1,3-Dipolar Cycloaddition Reaction of Benzodiazinium and Naphthyridinium *N*-Imines with Acetylenic Esters

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1,3-Dipolar cycloaddition of *N*-imines derived from mono-*N*-amino salts of phthalazines, 2-phenylquinoxaline, 1,5- and 1,8-naphthyridines with dimethyl acetylenedicarboxylate and methyl propiolate resulted in the formation of new tricyclic heterocyclic ring systems with bridgehead nitrogen.

The 1,3-dipolar cycloaddition reaction of activated alkynes and alkenes with heteroaromatic *N*-imines, especially pyridinium *N*-imines, has been extensively studied (1). Recently we observed that benzodiazines and some naphthyridines can be readily aminated by *O*-mesitylenesulfonylhydroxylamine (2) to give good to high yields of the corresponding mono-*N*-amino mesitylenesulfonates (3). As part of our studies on the chemical properties of the *N*-amino salts of benzodiazines and naphthyridines, we have now investigated the 1,3-dipolar cycloaddition reaction of the *N*-imines derived from these *N*-amino salts with dimethyl acetylenedicarboxylate and methyl propiolate, which produce novel heterocyclic ring systems.

Solutions of 1 mole equiv of the mono-*N*-amino salts and 1.5 molar equiv of dimethyl acetylenedicarboxylate or methyl propiolate in dimethylformamide in the presence of potassium carbonate were stirred at room temperature for 1 day. After evaporation of the solvent, the product was isolated by preparative tlc. In this manner, the *N*-amino salts of 2-phenylquinoxaline (I), phthalazine (II), 1-phenylphthalazine (III), 1,5- (IV) and 1,8-naphthyridines (V) gave 1:1 adducts in 7-30% yields. However, the *N*-amino salt of 4-phenylquinazoline (VI) afforded only a complex mixture, which was not further examined. The structures of the adducts were assigned on the basis of analyses (Table I), and ir, uv, mass (Table II), and nmr spectral data (Table III).

Comparisons of the nmr spectra of the adducts with those of the adducts (XVI-XIX) obtained from the *N*-amino salts of quinoline (VII) and isoquinoline (VIII) were particularly helpful (4). The methoxycarbonyl proton signals appear at *ca.* τ 6.0 except for ones at the 3-position of IX and X which are shielded by *ca.* 0.5-0.7 ppm as expected for the anisotropic effect exerted by the phenyl group at the 4-position. The signals of H-2 appear at τ 1.44-1.67 as a singlet. As in the cases of adducts XVIII and XIX, the

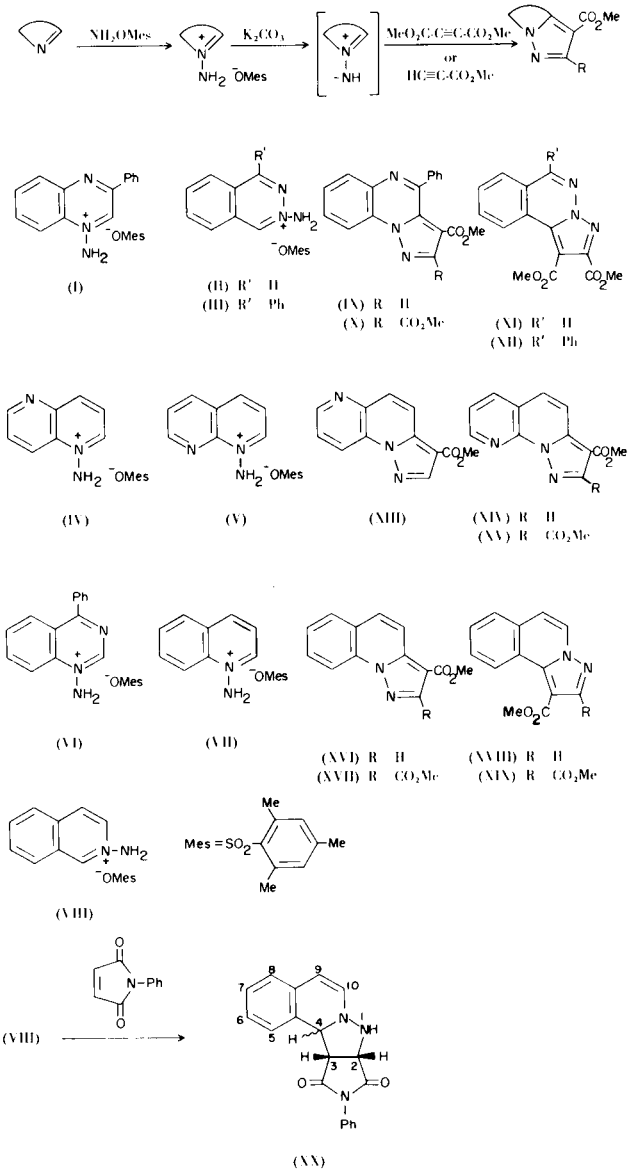


TABLE I

1,3-Dipolarcycloaddition Reaction of *N*-Imines derived from *N*-Amino Salts (I-V, VII and VIII)

Compd.	M.p. °C	Recrystallized from	Yield %	Formula	Anal.	C%	H%	N%
IX	137-138	methanol	13	$C_{18}H_{13}N_3O_2$	Calcd.	71.27	4.32	13.86
					Found	71.27	4.36	13.88
X	185-186	ethyl acetate	26	$C_{20}H_{15}N_3O_4$	Calcd.	66.47	4.18	11.63
					Found	66.50	4.24	11.58
XI	118-119	benzene-petroleum ether	7	$C_{14}H_{11}N_3O_4$	Calcd.	58.94	3.89	14.73
					Found	59.01	3.94	14.88
XII	203-204	benzene-petroleum ether	12	$C_{20}H_{15}N_3O_4$	Calcd.	66.47	4.18	11.63
					Found	66.27	4.07	11.45
XIII	151-152	benzene-petroleum ether	9	$C_{12}H_9N_3O_2$	Calcd.	63.43	3.99	18.49
					Found	63.45	4.18	18.26
XIV	179-181	benzene-petroleum ether	19	$C_{12}H_9N_3O_2$	Calcd.	63.43	3.99	18.49
					Found	63.41	4.11	18.20
XV	207-208	benzene	30	$C_{14}H_{11}N_3O_4$	Calcd.	58.94	3.89	14.73
					Found	58.91	3.91	14.54
XVI	123-124	methanol	27	$C_{13}H_{10}N_2O_2$	Calcd.	69.01	4.46	12.38
					Found	68.89	4.51	12.21
XVII	127-128	methanol	10	$C_{15}H_{12}N_2O_4$	Calcd.	63.38	4.26	9.86
					Found	63.45	4.35	9.66
XVIII	161-162	methanol	31	$C_{13}H_{10}N_2O_2$	Calcd.	69.01	4.46	12.38
					Found	69.12	4.54	12.29
XIX	125-126	methanol	14	$C_{15}H_{12}N_2O_4$	Calcd.	63.38	4.26	9.86
					Found	63.64	4.30	9.75

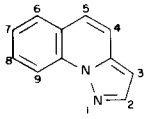
TABLE II

Spectral Data for 1,3-Dipolarcycloaddition Products

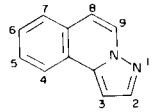
Compd.	Ir (KCl) cm^{-1}	Uv λ max (ethanol) nm (log ε)	M^+ m/e
IX	1730	257 (4.45), 319 (3.97), 346 (4.12) 361sh (4.00)	303
X	1730 1720	259 (4.53), 304sh (3.99), 317 (4.02) 336 (3.99), 349sh (3.89)	361
XI	1725 1720	251sh (4.48), 257 (4.56), 265 (4.46) 283 (3.95), 294sh (3.73), 316 (3.13)	285
XII	1720	262 (4.55), 271sh (4.48), 289sh (4.07)	361
XIII	1705	248 (4.28), 290 (3.47), 305 (3.64) 331sh (4.08), 341 (4.18), 356 (4.05)	227
XIV	1700	235 (4.31), 246sh (4.22), 293 (3.63) 307 (3.84), 329sh (4.13), 336 (4.22) 350 (4.07)	227
XV	1740 1705	233 (4.46), 294 (3.79), 307 (3.95) 321sh (4.09), 332 (4.22), 346 (4.11)	285
XVI	1700	257 (4.51), 280 (3.91), 290 (3.94) 304 (3.97), 320 (3.98), 329 (3.03) 334 (3.05), 344 (3.86)	226
XVII	1735 1700	239 (4.37), 250 (4.70), 254 (4.50) 293 (4.02), 304 (4.10), 310sh (4.04) 325 (4.09), 340 (4.05)	248
XVIII	1700	259sh (4.55), 264 (4.60), 280sh (4.02) 305 (3.68), 319 (3.92), 334 (4.01)	226
XIX	1735 1710	254 (4.66), 258sh (4.64), 280sh (4.02) 302 (3.80), 317 (3.87), 332 (3.90)	248

TABLE III

Nmr Spectral Data of Cycloaddition Products



Compd.	NMR ($CDCl_3$) τ R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9
XVI	1.67 (s)	6.16 (s)	(a)	2.05 (d) J = 10 Hz	(a)	(a)	(a)	1.38-1.61 (m)
XVII	5.96 or 6.08 (s)	6.08 or 5.96 (s)	1.97 (d) J = 10 Hz	2.32 (d) J = 10 Hz		2.10-2.45 (m)		1.25-1.45 (m)
IX	1.53 (s)	6.68 (s)	phenyl	N	1.75-1.91 (m)	2.25-2.65 (m) (b)		1.35-1.51 (m)
X	5.97 (s)	6.55 (s)	phenyl	N	1.76-1.92 (m)	2.22-2.59 (m) (b)		1.27-1.41 (m)
XIII	1.56 (s)	6.06 (s)	1.68 (d) J = 10 Hz	2.10 (d) J = 10 Hz	N	1.12 (d) J = 7 Hz	2.15-2.48 (m)	1.12 (d) J = 7 Hz
XIV	1.44 (s)	6.02 (s)	1.84 J = 10 Hz	2.36 J = 10 Hz	1.79 (dd) J = 8; 2 Hz	2.44 (dd) J = 8; 5 Hz	1.00-1.20 (m)	N
XV	5.99 or 6.09 (s)	6.09 or 5.99 (s)	1 92 (d) J = 10 Hz	2.35 (d) J = 10 Hz	1.80 (dd) J = 8; 2 Hz	2.40 (dd) J = 8; 5 Hz	1.11 (dd) J = 5; 2 Hz	N



XVIII	1.62 (s)	6.11 (s)	0.15-0.35 (m)		2.30-2.52 (m)		1.81 (d) J = 7.5 Hz	2.93 (d) J = 7.5 Hz
XIX	5.97 (s)	5.97 (s)	1.05-1.30 (m)		2.15-2.50 (m)		1.70 (d) J = 7.5 Hz	2.77 (d) J = 7.5 Hz
XI	6.02 or 6.04 (s)	6.04 or 6.02 (s)	0.99 (br.d)		2.00-2.25 (m)		1.26 (s)	N
XII	6.01 (s)	6.01 (s)	0.88 (br.d)		1.97-2.73 (m) (b)		phenyl	N

(a) These signals give rise to complex multiplets in the region from τ 1.61 to 3.05. (b) These signals are overlapped by those of a phenyl substituent.

signals of H-4 in XI and XII shift to low field as a result of a deshielding effect by the carbomethoxyl group at the 3-position.

All the products (IX-XV) have new heterocyclic ring systems.

N-Phenylmaleimide was found to react with isoquinolinium *N*-imine to produce a 1:1 adduct, which was assigned the gross structure XX on the basis of the spectral data (Experimental Section). The nmr spectrum of the adduct shows vicinal coupling constant between H^2 and H^3 ($J_{2,3}$ = 8 Hz), in accord with the *cis*-configuration (5).

Attempts to cycloadd *N*-phenylmaleimide with I-III, and VII, however, were unsuccessful.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on an Hitachi EPI G-2 spectrophotometer, uv spectra on an Hitachi 124 spectrophotometer, nmr spectra on an Hitachi R-20A spectrometer, and mass spectra on an Hitachi RMU-6D mass spectrometer operating at 70 ev.

Materials.

Compound I-VI (3) and VII-VIII (6) were prepared as previously described.

General Procedure for 1,3-Dipolar Cycloaddition.

A mixture of an *N*-amino salt (1 mmole) in dimethylformamide (5 ml.) and potassium carbonate (1.5 mmoles) was stirred for 10 minutes and a solution of dimethyl acetylenedicarboxylate or methyl propiolate (1.5 mmoles) in dimethylformamide (2 ml.) was added. The reaction mixture was stirred for 1-2 days at room

temperature. The solvent was evaporated under reduced pressure and the residue was extracted with chloroform. The extract was washed with water, dried over magnesium sulfate and concentrated. The residue was purified by preparative tlc on alumina (Merck Alumina PF_{254}) with benzene, followed by recrystallization. For the elemental analyses, yields, and melting points, see Table I, and for the spectral data see Table II and III.

Cycloaddition of Isoquinolinium *N*-Imine with *N*-Phenylmaleimide.

A mixture of VIII (344 mg.) and potassium carbonate (207 mg.) in methanol (5 ml.) was stirred for 10 minutes at room temperature. To the stirring solution was added *N*-phenylmaleimide (208 mg.) and the mixture was stirred for 8 hours. The reaction mixture was evaporated to dryness and the residue was extracted with chloroform. The dried extract was concentrated to give white crystals of XX, m.p. 193-194° (from methanol), yield, 75 mg. (24%); ir (potassium chloride): 1705 cm^{-1}; nmr (dimethylsulfoxide-d_6): τ 2.45-3.10 (9H, m, aromatic H), 3.88 (1H, d, J = 8 Hz, H^{10}), 4.72 (1H, d, J = 8 Hz, H^9), 5.29 (1H, d, J = 9 Hz, H^4), 5.23-5.65 (1H, br.d, J = 8 Hz, H^2), 6.32 (1H, dd, J = 8;9 Hz, H^3), 6.55-6.80 (1H, br, -N*H*); mass spectrum showed the parent ion at m/e 317 (Calcd. 317).

Anal. Calcd. for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.88; H, 4.94; N, 13.10.

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