

## ON THE POSSIBILITY OF CHLOROTROPY IN AROMATIC AZOLES:

## THE CASE OF 1,2,3-TRIAZOLES AND BENZOTRIAZOLES

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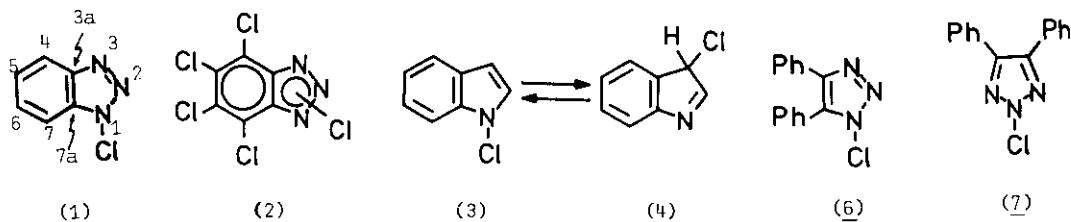
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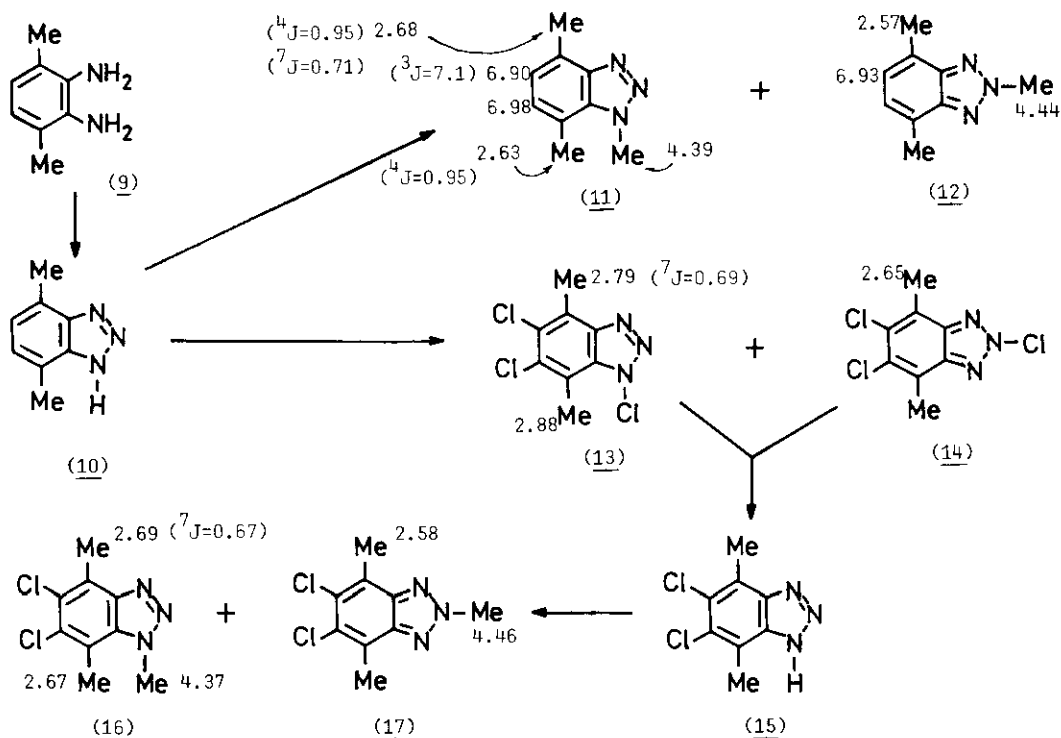
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**Abstract-** A <sup>13</sup>C n.m.r. study of *N*-chloro derivatives of 4,5-diphenyl-1,2,3-triazole and 5,6-dichloro-4,7-dimethylbenzotriazole reveals that neither a rapid chlorotropy nor a slow chlorine equilibration takes place. For the first time, a derivative of 2-chlorobenzotriazole has been characterized.

Although most tautomeric studies deal with prototropy,<sup>1</sup> almost any atom in a molecule could move from one tautomeric position to another, provided that sufficient energy is given to the system, and the heterocycle is stable under the conditions of the experiment. Thus, it is well established that methyltropies are too slow ( $\Delta G^\ddagger > 30 \text{ kcal.mol}^{-1}$ ) to detect equilibrium mixtures by n.m.r.,<sup>2</sup> and that metallotropies are rapid processes, in which separated<sup>3</sup> or averaged<sup>4</sup> signals are observed, depending on the metal. For halogenotropies, however, the literature results are contradictory, specially in the case of chlorotropies. <sup>1</sup>H n.m.r. showed that *N*-chlorobenzotriazole was a *N*-1 substituted derivative (1).<sup>5</sup> A comparative i.r. study showed a similar structure for *N*-bromo- and *N*-iodobenzotriazoles, but the extreme insolubility of these compounds, as well as of *N*,4,5,6,7-pentachlorobenzotriazole (2) precluded any n.m.r. study.<sup>6</sup> In the indole series, kinetic measurements lead De Rosa *et al.*<sup>7</sup> to propose an equilibrium between *N*-chloroindole (3) and 3-chloro-3*H*-indole (4). For 4,5-diphenyl-1,2,3-triazole (5), finally, the mass spectrum of the *N*-chloro-derivative was consistent with the 1-chloro structure (6), but the symmetry of the <sup>1</sup>H n.m.r. spectrum (220 MHz, CDCl<sub>3</sub>) suggested the authors<sup>8</sup> that "the chlorine is rapidly equilibrating between *N*-1 and *N*-3, or that the chlorine is on *N*-2", as in (7).



In order to have a better insight into the structure of this family of compounds, we registered the  $^{13}\text{C}$  n.m.r. spectrum of 1-chlorobenzotriazole (1). The chemical shifts were very close to those of 1-methylbenzotriazole (8)<sup>9</sup> (Table). No signals corresponding to the isomeric 2-chlorobenzotriazole were detected; there was neither chlorotropy (the signals were quite narrow at room temperature), nor equilibrium, although the 2-chloro "tautomer" could be in a very small proportion, not detectable by n.m.r. Searching for a steric effect that could favor the 2-Cl isomer over the 1-Cl, we prepared the chlorinated and *N*-methylated derivatives of 4,7-dimethylbenzotriazole (10) (Scheme).



Scheme

4,7-Dimethylbenzotriazole (10) (mp 276-278°C) was obtained in 91% yield from the diamine (9)<sup>10</sup> (sodium nitrite-aq. acetic acid). The methylation of (10) ( $\text{CH}_3\text{I}/\text{CH}_3\text{ONa}/\text{CH}_3\text{OH}$ ) gave a mixture of the 2-methyl- (mp 65-67°C) and 1-methyl- (mp 68-70°C) benzotriazoles (12) and (11) (ratio 33:67), which were separated by column chromatography (silica gel; hexane-ethyl acetate 60:40). Chlorination of (10), carried out by the Rees-Storr procedure<sup>5</sup> (sodium hypochlorite in acetic acid) afforded a 60:40 mixture of the trichlorobenzotriazoles (13) and (14). Our efforts to isolate the pure components by chromatography were unsuccessful (*N*-dechlorination, or chlorination of the benzylic methyl groups), and crystallization of the mixture in different solvents gave only new mixtures enriched in one or the other derivative. To our knowledge, (14) is the first

example of a 2-chlorobenzotriazole so far described. Compounds (16) (mp 186-190°C) and (17) (mp 143-146°C) were obtained by *N*-dechlorination of the mixture of (13) and (14) with methanol (84%), followed by methylation of the resulting benzotriazole (15) (mp 292°C) as above. The compounds were obtained in a ratio 70:30, and separated by column chromatography, the 2-methyl isomer (17) being eluted first.

<sup>13</sup>C n.m.r. data for the *N*-substituted benzotriazoles are collected in the Table. The signals were assigned by comparison to literature values for (8)<sup>9</sup> and by careful selective decoupling experiments. For the <sup>1</sup>H n.m.r. spectra (200 MHz, values typed on the Scheme), the most remarkable feature was the observation of the <sup>7</sup>J coupling constants between the protons of the methyl groups in C<sub>4</sub> and C<sub>7</sub> in the 1-substituted derivatives (11), (13), and (16). Analogous couplings have been observed previously in other heterocycles.<sup>11</sup>

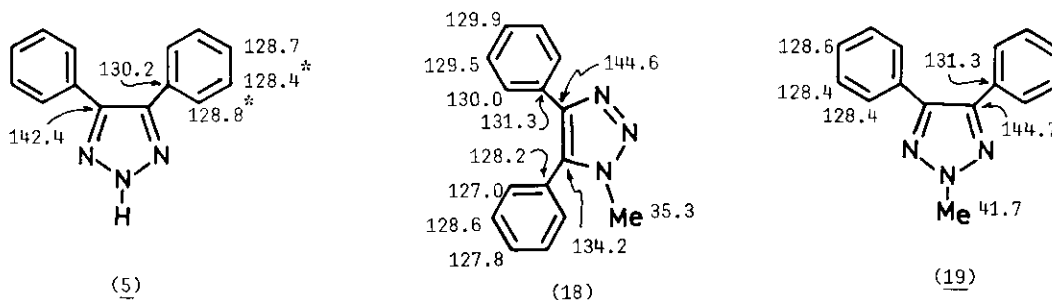
Table. <sup>13</sup>C Chemical shifts of *N*-substituted benzotriazoles (50.32 MHz, CDCl<sub>3</sub>)<sup>a</sup>

Compound	C <sub>3a</sub>	C <sub>4</sub>	C <sub>5</sub>	C <sub>6</sub>	C <sub>7</sub>	C <sub>7a</sub>	Me <sub>4</sub>	Me <sub>7</sub>	N-Me
(1) <sup>b</sup>	144.1	120.5	125.1	129.3	109.3	134.1	--	--	--
(8) <sup>b,c</sup>	145.5	119.3	123.4	126.8	108.8	133.1	--	--	33.7
(11)	146.5	128.2	123.6	128.2	117.7	132.7	16.2	17.6	36.5
(12)	145.0	125.5	125.5	125.5	125.5	145.0	16.7	16.7	42.9
(13)	142.6	128.3	129.6	134.4	117.7	131.1	14.6 <sup>d</sup>	14.7 <sup>d</sup>	--
(14)	143.6	124.5	131.4	131.4	124.5	143.6	15.4	15.4	--
(16)	145.1	128.2	127.7	132.4	117.4	131.4	15.1 <sup>d</sup>	15.8 <sup>d</sup>	37.3
(17)	143.4	124.9	129.8	129.8	124.9	143.4	15.4	15.4	43.2

<sup>a</sup>See formula (1) for the numbering of the carbon atoms; <sup>b</sup>20.15 MHz;

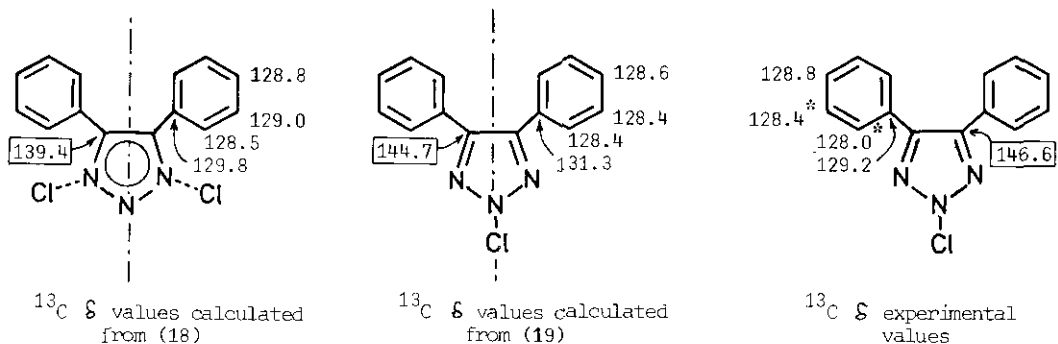
<sup>c</sup>From ref. 9); <sup>d</sup>These assignments can be reversed.

In the case of 4,5-diphenyl-1,2,3-triazole (5), both *N*-methyl derivatives (18) and (19) were prepared according to Gilchrist *et al.*<sup>12</sup> From the reported <sup>13</sup>C chemical shifts of 1-methyl-1,2,3-triazole,<sup>13</sup> the following assignments were made (those labelled with an asterisk could be reversed):



It was now possible to establish if the *N*-chloro derivative of (5) has the structure (6) (with a rapid *N*-1 ⇌ *N*-3 chlorotropy), or the structure (7). Since

there is almost no difference between  $^{13}\text{C}$  chemical shifts of *N*-methyl- and *N*-chlorobenzotriazoles (see Table), we can assume that chemical shifts for compound (6) should be similar to (18) (but with averaged values, to explain the "symmetry" of the spectra, both by  $^1\text{H}$ ,<sup>8</sup> or by  $^{13}\text{C}$  n.m.r.), and that structure (7) should be similar to (19). Only the heterocyclic carbon atom is significantly different in both structures. The experimental value, 146.6 ppm, proves without ambiguity that the chlorination product is (7).



In any of the compounds of this study we have observed neither a fast chlorotropic tautomerism nor an equilibrium between the *N*-chloro isomers [the mixtures of (13) and (14) of different ratios, obtained by crystallization, decompose on standing, but does not equilibrate]. Thus, the  $\text{C-Cl} \rightleftharpoons \text{N-Cl}$  equilibrium, claimed for the indoles (3)  $\rightleftharpoons$  (4), where a C-Cl bond has to be broken to obtain *N*-chloroindole from (4), seems unlikely.

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