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

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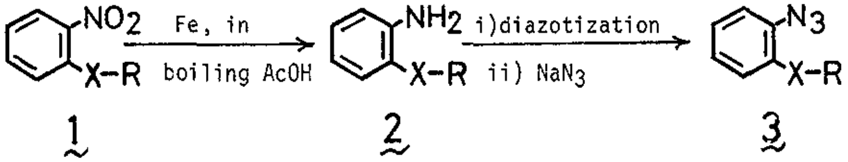
Aryl azides **3** containing alkynyl or alkenyl group as dipolarophile were prepared and thermally decomposed in benzene. Azides **3a**-**3d** gave the corresponding 1,3-cycloadducts, fused-ring 1,2,3-triazoles **8a**-**8d**, while bridgehead nitrogen aziridines **9** and **10**, were obtained from **3e** and **3f**, probably via unstable Δ^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,[1] azomethinimines,[2] nitrilimines,[3] and azides.[4] 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.[5] 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,[6] we learned that similar reactions have been recently reported by Fusco and his co-workers.[7]

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**,[8] are given in Table 1.



a: X=O, R= $CH_2C{\equiv}CH$; **b**: X=O, R= $CH_2C{\equiv}CPh$; **c**: X=S, R= $CH_2C{\equiv}CH$:

d: X=S, R= $CH_2C{\equiv}CPh$; **e**: X=O, R= $CH_2CH{=}CHPh$; **f**: X=O, R= 

Scheme 1

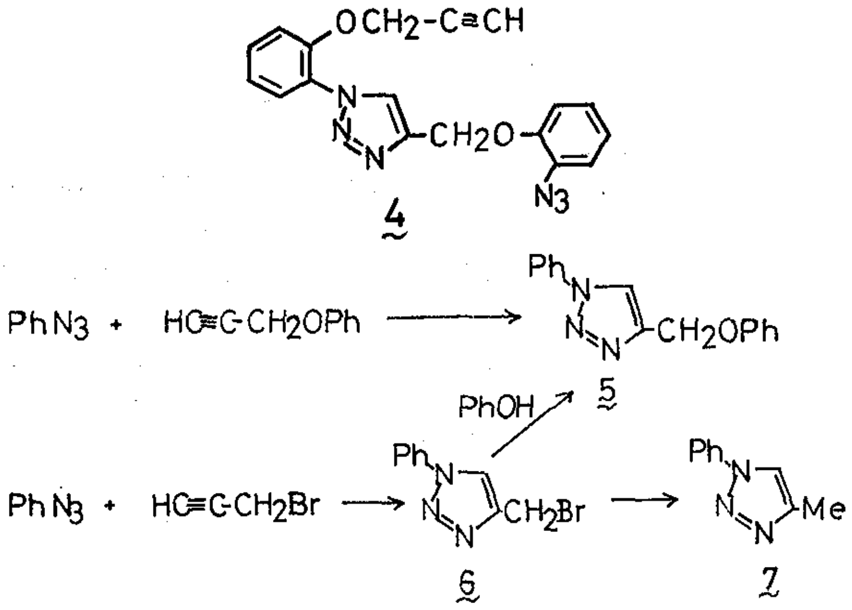
Azides **3**, with the exception of **3a**, were purified by chromatography over silica gel using benzene as eluent. On chromatography, **3a** was partially converted into dimer **4** and triazole **8a** (see later). The structure of **4**, mp 97-98.5°, was deduced on the basis of the following evidence. Ir ν_{max}^{KBr} cm^{-1}: 3240, 2100; nmr ($CDCl_3$) δ: 2.55 (1H, t, $\equiv C\underline{H}$, J=3 Hz), 4.75 (2H, d, $OC\underline{H_2}C\equiv$, J=3 Hz), 5.37 (2H, s, $OC\underline{H_2}$), 6.9-8.0 (8H, m, aromatic protons), 8.30 (1H, s, $=C\underline{H}$); mass m/e 346 (M^+), 318 ($M^+ - N_2$).

In addition, it has been found that the cycloaddition of phenyl azide to phenyl propargyl ether gave 1-phenyl-4-phenoxymethyl-1,2,3-triazole (**5**), mp 89.5-90.5°, in 61% yield [nmr ($CDCl_3$) δ: 5.28 (2H, s, $OC\underline{H_2}$), 6.9-7.8 (10H,

Table 1 Compounds 1, 2 and 3

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

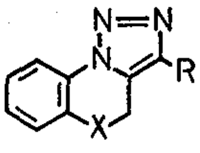
[a] Internal standard: TMS. Unless otherwise provided, the spectra were measured in CDCl$_3$. [b] Measured in CCl$_4$. [c] In the ir spectrum a strong band appered in the region 2100-2140 cm^{-1}.



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.[9] mp 81°), as depicted in Scheme 2.[10] 6: nmr ($CDCl_3$) δ 4.64 (2H, s, CH_2), 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.



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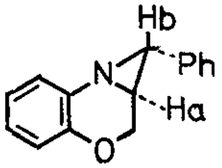
a: X=O, R=H
b: X=O, R=Ph
c: X=S, R=H
d: X=S, R=Ph

Table 2 Decomposition of Azides 3

Azide	Time hr	Product				
			Yield %	Mp. °C	Nmr($CDCl_3$), δ ppm (J, Hz)	Mass, m/e
3a	6	8a	81	58-59 (52[7])	5.4(2H, s, $C\underline{H}_2$), 6.9-7.4, 7.9-8.2 (3H and 1H, m, aromatic protons), 7.63(1H, s, =C$\underline{H}$)	173(M^+), 145 (M^+-N_2),[a] 119 117
3b	10	8b	86	193-194 (195[7])	5.55(2H, s, $C\underline{H}_2$), 7.0-8.2(9H, m, aromatic protons)	249(M^+), 221 (M^+-N_2),[a] 220
3c	3	8c	60	80-81	4.1(2H, s, $C\underline{H}_2$), 7.6(1H, s, =C$\underline{H}$), 7.2-7.5, 8.0-8.3(3H and 1H, m, aromatic protons)	189(M^+), 161 (M^+-N_2)[a]
3d	6	8d	68	156-157	4.25(2H, s, $C\underline{H}_2$), 7.2-8.3(9H, m, aromatic protons)	265(M^+), 237 (M^+-N_2)[a]
3e	6	9	65	86-87 (74[7])	2.91(1H, m, $\underline{H}_a$), 3.24(1H, d, $\underline{H}_b$, J=3.5), 4.32(2H, d, $OC\underline{H}_2$, J=3), 6.7-7.8(9H, m, aromatic protons)	223(M^+), 146 (M^+-Ph),[a] 144
3f	20	10	94	40-41	1.0-2.4(6H, m, $C\underline{H}_2$), 2.45-2.7(1H, m, $\underline{H}_a$), 2.92(1H, dd, $\underline{H}_b$, J=5 and 7.5), 4.55-5.0(1H, m, $\underline{H}_c$), 6.6-7.3(4H, m, aromatic protons)[b]	187(M^+),[a] 162 159, 145

[a] Base peak. [b] A double doublet (H_b) at δ 2.92 changed to a doublet with J=7.5 Hz when irradiated at δ 4.8. Thus, J_{ab}=5 and J_{bc}=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[7] 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_{ab}=3.5 Hz) of the vivinal coupling constant for aziridine ring protons of 9 compares to trans-coupling given in the literature.[11]



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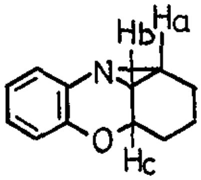

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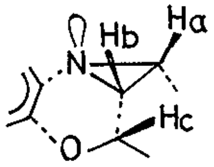
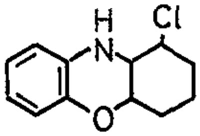


10A

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 ($J_{cis\text{-}anti}$) is about 5.3 Hz.[12] 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 84-84.5^0, in 46.5% yield [ir ν_{max}^{KBr} cm^{-1}: 3400; nmr ($CDCl_3$) δ: 1.4-2.5 (6H, m, $C\underline{H_2}$), 3.19 (1H, dd, $\geqslant C\underline{H}$), 4.05 (1H, m, $\geqslant C\underline{H}$), 4.45 (2H, m, $\geqslant C\underline{H}$ and $N\underline{H}$), 6.4-7.0 (4H, m, aromatic protons); mass m/e 223, 225 (M^+, rel. intensity 3:1)].



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On the basis of the formation of triazoles 8, and of the results of thermal decomposition of Δ^2-1,2,3-triazolines,[13] 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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