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## Cycloaddition Reactions Involving Two Heterocyclic Rings. Preparation of Novel Triazolophthalazine Ring Systems

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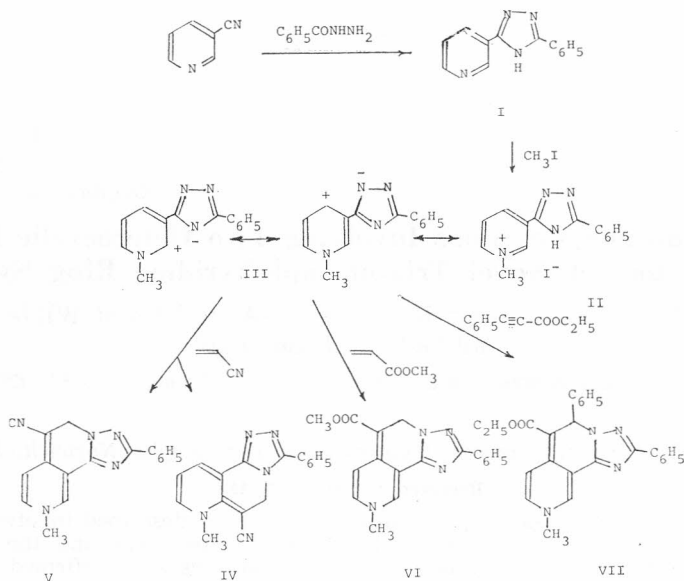
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A novel class of cycloaddition reactions is described involving the nitrogen atom of a 3-(s-triazol-3-yl) substituent and the 2- or 4- position of a pyridinium ring. Structures are confirmed by spectral data.

Extensive earlier work by our group has explored the cycloaddition reactions of 3-oxidopyridinium betaines. Thus reactions were uncovered in which  $2\pi$ ,  $4\pi$ , and  $6\pi$  electron systems underwent addition across (i) the 2, 6- and (ii) the 2,4-ring positions, (iii) the 2-ring position and the 3-oxygen atom and (iv) the 4-ring position with the 3-oxygen.<sup>4</sup> The present work was designed to explore the possibility of other substituents bearing a negative charge in the 3-position of a pyridinium ring entering into such cycloaddition reactions.

3-Cyanopyridine reacted readily with benzoic hydrazide to yield 3-phenyl-5-(3-pyridyl)-1,2,4-triazole *I*. This on reaction with methyl iodide gave the pyridinium salt *II* which exists in equilibrium with the betaine *III*. We tested the reactions of betaine *III* with a number of dipolarophiles. From the reaction with acrylonitrile two products were isolated using PLC, which were assigned by spectral methods (see later) as *IV* (30%) and *V* (44%). The corresponding reaction with methyl acrylate yielded only a single cycloadduct *VI* (55%). The stoichiometry of these reactions indicates that in each case an oxidation had taken place; we therefore carried out the reaction with ethyl phenylpropiolate and as expected obtained *VII* (18%).

The primary evidence for the structures of these products rests on their proton resonance spectra as summarized in Table I. In particular the compounds in which the 4-position of the pyridine ring has been substituted showed the remaining 5 and 6 ring protons as an AB pattern and which are not significantly coupled to the remaining ring proton in the 2-position; which shows as a singlet. By contrast, in compound *IV* in which the 2-position has undergone reaction, the 4,5,6-protons show as an ABC pattern in which the 4- and 6-protons are doublets with a coupling constant of 7 Hz and the 5 proton is seen as a triplet. The *N*-methyl group appears as a characteristic singlet near  $\delta$  3.6 and the methylene group of the new ring in compounds *IV*, *V* and *VI* is seen as a 2 proton singlet at 5.2.



The structures of the above triazonaphthyridine derivatives were further confirmed by their  $^{13}C$  NMR spectra (Table II), which displayed appropriate peaks corresponding to the expected numbers of carbon atoms for these compounds. The methylene carbon of the new ring in compounds IV, V and VI is seen near 67.2, while the R—C= carbon (R=CN,  $COOCH_3$  or  $COOC_2H_5$ ) appeared near 161.1. The CN carbon in compounds IV and V is seen near 121.0 while the CO carbon of compounds VI and VII occurs at 164.9. The N—CH<sub>3</sub> carbon of all the above compounds is seen near 48.0 ppm.

The ultraviolet spectra (Table II) of the esters VI and VII showed two maxima in the regions 248—253 and 365—372 nm. The nitriles IV and V exhibited three maxima in the regions 243—250, 335—352 and 348—368 nm. In addition to these three maxima, compound IV showed another maximum at 450 nm.

#### EXPERIMENTAL

$^1H$  NMR spectra were recorded on a Varian EM 360L spectrometer or a Nicolet NT-300 spectrometer, operating at a field of 7 tesla with tetramethylsilane as internal standard.  $^{13}C$  NMR spectra were recorded on Jeol JNM-FX100 NMR spectrometer. IR spectra were obtained using sodium-chloride plates on a Perkin-Elmer 297 spectrometer as solutions in bromoform. UV spectra were measured for ethanolic solutions with a Perkin-Elmer 330 spectrometer. Mass spectra were recorded on a Kratos MS 30. Melting points were measured on a Kofler hot stage apparatus and are uncorrected.

#### 3-Phenyl-5-(pyrid-3-yl)-1,2,4-triazole

Benzoylhydrazine (2.72 g, 0.02 mole) and 3-cyanopyridine (6.2 g, 0.06 mole) were shaken at 200 °C in an autoclave for 2h. The resulting yellow oil was dissolved in hot benzene. On cooling, the product (2.8 g, 56% yield) separated out in prisms, which after recrystallization from benzene had m. p. 211—214 °C. (lit. 5, m. p. 211 °C).

*Anal.*  $C_{13}H_{10}N_4$  (222.3) calc'd.: C 70.3; H 4.5; N 25.2%,  
found: C 70.2; H 4.4; N 25.4%.

TABLE I  
<sup>1</sup>H NMR and IR Spectral Data of Triazolonaaphthyridine Derivatives

Compound	<sup>1</sup> H NMR <sup>a</sup>							IR		
	2-CH (1H, s)	4-CH (1H, d)	5-CH (1H, d)	6-CH (1H, d)	ArH (5H, 2m)	CH <sub>2</sub> (2H, s)	CH <sub>3</sub> (3H, s)	others	C=O or CN ν/cm <sup>-1</sup>	C=N ν/cm <sup>-1</sup>
IV	—	7.44	6.14 <sup>b</sup>	7.62	7.50, 7.55	5.20	3.71	—	2200	1625
V	7.69	—	6.35	6.88	7.46, 8.10	5.17	3.55	—	2195	1660
VI	7.79	—	7.20	7.80	7.47, 8.02	5.16	3.60	3.58 (3H, s, COOCH <sub>3</sub> )	1685	1625
VII	<sup>c</sup>	—	8.54	9.10	7.74, 8.24	—	4.65	4.18 (2H, q, J = 7, CH <sub>2</sub> ) 0.92 (3H, t, J = 7, CH <sub>3</sub> )	1690	1630

<sup>a</sup> δ in ppm, J = coupling constant in Hz, solu. in DMSO-d<sub>6</sub>. <sup>b</sup> t, J = 7. <sup>c</sup> Overlapped with aromatic protons.

TABLE II  
 $^{13}\text{C}$  NMR and UV Spectral Data of Triazolonaaphthyridine Derivatives<sup>a</sup>

Triazole C	Pyridine C	Phenyl C	CH <sub>2</sub>	R—C=	$^{13}\text{C}$ NMR <sup>a</sup>		UV Maxima (extinction coefficients)
					N—CH <sub>3</sub>	others	
IV 106.2, 114.2	148.0, 144.8, 143.1, 137.0	130.3, 129.4, 128.8, 125.8	55.9	161.1	48.3	121.9 (CN)	218 (22386)    243 (24969)    335 (10188)    348 (9184)    450 (2296)
V 105.6, 109.8	147.6, 140.9, 137.7, 133.9	130.6, 129.2, 128.7, 125.8	65.2	161.0	47.4	120.2 (CN)	210 (24682)    250 (25830)    352 (19229)    368 (18942)
VI 106.8, 111.4	149.1, 139.0, 137.3, 134.5	130.9, 129.2, 128.7, 125.8	85.0	161.0	48.2	165.7 (CO) 50.1 (OCH <sub>3</sub> )	212 (27200)    248 (30080)    372 (24640)
VII 115.9, 117.2	148.7, 145.9, 136.9, 134.5	122.7, 127.0, 128.6, 129.3, 129.6, 129.1, 130.0, 131.2	62.5	162.0	48.2	164.1 (CO) 13.3 (CH <sub>3</sub> )	213 (22686)    253 (23233)    365 (9298)

<sup>a</sup>  $\delta$  ppm., solu. in DMSO-d<sub>6</sub>. <sup>b</sup> R = CN, COOCH<sub>3</sub> or COOC<sub>2</sub>H<sub>5</sub>.

TABLE III  
Preparation Details for Triazolophthyridine Derivatives

Compound No.	Yield %	M. p. °C	Solvent/crystal form	Found %			Elem. Analysis (Formula)	Calc'd %		
				C	H	N		C	H	N
V	30	210	benzene/orange needles	70.7	4.4	24.2	C <sub>17</sub> H <sub>13</sub> N <sub>5</sub> (287.3)	71.0	4.5	24.3
IV	44	230	methanol-benzene/yellow needles	70.7	4.5	24.3	C <sub>17</sub> H <sub>13</sub> N <sub>5</sub> (287.3)	71.0	4.6	24.4
VI	55	250	benzene/yellow prisms	67.3	5.1	17.0	C <sub>18</sub> H <sub>16</sub> N <sub>4</sub> O <sub>2</sub> (320.4)	67.5	5.0	17.5
VII	18	212	methanol/yellow prisms	73.3	5.8	13.2	C <sub>25</sub> H <sub>22</sub> N <sub>4</sub> O <sub>2</sub> (410.5)	73.2	5.4	13.7

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ 7.35—8.65 (9H, m, Aromatic protons); 9.20 (1H, s, NH); MS: *m/e* (relative abundance); M<sup>+</sup> 222(100), 208(1), 194(3.3), 193(2), 167(2), 120(8), 119(64), 118(31), 111(5), 106(6), 105(6), 104(11), 103(5), 92(17), 91(31), 90(13), 89(15), 79(3), 78(17), 77(20), 76(5), 66(4), 63(22), 51(18). UV (EtOH): Maxima (extinction coefficient) 210 (14080), 232 (15930) 255 (16670).

#### 1-Methyl-3-(3-phenyl-1,2,4-triazol-5-yl)pyridinium iodide

3-phenyl-5-(pyrid-3-yl)-1,2,4-triazole (2.22 g, 0.01 mole) and methyl iodide (1.42 g, 0.01 mole) in *n*-propanol (100 ml) were stirred for 24 h at 50 °C. On cooling the yellowish iodide (2.7 g, 75% yield) separated, it crystallized from *n*-propanol in fine needles, m. p. 236 °C.

Anal. C<sub>14</sub>H<sub>13</sub>IN<sub>4</sub> (364.2) calc'd.: C 46.1; H 3.6; N 15.4%,  
found: C 45.8; H 3.8; N 15.2%.

<sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ 4.39 (3H, s, CH<sub>3</sub>, s, CH<sub>3</sub>); 7.50—9.18 (9H, m, aromatic protons); 9.60 (1H, s, NH).

UV (EtOH): Maxima (extinction coefficient) 212 (26870), 222 (24480), 254 (20300).

#### Cycloaddition products

A suspension of the methiodide (2.5 g, 0.007 mole) in acetonitrile (50 ml) and the appropriate acrylic or acetylenic compound was refluxed for 30 min. Triethylamine (3 ml) was then added and the whole heated for another 12 hr. The solvent was then evaporated at 20 mm/50 °C and the residue subjected to column chromatography on silica gel (benzene/ethyl acetate 9:1): for details see Table III.

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## POVZETEK

### Cikloadicije, ki potekajo na dveh heterocikličnih obročih

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Opisana je nova vrsta cikloadicij, ki obsega dva obroča in sicer dušikov atom v 3-(stiazol-3-il)nem substituentu in položaj 2 ali 4 v piridinijevem obroču. Strukture produktov potrjujejo spektroskopski podatki.