1,2,4-Triazoles. XXV. The Effect of Pyridine Substitution on the Isomerization of *s*-Triazolo[4,3-*a*]pyridines into *s*-Triazolo[1,5-*a*]pyridines (1)

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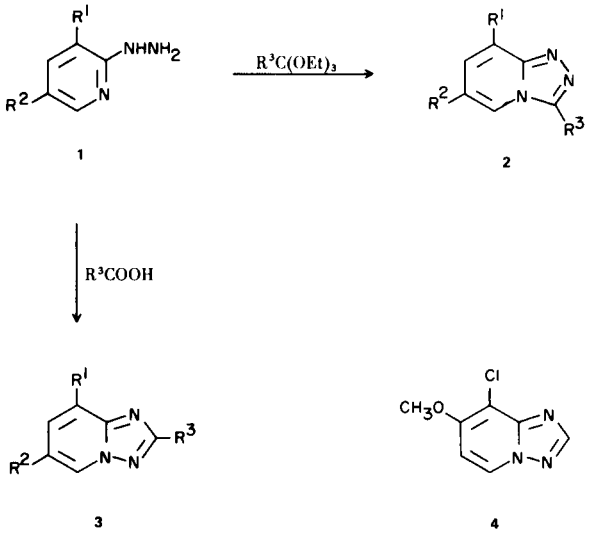
The isomerization of *s*-triazolo[4,3-*a*]pyridines into *s*-triazolo[1,5-*a*]pyridines is greatly facilitated by electron withdrawing nitro substituents in the pyridine ring and retarded by electron donating amino groups.

Isomerization in several ring-fused *s*-triazole systems induced by acid, base, or by heat, has been described previously (2) and we now report the effect of *py*-substitution (*py* = pyridine) on the isomerization of *s*-triazolo-[4,3-*a*]pyridines. These rearrangements may be considered analogous to the Dimroth rearrangement (3) which has recently been shown to involve ring fission and recyclization, as in the conversion of 1,2-dihydro-2-imino-1-methylpyrimidine into 2-methylaminopyrimidine (4). Numerous examples in related heterocyclic systems (5) also follow this reaction pathway. These studies, and also the failure of rearrangements in some systems (6), suggested that the ease of the rearrangement increases with the electron depletion of the ring and decreases with its electron enrichment.

3-Alkyl-*s*-triazolo[4,3-*a*]pyridine derivatives (**2**) are prepared very conveniently by the reaction of 2-hydrazinopyridine with aliphatic acids (7) or with orthoesters (7b), procedures utilized in the synthesis of other fused-ring systems of this type (2,8). 8-Nitro-*s*-triazolo[4,3-*a*]-pyridine (**2**; $R^1 = NO_2$; $R^2 = R^3 = H$) and 3-methyl-8-nitro-*s*-triazolo[4,3-*a*]pyridine (**2**; $R^1 = NO_2$; $R^2 = H$; $R^3 = CH_3$) were prepared in very good yields by the reaction of 2-hydrazino-3-nitropyridine (**1**; $R^1 = NO_2$; $R^2 = H$) with triethylorthoformate and triethylorthoacetate, respectively (Table I). These structural assignments were made on the basis of the spectral characteristics of the products (Table I) and also by the differences in their physical properties when compared to those of corresponding authentic *s*-triazolo[1,5-*a*]pyridine derivatives described below. The ultraviolet absorption spectra of the *s*-triazolo[4,3-*a*]pyridines show significant differences from the spectra of the *s*-triazolo[1,5-*a*]pyridines, differences which have also been observed in the spectra of similar ring systems (2a,2e,9). Reduction of 8-nitro-*s*-triazolo[4,3-*a*]pyridine and its methyl derivative with hydrogen over 10% palladium-on-charcoal catalyst gave excellent yields of the corresponding 8-amino-*s*-triazolo-[4,3-*a*]pyridines (**2**; $R^1 = NH_2$; $R^2 = H$; $R^3 = H$ and CH_3, respectively) (Table I).

The electron withdrawing 8-nitro substituent would be expected to facilitate the rearrangement to the isomeric system. Thus, when 8-nitro-*s*-triazolo[4,3-*a*]pyridine (**2**; $R^1 = NO_2$; $R^2 = R^3 = H$) was warmed gently with formic acid for 1 hour, or at room temperature over a longer reaction period, the product obtained was identified as 8-nitro-*s*-triazolo[1,5-*a*]pyridine (**3**; $R^1 = NO_2$; $R^2 = R^3 = H$). Similarly, 3-methyl-8-nitro-*s*-triazolo-[4,3-*a*]pyridine (**2**; $R^1 = NO_2$; $R^2 = H$; $R^3 = CH_3$) was also converted into 2-methyl-8-nitro-*s*-triazolo[1,5-*a*]pyridine (**3**; $R^1 = NO_2$; $R^2 = H$; $R^3 = CH_3$) by glacial acetic acid under similar reaction conditions. These isomerizations were also achieved very readily by the action of base (10% sodium hydroxide solution, 30 minutes) or by fusion of the compounds. The structures of the isomerized products were established on the basis of their spectral characteristics and also by comparison with the products obtained by nitration of the *s*-triazolo[1,5-*a*]pyridine system described later.

In 8-amino-*s*-triazolo[4,3-*a*]pyridine (**2**; $R^1 = NH_2$; $R^2 = R^3 = H$), the electron releasing amino group should retard the isomerization to the [1,5-*a*] series and it was



found that when **2** ($R^1 = NH_2$; $R^2 = R^3 = H$) was refluxed with formic acid for 2 hours, 8-formamido-*s*-triazolo[4,3-*a*]pyridine (**2**; $R^1 = NHCHO$; $R^2 = R^3 = H$) only was obtained (Table I). The structure of **2** ($R^1 = NHCHO$; $R^2 = R^3 = H$) was evident from analytical and spectral data, and also from the differences in its physical properties when compared to those of the corresponding *s*-triazolo[1,5-*a*]pyridine prepared by an alternate method described below. Heating with 10% sodium hydroxide solution for 4 hours did not bring about isomerization of the 8-amino compound but extension of the reaction period to 48 hours was effective. No isomerization was observed on prolonged heating of the compound above its melting point.

The above results indicate that reaction of 2-hydrazino-3-nitropyridine (**1**; $R^1 = NO_2$; $R^2 = H$) with aliphatic acids should result in the isolation of 8-nitro-*s*-triazolo[1,5-*a*]pyridines (**3**; $R^1 = NO_2$; $R^2 = R^3 = H$, CH_3) directly and such was observed to be the case. Similarly, reaction with benzoic acid at 170° for 5 hours gave 8-nitro-2-phenyl-*s*-triazolo[1,5-*a*]pyridine (**3**; $R^1 = NO_2$; $R^2 = H$; $R^3 = Ph$), clearly showing how possible isomerization should be considered in structural assignments in these ring systems.

Reduction of the 8-nitro-*s*-triazolo[1,5-*a*]pyridines (**3**; $R^1 = NO_2$; $R^2 = H$) to the corresponding 8-amino compounds (**3**; $R^1 = NH_2$; $R^2 = H$) occurred readily (Table I). These amino compounds readily formed formyl derivatives useful as comparison compounds in establishing that isomerization had not occurred on treatment of the 8-amino-*s*-triazolo[4,3-*a*]pyridines with formic acid.

Attempts to prepare 2-alkyl(aryl)-8-nitro-*s*-triazolo-[1,5-*a*]pyridines (**3**; $R^1 = NO_2$; $R^2 = H$) by the amidine dehydrogenation route (10a,10b) or utilizing 1,2-diaminopyridinium salts (10a) were unsuccessful. 2-Amino-3-nitropyridine (11) has a pK_a 2.42 (pK_a of 2-aminopyridine, 6.86) and because of the low basicity amidine or salt formation did not occur. Similar results have been obtained with 2-aminopyrazines (9) (pK_a 3.14) and in various other systems (12).

In view of the results obtained above, 3-alkyl-6-nitro-*s*-triazolo[4,3-*a*]pyridines (**2**; $R^1 = H$; $R^2 = NO_2$) were of particular interest for the isomerization study as the electron withdrawing nitro group is now adjacent to the electron deficient 5-position. Following the procedure used above, 2-hydrazino-5-nitropyridine (**1**; $R^1 = H$; $R^2 = NO_2$) and orthoesters gave 2-alkyl-6-nitro-*s*-triazolo-[1,5-*a*]pyridines (**3**; $R^1 = H$; $R^2 = NO_2$) and not the expected [4,3-*a*] derivatives. Numerous variations in the reaction conditions were unsuccessful in altering the course of this reaction which occurred with equal facility using aliphatic acids. However, with acetic acid for a

TABLE I

Some Substituted *s*-Triazolo[4,3-*a*]pyridine Derivatives (**2**)

R^1	R^2	R^3	Solvent (a)	M.p. °C	Form (b)	Yield %	Formula		C	H	N	Ultraviolet absorption data λ max (methanol) nm (log ε)
NO_2	H	H	A	226	yellow flakes	87	$C_6H_4N_4O_2$	Calcd. %	43.90	2.44	34.15	347 (3.78), 222 (4.24)
								Found %	43.74	2.36	34.36	
NO_2	H	CH_3	A	288 dec.	yellow needles	84	$C_7H_6N_4O_2$	Calcd. %	47.20	3.37	31.47	360 (3.69), 226 (4.18)
								Found %	47.24	3.47	31.39	
NH_2	H	H	B	154	needles	61	$C_6H_6N_4$	Calcd. %	53.72	4.51	41.77	292 (4.11), 222 (c) (3.73), 203 (4.29)
								Found %	53.54	4.54	41.62	
NH_2	H	CH_3	B	188	needles	63	$C_7H_8N_4$	Calcd. %	56.74	5.44	37.82	297 (4.20), 227 (3.99)
								Found %	56.90	5.33	37.61	
NHCHO	H	H	A	314	needles	85	$C_7H_6N_4O$	Calcd. %	51.85	3.73	34.56	312 (c) (3.89), 299 (4.06), 289 (c) (4.00), 277 (c) (3.83), 227 (4.23)
								Found %	52.14	3.77	34.53	

TABLE I - Continued

Some Substituted *s*-Triazolo[1,5-*a*]pyridine Derivatives (3)

H	NO_2	H	A	207	irreg. prisms	90	$C_6H_4N_4O_2$	Calcd. %	43.90	2.44	34.15	315 (3.60), 246 (4.37)
								Found %	43.79	2.53	34.09	
H	NO_2	CH_3	A	213.5	flakes	86	$C_7H_6N_4O_2$	Calcd. %	47.20	3.37	31.47	315 (3.56), 250 (4.29)
								Found %	47.00	3.60	31.20	
H	NO_2	NH_2	D	310	yellow flakes	50	$C_6H_5N_5O_2$	Calcd. %	40.22	2.79	39.11	333 (4.32), 259 (4.58),
								Found %	40.36	3.00	38.94	206 (4.55)
H	NO_2	SH	C	261 dec.	yellow flakes	30	$C_6H_4N_4O_2S$	Calcd. %	36.73	2.04	28.57	258 (4.17), 240 (4.25)
								Found %	36.46	2.00	28.68	
H	NO_2	Ph	A	199	needles	58	$C_{12}H_8N_4O_2$	Calcd. %	60.00	3.36	23.33	307 (4.18), 259 (4.45)
								Found %	59.85	3.35	23.08	
NO_2	H	H	A	204	needles	66	$C_6H_4N_4O_2$	Calcd. %	43.90	2.44	34.15	322 (3.73), 225 (4.16)
								Found %	43.65	2.57	34.30	
NO_2	H	CH_3	A	195	needles	65	$C_7H_6N_4O_2$	Calcd. %	47.20	3.37	31.47	325 (3.76), 232 (4.16)
								Found %	47.13	3.52	31.30	
NO_2	H	Ph	A	226	yellow flakes	59	$C_{12}H_8N_4O_2$	Calcd. %	60.00	3.36	23.33	332 (3.97), 250 (4.46)
								Found %	59.89	3.32	23.39	
H	NH_2	Ph	B	214 dec.	prisms	62	$C_{12}H_{10}N_4$	Calcd. %	68.55	4.79	26.65	257 (4.55), 245 (c) (4.50)
								Found %	68.77	4.75	26.50	
H	NH_2	H	B	121	needles	76	$C_6H_6N_4$	Calcd. %	53.72	4.51	41.77	320 (3.35), 255 (c) (3.73),
								Found %	53.82	4.62	41.77	230 (4.57)
NH_2	H	H	B	103.5	needles	80	$C_6H_6N_4$	Calcd. %	53.72	4.51	41.77	275 (4.15), 209 (4.40)
								Found %	53.93	4.56	41.90	
NH_2	H	Ph	B	133	needles	75	$C_{12}H_{10}N_4$	Calcd. %	68.55	4.79	26.65	293 (4.10), 257 (c) (4.58),
								Found %	68.75	4.68	26.56	248 (4.65)
NHCHO	H	H	A	200	needles	85	$C_7H_6N_4O$	Calcd. %	51.85	3.73	34.56	285 (c) (3.43), 261 (c) (3.85),
								Found %	52.07	3.86	34.34	235 (4.60)

(a) A = Ethanol; B = Benzene-petroleum ether; C = Acetic Acid; D = Methanol (b) All colorless except where noted. (c) Shoulder

TABLE II

Principal Ions Present in the Mass Spectra of Some Substituted *s*-Triazolo[4,3-*a*]pyridines (**2**)

Substituents																		
R^1	R^2	R^3																
NO_2	H	H	m/e	165	164	148	134	118	107	92	91	80	77	65	64	63	62	53	52	51
			% rel int	9	100	5	20	5	29	5	49	6	5	6	30	12	6	17	12	6
NO_2	H	CH_3	m/e	179	178	149	148	132	117	107	105	92	91	80	79	78	77	65	64	63
			% rel int	9	100	5	24	5	8	24	9	6	30	15	7	7	10	6	20	6
			m/e	62	53	52	51	43												
			% rel int	5	22	18	16	26												
NH_2	H	H	m/e	135	134	107	106	80	79	67	54	53	52							
			% rel int	8	100	13	5	20	7	6	5	20	8							
NH_2	H	CH_3	m/e	149	148	107	106	81	80	79	78	77	74	66	65	54	53	52	51	
			% rel int	9	100	35	10	5	67	11	5	11	10	6	6	7	33	11	10	
Some Substituted *s*-Triazolo[1,5-*a*]pyridines (**3**)																		
H	NO_2	H	m/e	165	164	148	134	118	107	92	91	90	80	79	78	65	64	63	62	
			% rel int	8	48	6	62	5	10	7	100	20	13	5	5	7	48	15	9	
			m/e	61	54	53	52	51	50											
			% rel int	6	7	13	11	7	5											
H	NO_2	CH_3	m/e	179	178	162	149	148	133	132	105	104	91	80	79	78	77	64	63	
			% rel int	9	100	6	7	32	8	65	5	8	19	20	5	8	6	30	41	
			m/e	62	53	52	51	50												
			% rel int	6	5	12	10	8												
H	NO_2	Ph	m/e	241	240	224	210	194	168	167	140	139	106	105	104	103	91	80	78	
			% rel int	15	100	5	6	5	5	10	5	5	5	6	7	5	6	7	5	
			m/e	77	76	64	63	62	52	51	50									
			% rel int	6	5	7	23	5	5	6	5									
NO_2	H	H	m/e	165	164	149	148	135	134	118	107	106	92	91	80	79	78	65	64	
			% rel int	8	48	6	5	5	62	5	10	5	7	100	13	5	5	7	48	
			m/e	63	62	61	54	53	52	51	50									
			% rel int	15	9	6	7	13	11	7	5									

TABLE II - Continued

NO_2	H	CH_3	m/e	179	178	149	148	132	107	105	92	91	80	65	64	63	54	53	52	51	50
			% rel int	9	100	12	46	6	11	5	10	60	15	5	28	7	5	5	9	5	5
NO_2	H	Ph	m/e	241	240	210	194	140	104	103	91	89	80	77	76	64	63	53	52	51	
			% rel int	15	100	11	13	5	10	20	15	5	5	25	7	9	5	5	5	7	
H	NH_2	H	m/e	135	134	133	107	93	80	79	78	67	66	53	52	51					
			% rel int	8	100	5	7	7	21	5	5	5	5	14	9	5					
NH_2	H	H	m/e	135	134	133	107	106	92	81	80	79	67	66	54	53	52	51			
			% rel int	8	100	5	28	5	5	5	33	11	9	5	6	40	17	5			
H	NH_2	Ph	m/e	211	210	209	107	105	104	103	93	80	79	78	77	76	66	53	52	51	50
			% rel int	14	100	12	5	10	5	5	20	30	9	13	8	5	12	20	10	8	5
NH_2	H	Ph	m/e	211	210	209	107	105	80	79	77	53	52	51							
			% rel int	14	100	6	5	7	10	5	5	18	5	5							

TABLE III

Metastable Ions Present in the Mass Spectra of Some Representative Substituted *s*-Triazolo[4,3-*a*]pyridines (**2**)

R^1	R^2	R^3	Transition	m* Calculated	m* Observed	Fragment Expelled
NH_2	H	H	107 → 80	59.98	60.0	HCN
NH_2	H	CH_3	107 → 80	59.98	60.0	HCN
			Some Substituted *s*-Triazolo[1,5-*a*]pyridines (**3**)			
NO_2	H	H	164 → 134	109.49	109.5	NO
NO_2	H	CH_3	178 → 148	123.10	123.0	NO
H	NO_2	H	118 → 91	70.33	70.2	HCN
			164 → 134	109.49	109.5	NO
H	NO_2	CH_3	178 → 148	123.10	123.0	NO
H	NH_2	Ph	93 → 66	47.00	47.0	HCN
			210 → 209	208.00	208.0	H
NH_2	H	H	107 → 80	59.98	60.0	HCN
			134 → 107	85.44	85.5	HCN
NH_2	H	Ph	210 → 209	208.00	208.0	H

short reaction period the intermediate acethydrazide (ν NH 3260, ν CO 1652 cm^{-1}) was obtained which readily underwent cyclodehydration on heating at 230° for 5 minutes. It is quite clear that the initially formed [4,3-*a*] isomer undergoes a very facile thermal rearrangement to the [1,5-*a*] isomer, no doubt due to the nitro group in the 6-position of the [4,3-*a*] nucleus. As would be expected from the above results, attempts to prepare 3-methyl-6-nitro-*s*-triazolo[4,3-*a*]pyridine and 3-methyl-8-nitro-*s*-triazolo[4,3-*a*]pyridine by nitration of 3-methyl-*s*-triazolo[4,3-*a*]pyridine (**2**; $R^1 = R^2 = H$; $R^3 = CH_3$) with potassium nitrate-concentrated sulfuric acid at 120° for 10 hours gave 2-methyl-8-nitro-*s*-triazolo[1,5-*a*]-pyridine (**3**; $R^1 = NO_2$; $R^2 = H$; $R^3 = CH_3$), no isolatable amount of the other isomer being observed.

6-Nitro-*s*-triazolo[1,5-*a*]pyridine was converted into 6-amino-*s*-triazolo[1,5-*a*]pyridine (**3**; $R^1 = R^3 = H$; $R^2 = NH_2$) by catalytic hydrogenation and the amino compound was then deaminated to *s*-triazolo[1,5-*a*]-pyridine (**3**; $R^1 = R^2 = R^3 = H$). This last product was also prepared from 1,2-diaminopyridinium iodide and formic acid (10a). Additional reference compounds, the 6- and 8-nitro compounds, were obtained by nitration of 2-methyl-*s*-triazolo[1,5-*a*]pyridine (13) (**3**; $R^1 = R^2 = H$; $R^3 = CH_3$) with potassium nitrate and concentrated sulfuric acid.

It has been reported (14) that the reaction of 2-hydrazino-5-nitropyridine (**1**; $R^1 = H$; $R^2 = NO_2$) with benzoyl chloride gave 2-benzhydrazido-5-nitropyridine which, when heated in the presence of polyphosphoric acid at 150° for 6 hours, gave 6-nitro-3-phenyl-*s*-triazolo[4,3-*a*]pyridine (**2**; $R^1 = H$; $R^2 = NO_2$; $R^3 = Ph$). The same product was obtained in this laboratory when 2-hydrazino-5-nitropyridine was heated with benzoic acid at 170° for 4 hours and our data indicate that the structure of this product should be regarded as 6-nitro-2-phenyl-*s*-triazolo[1,5-*a*]-pyridine (**3**; $R^1 = H$; $R^2 = NO_2$; $R^3 = Ph$) (Table I). This was confirmed by its synthesis from *N*-(5-nitro-2-pyridyl)benzamidine and lead tetraacetate.

The above facile isomerizations induced by the presence of a nitro group in the *py*-ring provide a convenient route to difficulty accessible 2-substituted-*s*-triazolo[1,5-*a*]pyridines where the 2-substituent is a reactive functional group. 2-Hydrazino-5-nitropyridine (**1**; $R^1 = H$; $R^2 = NO_2$), on reaction with cyanogen bromide gave 2-amino-6-nitro-*s*-triazolo[1,5-*a*]pyridine (**3**; $R^1 = H$; $R^2 = NO_2$; $R^3 = NH_2$). The same hydrazine with carbon disulfide likewise gave the isomerized product, 6-nitro-*s*-triazolo-[1,5-*a*]pyridine-2-thiol (**3**; $R^1 = H$; $R^2 = NO_2$; $R^3 = SH$). Analytical and spectral data (Table I and Experimental) showed that these products belonged to the [1,5-*a*] series.

These nitro compounds were also convenient for introducing more diversified substituents into the *py*-ring. Utilizing the haloalkoxy reaction (15), 8-nitro-*s*-triazolo-[1,5-*a*]pyridine readily gave 8-chloro-7-methoxy-*s*-triazolo-[1,5-*a*]pyridine (**4**). Its structure was immediately apparent on the basis of analytical and spectral data, especially the nmr spectrum which showed resonances at δ 4.25 (s, 1, OCH_3), 8.45 (s, 1, 2-H) and an AB doublet (J = 9.0 Hz) at 7.60 and 6.30 (5- and 6-H).

The principal ions present in the mass spectra of some of the products described above are shown in Table II. All these derivatives, with the exception of 6-nitro- and 8-nitro-*s*-triazolo[1,5-*a*]pyridine, had their molecular ions as the most abundant ion. When there was a nitro group (R^1 or $R^2 = NO_2$) present in the *py*-moiety of the fused-ring system, the major fragmentation pathway involved the loss of the NO_2 group from the molecular ion, either as such, or by a combination of fragmentations involving NO and O·. This was then followed by the loss of R^3CN and HCN. The second pathway involved the loss of NO from the molecular ion followed by the loss of R^3CN, HCN and CO in that order, the notable exception being 8-nitro-2-phenyl-*s*-triazolo[1,5-*a*]pyridine. When there was an animo group (R^1 or $R^2 = NH_2$) present in the *py*-moiety of the fused ring system, the loss of R^3CN and HCN was first observed. The resulting ion then underwent fragmentation by two different pathways, one involving rearrangement followed by the loss of HCN and, in the other, loss of H followed by rearrangement and subsequent loss of HCN, was observed. Table III lists metastable transitions which support the above fragmentation pathways.

EXPERIMENTAL (16)

2-Hydrazino-3-nitropyridine.

2-Chloro-3-nitropyridine (27.7 g., 0.2 mole), dissolved in ethanol (150 ml.), was treated with hydrazine hydrate (50 ml., 85%) slowly with vigorous stirring and the mixture was then refluxed for 15 minutes. The product that separated after cooling crystallized from ethanol as yellow needles, 27.5 g. (90%), m.p. 170° dec; ir (Nujol) 3300, 1610, 1570, 1315, 1255, 1160, 1055, 990, 880, 840, 805, 760, 735 cm^{-1}; uv λ max (methanol) 255 sh nm (log ε 3.68), 224 (4.26).

Anal. Calcd. for $C_5H_6N_4O_2$: C, 38.96; H, 3.90; N, 36.37. Found: C, 39.03; H, 3.98; N, 36.55.

The picrate crystallized from ethanol as yellow needles, m.p. 177° dec.

Anal. Calcd. for $C_{11}H_9N_7O_9$: C, 34.46; H, 2.35; N, 25.59. Found: C, 34.32; H, 2.52; N, 25.64.

2-Hydrazino-5-nitropyridine.

This compound was prepared from 2-chloro-5-nitropyridine as above. It was obtained as yellow needles (75%) on crystallization from ethanol, m.p. 206° dec. (lit. (17) m.p. 206° dec.); ir (Nujol) 3325, 1660, 1604, 1587, 1418, 1323, 1290, 1110, 1000, 946, 825, 755, 715 cm^{-1}.

General Procedure for the Preparation of 3-Alkyl-8-nitro-*s*-triazolo[4,3-*a*]pyridines (Table I).

2-Hydrazino-3-nitropyridine (0.02 mole) and freshly distilled orthoester (0.14 mole) were refluxed for 4 hours. The orthoester was removed (18) and the residue was recrystallized from ethanol.

General Procedures. (I).

(A) The Isomerization of 3-Alkyl-8-nitro-*s*-triazolo[4,3-*a*]pyridines with Acid.

8-Nitro-*s*-triazolo[4,3-*a*]pyridine (0.2 g.) was heated with formic acid (98%, 1.0 ml.) on a steam bath for 1 hour. The product obtained after evaporation of the formic acid was recrystallized from ethanol whence colorless needles (80%) separated, m.p. 204°. The compound was identified as 8-nitro-*s*-triazolo[1,5-*a*]-pyridine on comparison (19) of its spectral characteristics with those of authentic 2-alkyl-8-nitro-*s*-triazolo[1,5-*a*]pyridines (13).

Isomerization at room temperature was found to take place over 6 hours.

(B) Thermal Isomerization.

8-Nitro-*s*-triazolo[4,3-*a*]pyridine (0.2 g.) was heated at 240° for 5 minutes. The black residue was dissolved in ethanol (20 ml.), filtered and the filtrate was concentrated to about 5 ml. On cooling, colorless needles (70%) of 8-nitro-*s*-triazolo[1,5-*a*]pyridine separated.

(C) Isomerization with Base.

8-Nitro-*s*-triazolo[4,3-*a*]pyridine (0.2 g.) was heated with 10% sodium hydroxide solution (2 ml.) on a steam bath for 1 hour. After neutralization with dilute hydrochloric acid and extraction with chloroform (3 x 50 ml.), the chloroform layer was separated and evaporated to dryness. Recrystallization of the residue from ethanol gave colorless needles of 8-nitro-*s*-triazolo[1,5-*a*]pyridine, m.p. 204° (70%).

(II) The Preparation of 2-Alkyl-8-nitro-*s*-triazolo[1,5-*a*]pyridines.

2-Hydrazino-5-nitropyridine (0.01 mole) and the aliphatic acid (0.20 mole) were refluxed for 3 hours and the excess acid removed. The residue was dissolved in water, neutralized by the addition of sodium bicarbonate and allowed to stand for 1 hour. The products which separated were recrystallized from ethanol and are described in Table I.

(III) The Preparation of 6- and 8-Nitro-2-phenyl-*s*-triazolo[1,5-*a*]-pyridines.

2-Hydrazino-3-nitropyridine (0.04 mole) and benzoic acid (0.16 mole) were heated at 170° for 5 hours. After cooling to room temperature, the dark viscous oil was dissolved in ethanol, neutralized by the addition of aqueous sodium bicarbonate, and filtered. The filtrate on cooling gave a crude product which was recrystallized from ethanol (charcoal) forming yellow flakes of 8-nitro-2-phenyl-*s*-triazolo[1,5-*a*]pyridine: 2.9 g. (59%), m.p. 226° (Table I). When 2-hydrazino-5-nitropyridine (0.04 mole) and benzoic acid (0.16 mole) were reacted together as above, 6-nitro-2-phenyl-*s*-triazolo[1,5-*a*]pyridine was obtained as colorless needles, 5.6 g. (58%), m.p. 199°.

(IV) Reduction of the Nitro Compounds.

6-Nitro-*s*-triazolo[1,5-*a*]pyridine (0.3 g., 0.002 mole) in ethanol (50 ml.) and palladium-on-powdered charcoal (1.0 g., 10% catalyst) were shaken under hydrogen. After completion of the reduction (135 ml. of hydrogen absorbed), the catalyst was removed and the filtrate was evaporated to dryness under reduced pressure. The residue was recrystallized from a mixture of benzene-petroleum ether and the 6-amino-*s*-triazolo[1,5-*a*]pyridine was obtained as colorless needles, 0.18 g., 76%; m.p. 121° (Table I).

The picrate crystallized from ethanol as yellow needles, m.p. 225° dec.

Anal. Calcd. for $C_{12}H_9N_7O_7$: C, 39.68; H, 2.48; N, 27.00. Found: C, 39.91; H, 2.79; N, 27.19.

(V) The Preparation of 2-Alkyl-6-nitro-*s*-triazolo[1,5-*a*]pyridines (Table I).

(A) Using Orthoesters.

2-Hydrazino-5-nitropyridine (0.2 mole) and the orthoester (0.135 mole) were refluxed for 4 hours. The orthoester was removed and the residue was recrystallized from ethanol (charcoal).

(B) With Aliphatic Acids.

The hydrazine (0.065 mole) was heated under reflux with the aliphatic acid (0.435 mole) for 2-5 hours. The excess acid was removed and the resulting mixture was poured into water, neutralized (sodium bicarbonate) and allowed to stand for 1 hour. The products obtained were recrystallized from ethanol (charcoal). When the hydrazine (5.0 g., 0.033 mole) was refluxed with dilute acetic acid (40 ml., 0.2 mole, 75%) for 1 hour, the product obtained separated from ethanol, giving 2-acetylhydrazino-5-nitropyridine as yellow, irregular prisms, 4.8 g. (75%), m.p. 228.5°; ir (Nujol) 3260, 1652, 1610, 1600, 1495, 1410, 1320, 1290, 1100, 750 cm^{-1}.

Anal. Calcd. for $C_7H_8N_4O_3$: C, 42.85; H, 4.08; N, 28.57. Found: C, 42.77; H, 4.24; N, 28.72.

The 2-acetyl compound (3.0 g.) was heated in an oil bath maintained at 230° for 30 minutes. The crystalline melt crystallized from ethanol giving colorless flakes of 2-methyl-6-nitro-*s*-triazolo[1,5-*a*]pyridine, m.p. 213.5° (73%).

Reaction of 8-Amino-*s*-triazolo[4,3-*a*]pyridine with Formic Acid.

8-Amino-*s*-triazolo[4,3-*a*]pyridine (1.0 g.) was heated with formic acid (98%, 4.0 ml.) on the steam bath for 2 hours. The formic acid was removed and the residue was dissolved in ethanol (charcoal) and filtered. The filtrate, on cooling, gave colorless needles of 8-formamido-*s*-triazolo[4,3-*a*]pyridine (Table I). Similarly, 8-amino-*s*-triazolo[1,5-*a*]pyridine gave colorless needles of 8-formamido-*s*-triazolo[1,5-*a*]pyridine (Table I).

Deamination of 6-Amino-*s*-triazolo[1,5-*a*]pyridine.

A mixture of concentrated sulfuric acid (10 ml.) and water (5 ml.) was cooled in an ice salt bath to −10°. Sodium nitrite (0.37 g.) was added in small portions over a period of 15 minutes followed by dropwise addition of cold 50% hypophosphorous acid (2 ml.). The temperature was kept below −10°, and 6-amino-*s*-triazolo[1,5-*a*]pyridine (0.27 g.) was added in small portions with vigorous stirring. The temperature was kept at −10° for 2 hours and the reaction mixture warmed slowly to 60° and stirred at this temperature for another 2 hours. After cooling to room temperature and making alkaline (*p*H 10) with sodium hydroxide solution. the product was extracted with chloroform. The chloroform layer was dried (sodium sulfate) and the chloroform was evaporated. The residue was recrystallized from benzene-petroleum ether and *s*-triazolo[1,5-*a*]pyridine was obtained as colorless needles, 0.1 g. (40%), m.p. 101° (lit. (10a) m.p. 102°).

The Preparation of 6-Nitro-2-phenyl-*s*-triazolo[1,5-*a*]pyridine by Dehydrogenative Ring Closure of *N*-(5-Nitro-2-pyridyl)benzamidine.

2-Amino-5-nitropyridine (2.8 g., 0.02 mole), aluminum chlo-

ride (0.02 mole) and benzonitrile (0.02 mole) were heated together at 170° for 30 minutes after the initial vigorous reaction had subsided. The complex was decomposed by the cautious addition of water and the reaction mixture was then made strongly alkaline with sodium hydroxide solution, keeping the temperature at 0-5°. After extraction into ether (5 x 20 ml.) and drying (sodium sulfate), the crude product was obtained as light yellow crystals. Recrystallization from ethanol yielded *N*-(5-nitro-2-pyridyl)benzamidine as yellow flakes, 3.4 g., 70%, m.p. 203°; ir (Nujol) 3370 to 3050, 1625, 1600, 1525, 1500, 1350, 1270, 1140, 1110, 1010, 950, 870, 860, 780, 725, 705, 650 cm^{-1}.

Anal. Calcd. for $C_{12}H_{10}N_4O_2$: C, 59.51; H, 4.13; N, 23.14. Found: C, 59.23; H, 4.20; N, 23.01.

The above amidine (2.4 g., 0.01 mole) was dissolved in dry benzene (30 ml.), dry lead tetraacetate (4.7 g., 0.01 mole) was added and the mixture was heated under reflux for 30-60 minutes. The reaction mixture was extracted with 30% aqueous sodium hydroxide (3 x 10 ml.) and the benzene solution was then dried (sodium sulfate) and evaporated under reduced pressure. The residue was recrystallized from benzene forming colorless needles, 1.4 g., 58%, m.p. 199°.

2-Amino-6-nitro-*s*-triazolo[1,5-*a*]pyridine.

2-Hydrazino-5-nitropyridine (0.013 mole) in ethanol (30 ml.) was treated cautiously with cyanogen bromide (0.013 mole) (mild exothermic reaction), and refluxed for 30 minutes. The ethanol was removed and the residue was dissolved in water. The aqueous solution was neutralized with sodium hydroxide solution and the product which separated collected. It was purified by recrystallization from methanol from which it separated as yellow flakes, m.p. 310° (Table I); ir (potassium bromide) 3450, 3325, 3240, 3110, 3033, 1640, 1560, 1530, 1490, 1355, 1335, 1295, 1260, 1210, 1140, 1080, 950, 890, 830, 760, 745, 730, 700 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 179 (100), 149 (14), 133 (5), 117 (5), 116 (5), 105 (5), 80 (9), 79 (6), 78 (30), 77 (7), 64 (6), 63 (5), 52 (7), 51 (13).

6-Nitro-*s*-triazolo[1,5-*a*]pyridine-2-thiol.

2-Hydrazino-5-nitropyridine (0.026 mole) in ethanol (150 ml.) and carbon disulfide (0.04 mole) were heated under gentle reflux for 4-6 days until evolution of hydrogen sulfide had ceased. The ethanol was removed and the residue was purified by repeated extraction with hot glacial acetic acid. (The reaction time was reduced to 5-6 hours by adding sodium hydroxide (0.04 mole) to the reaction mixture.) Evaporation of the acetic acid and recrystallization of the residue from the same solvent afforded yellow flakes of the thiol, 0.58 g. (30%), m.p. 261° dec. (Table I); ir (Nujol) 3100-3000, 1650, 1570, 1510, 1485, 1420, 1353, 1335, 1315, 1258, 1210, 1175, 1085, 1000, 940, 840, 825, 750, 710 cm^{-1}; mass spectrum (70 eV), m/e (rel intensity) 196 (100), 195 (5), 169 (6), 151 (5), 150 (69), 149 (5), 123 (10), 104 (11), 95 (11), 91 (5), 80 (5), 79 (5), 78 (19), 77 (8), 76 (5), 64 (15), 63 (30), 62 (5), 60 (5), 53 (5), 52 (8), 51 (10).

Nitration of 3-methyl-*s*-triazolo[4,3-*a*]pyridine.

To a solution of 3-methyl-*s*-triazolo[4,3-*a*]pyridine (5.8 g.) dissolved in concentrated sulfuric acid (145 g.), finely powdered potassium nitrate (8.7 g.) was added in small portions. The mixture was heated at 120-130° for 10 hours. After cooling, the reaction mixture was poured into ice water and neutralized with sodium carbonate. The separated product was extracted several times with chloroform, the chloroform layer was dried (sodium sulfate) and the solvent was evaporated. The residue was dissolved in ethanol (charcoal), filtered and, on cooling, gave colorless needles of 2-methyl-8-nitro-*s*-triazolo[1,5-*a*]pyridine, 3.5 g. (60%), m.p. 195°.

Nitration of 2-methyl-*s*-triazolo[1,5-*a*]pyridine under similar reaction conditions gave 2-methyl-8-nitro-*s*-triazolo[1,5-*a*]pyridine and 2-methyl-6-nitro-*s*-triazolo[1,5-*a*]pyridine (13).

8-Chloro-7-methoxy-*s*-triazolo[1,5-*a*]pyridine.

A solution of 8-nitro-*s*-triazolo[1,5-*a*]pyridine (3.3 g., 0.02 mole) and potassium hydroxide (6.4 g., 0.112 mole) in methanol (400 ml.) was stirred under reflux during the dropwise addition of aqueous sodium hypochlorite (520 ml., 0.745 mole) solution over a period of 15 minutes. The solution was maintained at 60-65° for 2 hours and the methanol then removed. The residue was dissolved in water and extracted with chloroform, dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The residual oil on standing at room temperature for several hours, gave a yellow solid which, after three recrystallizations from benzene-petroleum ether, afforded colorless needles, 1.6 g. (44%), m.p. 137°; ir (potassium bromide) 3050, 1640, 1560, 1520, 1450, 1380, 1325, 1290, 1270, 1210, 1190, 1160, 1110, 980, 970, 950, 920, 910, 810, 760, 720, 670, 640, 600 cm^{-1}; uv λ max (methanol) 291 nm (log ε 4.03), 265 (3.92), 208 (4.59); mass spectrum (70 eV) m/e (rel intensity) 183 (51), 168 (7), 143 (4), 142 (16), 141 (13), 140 (45), 128 (7), 127 (8), 126 (11), 121 (4), 120 (4), 115 (6), 114 (21), 113 (16), 112 (44), 104 (7), 99 (5), 94 (5), 93 (5), 92 (4), 89 (11), 87 (20), 86 (12), 85 (50), 84 (5), 78 (7), 77 (18), 76 (25), 75 (10), 73 (13), 72 (4), 67 (6), 66 (11), 65 (5), 64 (38), 63 (24), 62 (17), 61 (11), 60 (5), 54 (7), 53 (15), 52 (15), 51 (21), 50 (100), 49 (28), 42 (82).

Anal. Calcd. for $C_7H_6ClN_3O$: C, 45.77; H, 3.27; N, 22.89. Found: C, 45.69; H, 3.26; N, 22.70.

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(18) All evaporations were done under reduced pressure on the steam bath using a rotatory evaporator.

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