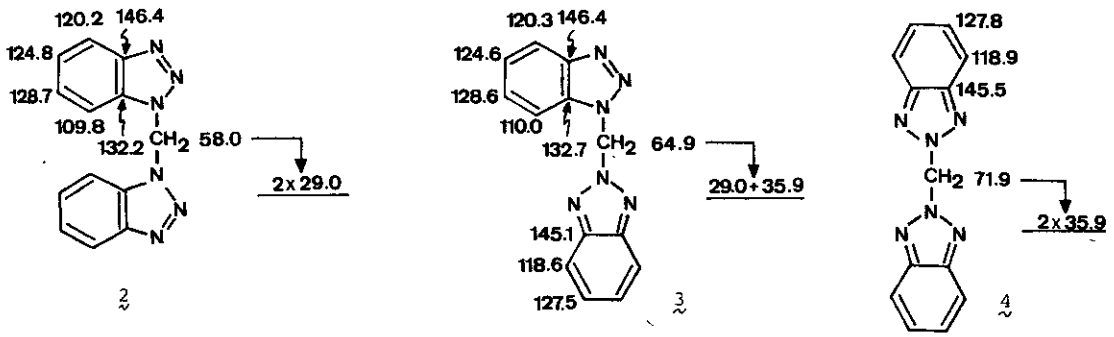
When the experiment was carried out, a complex mixture was obtained with an overall yield of 71%. A careful chromatographic separation allows to obtain three pure samples. The assignment of the structures has been made using concomitantly ^{1}H nmr (at 90 MHz), ^{13}C nmr (at 20 MHz) and mass spectrometry. The most characteristic features are gathered in Table I (the remaining data are to be found in Scheme 2 and in the experimental part).

Table I. Bisbenzotriazolylmethanes

Compound	mp °C	Yield	Rel. amount	^{1}H	^{13}C	ms
2	188	30.4%	50.8%	1 ABCD system, CH_2 at 7.43	6 aromatic carbons CH_2 at 58.0	$[M-N_2]^{+\cdot}$, m* 197 m/z 222 (88%)
3	165.5	24.4%	40.8%	Complex pattern, CH_2 at 7.40	9 aromatic carbons CH_2 at 64.9	$[M-N_2]^{+\cdot}$, m* 197 m/z 222 (43%)
4	153–4	5%	8.4%	1 AA'BB' system, CH_2 at 7.41	3 aromatic carbons CH_2 at 71.9	No loss of N_2 from the $M^{+\cdot}$ peak

Proton nmr spectrum clearly identifies the symmetrical nature of the isobenzotriazole structure 4 by the presence of two superimposed AA'BB' systems at 7.35 and 7.80 ppm (taking the two most intense peaks as an approximation to the real chemical shifts). The other isomers are more difficult to assign, although compound 2 presents an ABCD system (compare with 1-methylbenzotriazole[4]). Carbon-13 nmr spectrum is a perfect tool for this problem. It should be enough to count the number of aromatic carbons to identify 2 [2 x 6], 3 [6 + (2 x 3)], and 4 [4 x 3] (Scheme 2). The assignment of carbons has been made by analogy with those of 1-methyl- and 2-methylbenzotriazoles.[5]



Scheme 2

In the first paper of this series[1] we have found that there is a linear relationship (Eq. 1) between the ^{13}C chemical shifts of the CH_3 in N-methylazoles and the chemical shifts of the CH_2 in diazolylmethanes (separated into two individual contributions).

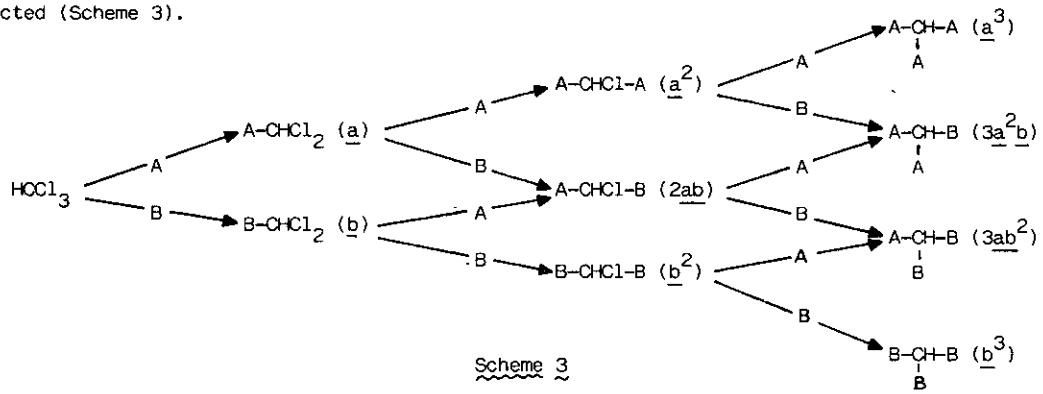
$$\delta(\text{N-Me}) = -3.15 + 1.28\ \delta(\text{N-CH}_2) \qquad [\text{Eq. 1}]$$

From the values of scheme 2 (1-benzotriazolyl, 29.0 ppm, 2-benzotriazolyl, 35.9 ppm) the following values for the N-methyl groups result: 33.9 and 42.8 ppm which compare very well with the experimental values (33.7 and 42.8 ppm respectively).[5]

Mass spectrometry provides an independent method of assignment which takes into account the fact that only 1-substituted derivatives lose nitrogen from the molecular peak.[6] The fragment m/z 222 is about two times more intense in the mass spectrum of 2 (1,1'-derivative) than in the mass spectrum of 3 (1,2'-derivative). The spectrum of 2 shows a peak at m/z 104 and that of 4 a peak at m/z 105; in compound 3 both peaks are present.

The three isomers unambiguously assigned, it is now possible to examine the relative amounts of table I searching for a verification of the rule $(\underline{a} + \underline{b})^2$. For $\underline{a}$ = 71 and $\underline{b}$ = 29, the relation gives 50.5% of $\underline{a}^2$, 41% of 2$\underline{ab}$, and 8.5% of $\underline{b}^2$, almost exactly the values of table I. A ratio 71/29 for competition between positions 1(3) and 2 compares well with the results of N-methylation (62/38) and of N-amination (78/22).[7]

After verifying that both the equation of the percentages (Scheme 1) and that of the ^{13}C chemical shifts (Eq. 1) were fulfilled, it was decided to extend the reaction to the more complex case of chloroform. Chloroform and azoles react under PTC conditions to yield either products resulting of dichlorocarbene addition[8] to an heterocyclic C = C double bond or triazolylmethanes (1,1',1''-methinetriazoles).[9] The yields were generally very low. A better PTC procedure having recently been discovered,[10] the reaction was tried with benzotriazole. In this case an $(\underline{a} + \underline{b})^3$ relationship was expected (Scheme 3).



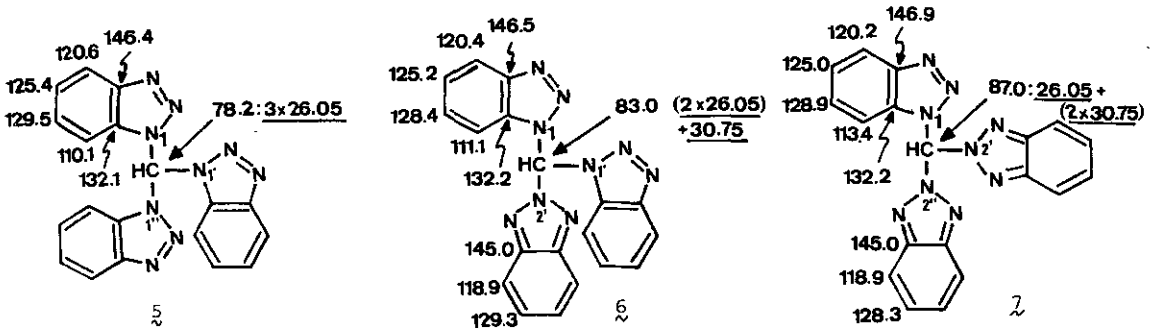
Scheme 3

Four products were isolated and a fifth one was observed in TLC but in a too low proportion to be identified (overall yield before separation about 45%). The same methods as previously described, were used to identify the four compounds (Table II).

Table II. Trisbenzotriazolylmethanes

Compound	mp °C	Yield	Rel.amount	^1H	^{13}C	ms
5	191	20.4%	65.05%	1 ABCD system, CH at 10.21	6 aromatic carbons CH at 78.2	$[M-C_6H_4N_3]^{+\cdot}$ m/z 249 (32%)
6	149	9.5%	30.3%	Complex pattern CH at 10.27	9 aromatic carbons CH at 83.0	$[M-C_6H_4N_3]^{+\cdot}$ m/z 249 (30%)
7	188	1.45%	4.65%	Complex pattern CH at 10.23	9 aromatic carbons CH at 87.5	$[M-C_6H_4N_3]^{+\cdot}$ m/z 249 (36%)
9	77.5	2.3%	----	1 AA'BB' system CH at 8.12	3 aromatic carbons CH at 79.5	$M^{+\cdot}$ 201 (40%), 203 (25%), 205 (5%)

The ^1H nmr spectrum of the low melting compound shows the CH signal at 8.12 ppm, too different from the other values to be the 2,2',2''-isomer 8. The ^{13}C spectrum confirms the 2-substituted benzotriazole structure, but here the CH signal is in the same region than the others.[11] Finally, the mass spectrum identifies the compound as a dichloromethyl derivative ; this fact together with nmr results establishes definitively the structures as 2-dichloromethylbenzotriazole 9. Mass spectrometry was not useful to identify the 5, 6, 7 isomers, since all of them lose benzotriazole from the molecular peak. However, ^{13}C nmr spectrum allows to assign the three isomers as the 1,1',1''-, 1,1',2''-, and 1,2',2''-isomers respectively by simply counting the number of different aromatic carbons (Scheme 4).



Scheme 4

Comparing the contributions of each benzotriazole to the CH chemical shifts (Scheme 4) with those of Scheme 2, it appears that equation 1 still holds, simply changing N-Me by $N-CH_2$ and $N-CH_2$ by N-CH (Equation 2). Both equations could be written taking δ N-Me (the richest collection of available data) as independent variable (Equations 3 and 4).

$$\delta(N-CH_2) = -3.15 + 1.28\,\delta(N-CH) \quad [\text{Eq. } 2]$$

$$\delta(N-CH_2) = 2.46 + 0.78\,\delta(N-Me) \quad [\text{Eq. } 3]$$

$$\delta(N-CH) = 4.38 + 0.61\,\delta(N-Me) \quad [\text{Eq. } 4]$$

From the chemical shifts of the N-methyl groups in 1-benzotriazole (33.9 ppm[5]) and in 2-benzotriazole derivatives (42.8 ppm[5]), equations 3 and 4 gave the following values: 1-$N-CH_2$ 28.9 (exp. 29.0 ppm), 2-$N-CH_2$ 35.8 (exp. 35.9 ppm), 1-N-CH 25.1 (exp. 26.05), and 2-N-CH 30.5 (exp. 30.75ppm).

It is now possible to come back to scheme 3. The relative amounts in table II correspond to 86.7% a and 13.3% b: 5, a^3 = 65.2% (exp. 65.05%). 6, $3a^2b$ = 30.0% (exp. 30.3%), 7, $3ab^2$ = 4.6% (exp. 4.65%). The fourth isomer, 2,2',2''-trisbenzotriazolylmethane 8 corresponding to b^3 = 0.23% (about 0.005 g) is probably the non identified 2nd fraction of the chromatography.

With methylene chloride the ratio a/b was 71/29 and now with chloroform we obtain a value 86.7/13.3 *However, it must be considered that a part of the reaction stopped at the first step, since 2.3% of* compound 9 (B-$CHCl_2$ in scheme 3) was isolated unreacted. Thus, in the first step 80.3% of A-$CHCl_2$ and 19.7% of B-$CHCl_2$ was formed but, if the first one continued to react with more benzotriazolyl anions, B-$CHCl_2$ was partly isolated as such (9, 7.4% relative amount) and partly (12.3%) continued the reactions of scheme 3. Thus a more realistic ratio in the case of chloroform would be 80.3/19.7, closer to the methylene chloride ratio. Due to the relative fragility of compound 9 it is possible that the isolated quantity (0.087 g) does not correspond to the total amount of compound formed in the reaction.[13]

EXPERIMENTAL[14]

Synthesis of N,N'-Dibenzotriazolylmethanes

2.00 g (16.8 mmoles) of benzotriazole, 2.32 g (16.8 mmoles) of anhydrous potassium carbonate, 1.11 g (16.8 mmoles) of powdered potassium hydroxide, 0.289 g (0.85 mmoles) of tert-butylammonium bisulphate and 50 ml of methylene chloride were vigorously stirred and refluxed overnight. Then, the mixture was filtered and the residue washed twice whith hot methylene chloride (2 X 50 ml). The combined organic phases were dried and evaporated under reduced pressure yielding 1.5 g of a white solid (pure mixture of isomers by ^1H nmr), yield = 71.5%. The crude product so obtained was chromatographed on 150 g silica gel 70-230 mesh affording two fractions:

The 1st fraction eluted with methylene chloride (r_f : 0.75, methylene chloride) gave 0.105 g, corresponding to 2,2'-dibenzotriazolylmethane 4. Yield in isolated product = 5 %, mp 153-154°C. IR (KBr

pellet) 3090, 3040, 2980, 1560, 1450, 850, 750 cm^{-1}. ^{1}H-nmr ($CDCl_3$ plus TMS) δ 7.75–7.95 (4H, m), 7.41 (2H, s), 7.20–7.40 (4H, m). Ms: $M^{+\cdot}$ 250 (50), m/z 132 (60), 105 (69), 77 (100). UV (EtOH) λ_{max} 282 (23500), 289 (23500).

The 2nd fraction eluted with methylene chloride (r_f: 0.45, methylene chloride gave 1.20 g, corresponding to a mixture which was chromatographed again on 120 g silica gel 70–230 mesh affording two products: 1st product eluted with hexane/ether (1:1)(r_f: 0.28 hexane/ether 1:1) gave 0.513 g, corresponding to 1,2'-dibenzotriazolylmethane 3. Yield in isolated product: 24.4%, mp 165.5°C. IR (KBr pellet) 3060, 3040, 2980, 1560, 1450, 850, 750 cm^{-1}. ^{1}H-nmr ($CDCl_3$ plus TMS) δ 7.80–8.10 (4H, m), 7.40 (2H, s), 7.25–7.65 (4H, m). Ms: $M^{+\cdot}$ 250 (43). m/z 222 (43), 132 (100), 105 (36), 104 (60), 77 (86). UV (EtOH) λ_{max} 279 (16880), 286 (15490). The 2nd product eluted with hexane/ether (1:1) (r_f: 0.16 hexane/ether 1:1) was 1,1'-dibenzotriazolylmethane 2 (0.638 g). Yield of isolated product 30.4%, mp. 188°C. IR (KBr pellet) 3090, 3010, 2960, 1610, 1590, 1490, 1450, 950, 750 cm^{-1}. ^{1}H-nmr ($CDCl_3$ plus TMS) δ 7.85–8.15 (4H, m), 7.43 (2H, s), 7.25–7.65 (4H, m). Ms: $M^{+\cdot}$ 250 (27), m/z 222 (88), 132 (87), 104 (100), 77 (86). UV (EtOH) λ_{max} 254 (34500), 282 (7247).

Synthesis of N,N',N''-Trisbenzotriazolylmethanes

2.00 g (16.8 mmoles) of benzotriazole, 12.0 g (85 mmoles) of anhydrous potassium carbonate, 0.289 g (0.85 mmoles) of tetrabutylammonium bisulphate and 50 ml chloroform were vigorously stirred and refluxed overnight. Then the mixture was filtered and the residue washed with hot chloroform (3 x 50 ml). The combined organic phases were dried and concentrated under vacuum to leave 1.2 g of a brown oil (purity of the crude from ^{1}H nmr: 77%, yield = 45%). The crude was purified by column chromatography on 160 g silica gel 70–230 mesh and eluted with methylene chloride giving five fractions. In increasing polarity order they were:

1st fraction: r_f: 0.76 (methylene chloride). 0.087 g of 2-benzotriazolyldichloromethane 9 were collected, yield in isolated product = 2.3%, mp 77.5°C. IR (film) 3060, 3005, 1560, 1450, 1340, 1255, 865, 775 cm^{-1}. ^{1}H nmr ($CDCl_2$ plus TMS) δ 8.12 (1H, s), 7.75–7.95 (2H, m), 7.30–7.50 (2H, m). ^{13}C nmr ($CDCl_2$ plus TMS) δ 145.1 (C_{3a}, C_{7a}), 128.6 (C_5, C_6), 118.9 (C_4, C_7), 79.5 ppm ($CHCl_2$). Ms $M^{+\cdot}$ 201 (40), 203 (25), 205 (5), m/z 166 (70), 168 (22), 111 (100), 113 (32).

2nd fraction: r_f: 0.65 (methylene chloride). Less than 0.005 g of an unidentified product were collected.[15]

3rd fraction: r_f: 0.55 (methylene chloride). 0.033 g of 1,2',2''-trisbenzotriazolylmethane 7 were collected. Yield in isolated product = 1.46%, mp 188°C. IR (film) 3070, 2940, 1560, 1450, 1330, 1250, 875, 740 cm^{-1}. ^{1}H nmr ($CDCl_3$ plus TMS) δ 10.23 (1H, s), 8.3 (1H, m), 7.65–7.85 (4H, m), 7.25–7.45 (7H, m). Ms $M^{+\cdot}$ 367 (4), m/z 249 (50), 193 (34), 192 (37), 166 (100), 140 (36), 90 (32), 76 (32). UV (EtOH) λ_{max} 212 (48700), 282 (28500), 290 (27670).

4th fraction: r_f: 0.43 (methylene chloride). 0.212 g of 1,1',2''-trisbenzotriazolylmethane 6 were collected. Yield in isolated product = 9.5%, mp 149°C. IR (KBr pellet) 3060, 2940, 1610, 1590, 1560, 1450, 1330, 1270, 825, 740 cm^{01}. ^{1}H nmr ($CDCl_2$ plus TMS) δ 10.27 (1H, 2), 7.30–8.30 (12H, m). Ms $M^{+\cdot}$ 367 (4), m/z 249 (35), 193 (25), 192 (28), 166 (73), 140 (58), 103 (61), 90 (42), 77 (100). UV (EtOH) λ_{max} 258 (18110), 282 (19750), 288 (18700).

5th fraction: r_f: 0.31 (methylene chloride). 0.458 g of 1,1',1''-trisbenzotriazolylmethane 5 were collected. Yield in isolated product 20.4%, mp 191°C. IR (KBr pellet) 3080, 2940, 2910, 2840, 1610, 1590, 1450, 1350, 1290, 820, 740 cm^{-1}. ^{1}H nmr ($CDCl_3$ plus TMS) δ 10.21 (1H, s), 7.95–8.10 (3H, m), 7.20–7.40 (9H, m). Ms. $M^{+\cdot}$ 367 (5). m/z 249 (33), 221 (18), 193 (14), 192 (20), 166 (33), 140 (28), 103 (78), 90 (24), 77 (100). UV (EtOH) λ_{max} 253 (21370), 284 (10500).

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11. This difference between both nuclei is due to the fact that ^{1}H chemical shifts are more sensitive to ring current anisotropies whereas ^{13}C chemical shifts are more sensitive to electronic effects. Since chlorine and benzotriazoles are arenologues[1,12], the chemical shift of the CH is rather insensitive to the replacement of Cl by the heterocycle (the signal of chloroform itself appears at 78.0 ppm).
12. T. Kauffmann, Angew. Chem., Int. Ed. Eng., 1971, 10, 743.
13. A 71/29 ratio would involve the formation of 0.26 g (6.9% yield) of 9.
14. All the new compounds described here give correct analytical results (C,H,N). The nmr spectra were recorded in $CDCl_3$ at 90 MHz for the proton (Varian EM-390) and at 20 MHz for carbon-13 (Bruker WP80SY). Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6M working at 70 eV.
15. Analogously to the ^{13}C chemical shifts of the CH groups (Scheme 4), the r_f values can be divided into individual contributions of each benzotriazole. A 1-benzotriazolyl substituent contributed with a 0.105 increment to the total r_f and a 2-benzotriazolyl one with 0.220. Thus for compounds 5, 6, and 7, the calculated (and experimental) r_f will be respectively 0.315 (0.31), 0.43 (0.43), and 0.545 (0.55). The fourth isomer, the 2,2',2''-trisbenzotriazolylmethane will have an r_f values of 0.66, confirming that the non identified compound (r_f = 0.65) is probably the isomer 8.

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