

# INTRAMOLECULAR 1,3-DIPOLAR CYCLOADDITIONS OF ARYL AZIDES ON ALKYNYL AND ALKENYL GROUPS

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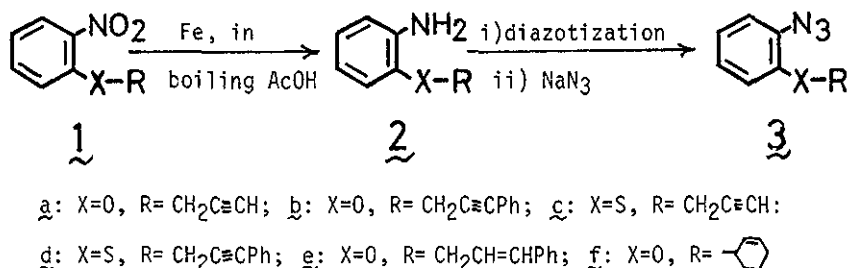
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Aryl azides 3 containing alkynyl or alkenyl group as dipolarophile were prepared and thermally decomposed in benzene. Azides 3a-3d gave the corresponding 1,3-cycloadducts, fused-ring 1,2,3-triazoles 8a-8d, while bridgehead nitrogen aziridines 9 and 10, were obtained from 3e and 3f, probably via unstable  $\Delta^2$ -1,2,3-triazolines.

In spite of a large number of studies on intermolecular 1,3-dipolar cycloadditions, the intramolecular ones are not yet extensively investigated. Only few intramolecular cycloadditions have been reported on alkenyl and/or alkynyl nitrones,<sup>1</sup> azomethanimines,<sup>2</sup> nitrilimines,<sup>3</sup> and azides.<sup>4</sup> As seen in these examples, the intramolecular cycloaddition of a properly functionalized 1,3-dipoles provides a useful route for the preparation of fused heterocycles. In addition, Hall, et al.<sup>5</sup> have demonstrated that an intramolecular 1,3-dipolar cycloaddition of the azido group to the carbonyl function is involved in the formation of 3-phenylanthranils from 2-azidobenzophenones.

Therefore, we planned to investigate the intramolecular cycloadditions of azides where the azido and alkynyl or alkenyl groups are connected through an aromatic ring, and here wish to report our findings. After the completion of this work,<sup>6</sup> we learned that similar reactions have been recently reported by Fusco and his co-workers.<sup>7</sup>

Azides 3 were prepared from the corresponding nitrobenzenes 1, which were obtained by the reaction of o-nitrophenol or o-nitrothiophenol with propargylic or allylic bromides, as shown in Scheme 1. The yields, physical and spectral data of new nitrobenzenes 1, anilines 2, and azides 3,<sup>8</sup> are given in Table 1.



Scheme 1

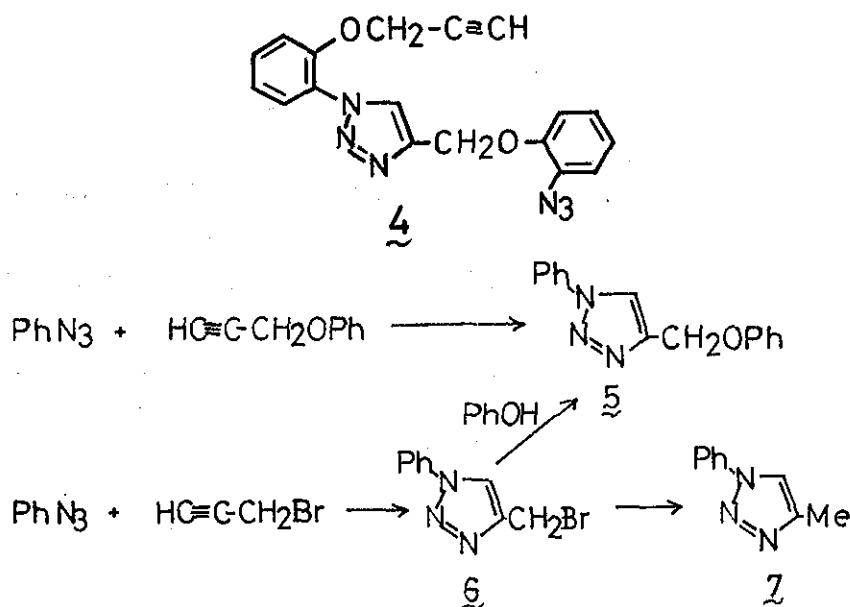
Azides 3, with the exception of 3a, were purified by chromatography over silica gel using benzene as eluent. On chromatography, 3a was partially converted into dimer 4 and triazole 8a (see later). The structure of 4, mp 97-98.5°, was deduced on the basis of the following evidence. Ir  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup>: 3240, 2100; nmr (CDCl<sub>3</sub>)  $\delta$ : 2.55 (1H, t, ≡CH, J=3 Hz), 4.75 (2H, d, OCH<sub>2</sub>C≡, J=3 Hz), 5.37 (2H, s, OCH<sub>2</sub>), 6.9-8.0 (8H, m, aromatic protons), 8.30 (1H, s, =CH); mass m/e 346 (M<sup>+</sup>), 318 (M<sup>+</sup> - N<sub>2</sub>).

In addition, it has been found that the cycloaddition of phenyl azide to phenyl propargyl ether gave 1-phenyl-4-phenoxyethyl-1,2,3-triazole (5), mp 89.5-90.5°, in 61% yield [nmr (CDCl<sub>3</sub>)  $\delta$ : 5.28 (2H, s, OCH<sub>2</sub>), 6.9-7.8 (10H,

Table 1 Compounds 1, 2 and 3

| Compound               | Yield<br>% | Mp., °C<br>(Bp., °C/mm) | Nmr, $\delta$ ppm (J, Hz) <sup>a</sup>                                                                                                                             |
|------------------------|------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>1c</u>              | 99         | 96-97                   | 2.28(1H, t, $\equiv\text{CH}$ , J=3), 3.7(2H, d, $\text{CH}_2$ , J=3), 7.2-8.3(4H, m, aromatic protons)                                                            |
| <u>1d</u>              | 65         | 88.5-90                 | 3.75(2H, s, $\text{CH}_2$ ), 7.26, 7.5-8.3(5H, s, and 4H, m, aromatic protons) <sup>b</sup>                                                                        |
| <u>1f</u>              | 67         | oil<br>(151.5/3)        | 1.5-2.3(6H, m, $\text{CH}_2$ ), 4.8(1H, m, $\geq\text{CH}$ ), 5.5-6.1(2H, m, $=\text{CH}$ ), 6.7-8.0(4H, m, aromatic protons) <sup>b</sup>                         |
| <u>2c</u>              | 51         | oil<br>(131/3)          | 2.2(1H, t, $\equiv\text{CH}$ , J=3), 3.42(2H, d, $\text{CH}_2$ , J=3), 4.24(2H, br, $\text{NH}_2$ ), 6.5-7.6(4H, m, aromatic protons)                              |
| <u>2d</u>              | 21         | oil                     | 3.65(2H, s, $\text{CH}_2$ ), 4.35(2H, br, $\text{NH}_2$ ), 6.5-7.6(4H, m, aromatic protons)                                                                        |
| <u>2f</u>              | 48         | oil<br>(144.5-147/5)    | 1.5-2.2(6H, m, $\text{CH}_2$ ), 3.6(2H, br, $\text{NH}_2$ ), 4.65(1H, m, $\geq\text{CH}$ ), 5.83(2H, m, $=\text{CH}$ ), 6.3-6.8(4H, aromatic protons) <sup>b</sup> |
| <u>3c</u> <sup>c</sup> | 31         | oil                     | 2.2(1H, t, $\equiv\text{CH}$ , J=3), 3.52(2H, d, $\text{CH}_2$ ), 7.0-8.1(4H, m, aromatic protons)                                                                 |
| <u>3d</u> <sup>c</sup> | 50         | oil                     | 3.8(2H, s, $\text{CH}_2$ ), 6.9-7.6(9H, m, aromatic protons)                                                                                                       |
| <u>3f</u> <sup>c</sup> | 50         | oil                     | 1.3-2.4(6H, m, $\text{CH}_2$ ), 4.7(1H, m, $\geq\text{CH}$ ), 5.88(2H, m, $=\text{CH}$ ), 6.6-7.3(4H, m, aromatic protons)                                         |

<sup>a</sup>Internal standard: TMS. Unless otherwise provided, the spectra were measured in  $\text{CDCl}_3$ . <sup>b</sup>Measured in  $\text{CCl}_4$ . <sup>c</sup>In the ir spectrum a strong band appeared in the region 2100-2140  $\text{cm}^{-1}$ .

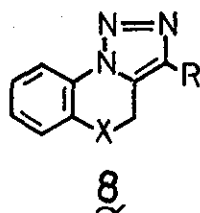


Scheme 2

m, aromatic protons), 8.02 (1H, s, =CH)]. Triazole 5 was identical with an authentic sample prepared from 1-phenyl-4-bromomethyl-1,2,3-triazole (6), mp 120.5-121.5°, which was converted into the known 4-methyl derivative 7, mp 81-82° (lit.<sup>9</sup> mp 81°), as depicted in Scheme 2.<sup>10</sup> 6: nmr (CDCl<sub>3</sub>) δ 4.64 (2H, s, CH<sub>2</sub>), 7.3-7.8 (5H, m, aromatic protons), 8.01 (1H, s, =CH).

When azide 3a was heated in boiling benzene for 6 hr until the starting material was consumed, the expected 1,3-cycloadduct 8a was obtained in good yield. Under similar conditions, azides 3b-3d gave the corresponding 1,3-cycloadducts, triazoles 8b-8d, respectively.

The reaction times, and yields, physical and spectral data are given in Table 2. The structures of all 8 were confirmed on the basis of their spectral data.



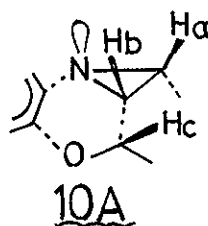
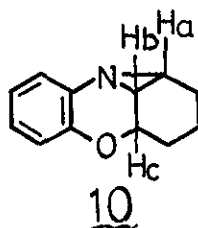
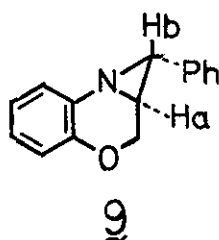
- a: X=O, R=H
- b: X=O, R=Ph
- c: X=S, R=H
- d: X=S, R=Ph

Table 2 Decomposition of Azides 3

| Azide     | Time<br>hr | Product      |                                |                                                                                                                                                                                                           |                                                                                         |
|-----------|------------|--------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
|           |            | Yield<br>%   | Mp.<br>°C                      | Nmr(CDCl <sub>3</sub> ), $\delta$ ppm (J, Hz)                                                                                                                                                             | Mass, m/e                                                                               |
| <u>3a</u> | 6          | <u>8a</u> 81 | 58-59<br>(52 <sup>7</sup> )    | 5.4(2H, s, CH <sub>2</sub> ), 6.9-7.4, 7.9-8.2<br>(3H and 1H, m, aromatic protons),<br>7.63(1H, s, =CH)                                                                                                   | 173(M <sup>+</sup> ), 145<br>(M <sup>+</sup> -N <sub>2</sub> ), <sup>a</sup> 119<br>117 |
| <u>3b</u> | 10         | <u>8b</u> 86 | 193-194<br>(195 <sup>7</sup> ) | 5.55(2H, s, CH <sub>2</sub> ), 7.0-8.2(9H, m,<br>aromatic protons)                                                                                                                                        | 249(M <sup>+</sup> ), 221<br>(M <sup>+</sup> -N <sub>2</sub> ), <sup>a</sup> 220        |
| <u>3c</u> | 3          | <u>8c</u> 60 | 80-81                          | 4.1(2H, s, CH <sub>2</sub> ), 7.6(1H, s, =CH),<br>7.2-7.5, 8.0-8.3(3H and 1H, m,<br>aromatic protons)                                                                                                     | 189(M <sup>+</sup> ), 161<br>(M <sup>+</sup> -N <sub>2</sub> ) <sup>a</sup>             |
| <u>3d</u> | 6          | <u>8d</u> 68 | 156-157                        | 4.25(2H, s, CH <sub>2</sub> ), 7.2-8.3(9H, m,<br>aromatic protons)                                                                                                                                        | 265(M <sup>+</sup> ), 237<br>(M <sup>+</sup> -N <sub>2</sub> ) <sup>a</sup>             |
| <u>3e</u> | 6          | <u>9</u> 65  | 86-87<br>(74 <sup>7</sup> )    | 2.91(1H, m, H <sub>a</sub> ), 3.24(1H, d, H <sub>b</sub> ,<br>J=3.5), 4.32(2H, d, OCH <sub>2</sub> , J=3),<br>6.7-7.8(9H, m, aromatic protons)                                                            | 223(M <sup>+</sup> ), 146<br>(M <sup>+</sup> -Ph), <sup>a</sup> 144                     |
| <u>3f</u> | 20         | <u>10</u> 94 | 40-41                          | 1.0-2.4(6H, m, CH <sub>2</sub> ), 2.45-2.7(1H,<br>m, H <sub>a</sub> ), 2.92(1H, dd, H <sub>b</sub> , J=5 and<br>7.5), 4.55-5.0(1H, m, H <sub>c</sub> ), 6.6-<br>7.3(4H, m, aromatic protons) <sup>b</sup> | 187(M <sup>+</sup> ), <sup>a</sup> 162<br>159, 145                                      |

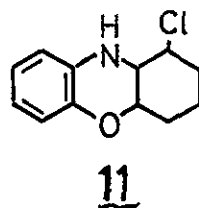
<sup>a</sup>Base peak. <sup>b</sup>A double doublet (H<sub>b</sub>) at  $\delta$  2.92 changed to a doublet with J=7.5 Hz when irradiated at  $\delta$  4.8. Thus, J<sub>ab</sub>=5 and J<sub>bc</sub>=7.5 Hz.

On the other hand, thermal decomposition of azides 3e and 3f in boiling benzene for 6 and 20 hr afforded the aziridine derivatives 9<sup>7</sup> and 10, respectively. The yields, physical and spectral data of the products are also given in Table 2. The spectral data support well the assigned structures. The observed value (J<sub>ab</sub>=3.5 Hz) of the vicinal coupling constant for aziridine ring protons of 9 compares to trans-coupling given in the literature.<sup>11</sup>



An inspection of Dreiding models indicates that a configuration 10A in which three hydrogens  $H_a$ ,  $H_b$  and  $H_c$  are situated cis each other, is possible for the structure of 10. It has been reported that in 1-alkylaziridine the value of cis-vicinal coupling constant for two protons anti to the alkyl group ( $J_{cis-anti}$ ) is about 5.3 Hz.<sup>12</sup> As shown in Table 2, the vicinal coupling constant,  $J_{ab}$ , in 10 is 5 Hz.

Treatment of 10 with hydrochloric acid in ethanol at room temperature gave the hexahydrophenoxazine 11, mp 84-84.5°, in 46.5% yield [ir  $\nu_{max}^{KBr}$  cm<sup>-1</sup>: 3400; nmr (CDCl<sub>3</sub>)  $\delta$ : 1.4-2.5 (6H, m,  $\underline{CH_2}$ ), 3.19 (1H, dd,  $\underline{\geq CH}$ ), 4.05 (1H, m,  $\underline{\geq CH}$ ), 4.45 (2H, m,  $\underline{\geq CH}$  and  $\underline{NH}$ ), 6.4-7.0 (4H, m, aromatic protons); mass  $m/e$  223, 225 ( $M^+$ , rel. intensity 3:1)].



On the basis of the formation of triazoles 8, and of the results of thermal decomposition of  $\Delta^2$ -1,2,3-triazolines,<sup>13</sup> the formation of aziridines 9 and 10 can be explained by an initial intramolecular 1,3-cycloaddition to form triazolines, followed by the concurrent elimination of nitrogen.

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Received, 2nd September, 1975