(0.2 mole) in chloroform (125 ml.) was treated with carbon disulfide (0.25 mole), a precipitate forming immediately. This dissolved when the reaction mixture was heated under gentle reflux and the heating was continued for 1–7 days, depending on the rate of separation of the product and until no appreciable amount of hydrogen sulfide was being evolved. The insoluble products, described in Table VII, were purified by crystallization from methanol.

B. Attempted Synthesis from Thiourea.—2-Pyridylhydrazine (6.0 g., 0.056 mole) was heated with thiourea (6.0 g., 0.07 mole) at 200° for 3 hr. During this time there was a noticeable amount of ammonia being evolved and, after cooling to room temperature, a dark yellow, viscous oil formed.

The dark yellow semisolid was dissolved in methanol and the small amount of insoluble material was discarded. After removal of the methanol, the residue was distilled under reduced pressure. Fraction I (0.3 g.), b.p. 40–44° (0.1 mm.), crystallized from benzene as colorless plates and was identified as 2-aminopyridine, by mixture melting point data and its infrared spectrum.

Fraction 2, b.p. 125° (0.1 mm.), which collected in the condenser as a pale yellow semisolid, crystallized from methanol–chloroform as pale pink plates, 1.0 g. (12%), m.p. 109–110°. The product was recrystallized twice from acetone–ether, and formed pale pink plates, m.p. 115–119°, infrared (Nujol), cm.$^{-1}$, 2020 (NCS^-). It was identified as 2-aminopyridinium isothiocyanate.

Anal. Calcd. for $C_6H_7N_3S$: C, 47.1; H, 4.6; N, 27.4; S, 20.9. Found: C, 47.1; H, 4.6; N, 27.0; S, 20.7.

3-Amino-*s*-triazolo[4.3-*a*]pyridines.—The 2-pyridylhydrazine (0.1 mole) was dissolved in methanol (125 ml.) and cyanogen bromide (0.1 mole) was added cautiously (mild exothermic reaction) after which the reaction mixture was refluxed for 2–7 hr. The methanol was removed under reduced pressure on the steam bath and the residual, crystalline hydrobromide salt was dissolved in water. The aqueous solution was basified with sodium acetate and a small volume of concentrated sodium hydroxide solution. The base that separated was purified by recrystallization from ethanol (Table VII), and in those cases where the base did not separate from solution, it was obtained by continuous ether extraction (24–48 hr.).

1,2,4-Triazoles. XIII. Derivatives of the *s*-Triazolo[1,5-*a*]pyridine Ring System[1a]

K. T. POTTS,[1b] H. R. BURTON, AND J. BHATTACHARYYA

Department of Chemistry, University of Louisville, Louisville, Kentucky 40208

Received June 8, 1965

Cyclization of N-(2-pyridyl)alkyl- (or aryl-) amidines (**1**) with lead tetraacetate resulted in the formation of 2-alkyl- (or aryl-) *s*-triazolo[1,5-*a*]pyridines (**2**) in good yield. The scope of this reaction sequence has been determined. A second method of synthesis of the ring system, from 1,2-diaminopyridinium salts and carboxylic acids or acid chlorides, has also been established. The parent ring and others unsubstituted in the 2-position were readily obtained by this procedure. The pyridinium salts yielded the corresponding 1-amino-2-imino-1,2-dihydropyridines by passage through Amberlite IRA-400 resin; these bases underwent extremely facile cyclizations to the bicyclic system in yields greater than 90%. Potassium permanganate oxidation of *s*-triazolo[1,5-*a*]-pyridine yielded *s*-triazole-3-carboxylic acid. The triazolopyridine nucleus was resistant to the usual electrophilic substitution reactions.

In a previous paper[2] in this series, syntheses of *s*-triazolo[4,3-*a*]pyridine derivatives were described. In a continuation of our interests in the chemistry and pharmacological evaluation of fused bicyclic systems with a common nitrogen atom, we now describe the syntheses of members of the isomeric ring system, the *s*-triazolo[1,5-*a*]pyridine system (**2**) by two methods that make members of this ring system readily available. The spectral characteristics of these derivatives will be described in a later communication, in particular the relationship of their proton magnetic resonance data to various properties associated with heteroaromatic systems.

A synthesis involving ring closure onto a preformed *s*-triazole nucleus to form the pyridine ring is again not practicable,[3a] but a satisfactory route is available by cyclization of an intermediate N-(2-pyridyl)alkyl- (or aryl-) amidine with lead tetraacetate. This oxidative-type ring closure was used by Bower and Ramage[3b] for the synthesis of the only known representatives of this ring system, the 2-methyl- and 2-phenyl-*s*-triazolo[1,5-*a*]pyridines (**2**, R^1 = CH_3 and Ph) and has also found application in the synthesis of the *s*-triazolo[1,5-*a*]pyrazine system.[4] A closely related oxidation reaction is the synthesis of 3-methyl-1-phenyl-*v*-triazolo[3,4-*a*]pyridinium chloride (**4**) from methyl 2-pyridyl ketone phenylhydrazone[5] (**3**). This present study has developed and extended this route to the bicyclic system and determined its limitations, results which are of special interest in view of the recent use[3c] of sodium hypochlorite and base in the oxidative ring closure of N-(2-pyridyl)benzamidine to 2-phenyl-*s*-triazolo[1,5-*a*]pyridine. Using this method, it was found that N′-(3-pyridyl)-4-thiazolecarboxamidine underwent ring closure to 2-(4-thiazolyl)-3H-imidazo[4,5-*b*]pyridine.[3c]

The *s*-triazolo[1,5-*a*]pyridine ring system is now also available from the reaction of aliphatic or aromatic acids (or their chlorides) with 1,2-diaminopyridinium salts (**7**) or the corresponding bases (**8**), and in addition the isomerization of the *s*-triazolo[4,3-*a*]pyridine systems, described in the following publication,[3d] offers an alternative route.

The intermediate N-(2-pyridyl)alkylamidines (Table I) can be prepared by two methods: (a) from the 2-aminopyridines, aluminum chloride, and the alkyl cyanide[6]; or (b) by treatment of an imino ether

(1) (a) This work was supported by Public Health Service Research Grant CA-05973, 01-04, National Cancer Institute, U. S. Public Health Service. (b) To whom correspondence should be sent: Department of Chemistry, Rensselaer Polytechnic Institute, Troy, N. Y.

(2) K. T. Potts and H. R. Burton, *J. Org. Chem.*, **31**, 251 (1966).

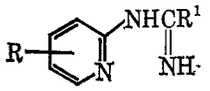
(3) (a) A recent example of this approach is the synthesis of 5-azaadenine from 3-amino-*s*-triazole [E. C. Taylor and R. W. Hendess, *J. Am. Chem. Soc.*, **87**, 1980 (1965)]; (b) J. D. Bower and G. R. Ramage, *J. Chem. Soc.*, 4506 (1957); (c) V. J. Grenda, R. E. Jones, G. Gal, and M. Stetzinger, *J. Org. Chem.*, **30**, 259 (1956); (d) K. T. Potts, H. R. Burton, and S. K. Roy, *ibid.*, **31**, 265 (1966).

(4) G. M. Badger, P. J. Nelson, and K. T. Potts, *ibid.*, **29**, 2542 (1964).

(5) R. Kuhn and W. Münzing, *Chem. Ber.*, **85**, 29 (1952).

TABLE I

N-(2-PYRIDYL)ALKYL- (OR ARYL-) AMIDINES AND THEIR PICRATES



R	R^1	M.p., °C.	Yield, %	Form[a]	Solvent[b]	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N	Picrates[c] M.p., °C.	Picrates[c] % N Calcd.	Picrates[c] % N Found
H	Et	92–95[d]	44	Yellow oil	..	$C_8H_{11}N_3$	64.4	7.4	28.2	65.5	7.4	27.5	219–221	22.2	22.1
H	Ph	97–98	37	Plates	A	$C_{12}H_{11}N_3$	73.1	5.6	21.3	73.4	5.6	21.1	203–204	17.8	17.5[e]
3-CH_3	CH_3	80–82[d]	44	Yellow oil	..	$C_8H_{11}N_3$	64.4	7.4	28.2	65.1	7.4	27.8	150–151	22.2	22.3
3-CH_3	Ph	68–69	63	Needles	B	$C_{13}H_{13}N_3$	73.9	6.2	19.9	73.8	6.3	20.0	171–172	19.1	19.3
4-CH_3	CH_3	52–53	49	Needles	A	$C_8H_{11}N_3$	64.4	7.4	28.2	61.0	8.2	26.4	179–181	22.2	22.0
4-CH_3	Ph	125–126	55	Plates	C	$C_{13}H_{13}N_3$	73.9	6.2	19.9	73.8	6.1	19.8	203	19.1	19.2
5-CH_3	CH_3	133–134	22	Needles	A	$C_8H_{11}N_3$	64.4	7.4	28.2	64.2	7.4	27.9			
5-CH_3	Ph	89–90	43	Needles	B	$C_{13}H_{13}N_3$	73.9	6.2	19.9	74.0	6.1	20.2			
6-CH_3	CH_3	102–104	12	Needles	C	$C_8H_{11}N_3$	64.4	7.4	28.2	64.7	7.5	28.4			
4,6-$(CH_3)_2$	CH_3[f]	124	37	Needles	C	$C_9H_{13}N_3$	66.2	8.0	25.8	65.8	7.9	26.0			

[a] All crystalline products were colorless. [b] A = benzene, B = benzene–petroleum ether, and C = petroleum ether. [c] All picrates crystallized from ethanol as yellow needles except the one where R = 3-CH_3, R^1 = CH_3, which separated from benzene. [d] Boiling point at 0.2 mm. [e] Contains 1 mole of ethanol. [f] Imino ether method.

hydrochloride with the 2-aminopyridine in dry pyridine.[7] In earlier work in the s-triazolo[1,5-a]pyrazine series,[4] the 2-aminopyrazines were such weak bases (pK_a = *ca.* 3.14) that the N-(2-pyrazinyl)alkylamidines could not be formed. However, the 2-aminopyridines are sufficiently strong bases (pK_a = 6.86) that the corresponding amidines were readily prepared. Fresh aluminum chloride was found to be a requisite in the reaction, neglect of this factor resulting in a decrease in yield of the amidine and, in some cases, no reaction at all. Decomposition in the work-up of the reaction intermediate occurred unless low temperatures were observed, and the most efficient method of purification of these amidines was by fractional distillation under reduced pressure, whereby a small amount of unchanged amine was obtained as a forerun. The crystalline amidines were purified easily by crystallization from petroleum ether. Some decomposition of the amidines occurred on storage, occasionally resulting in incorrect analytical values, but the amidines could be readily characterized as their picrates (Table I).

The N-(2-pyridyl)benzamidines used in this study were prepared by the standard amidine procedure described above and were purified by recrystallization from benzene or benzene–petroleum ether (Table I). The presence of the phenyl group had a stabilizing effect on these amidines which was reflected in very little decomposition occurring in the work-up procedure, even above room temperature.

In order to obtain the parent s-triazolo[1,5-a]pyridine by this route, it is necessary to synthesize N-(2-pyridyl)-formamidine.[8a] Several unsuccessful approaches were used in attempts to prepare this intermediate amidine. Taylor[8b] has reported the formation of some heterocyclic formimidates from the reaction of the corresponding amine with triethyl orthoformate and acetic anhydride, and alcoholic ammonia was then used to convert the imidate into the formamidine. Application of this procedure to a 2-aminopyridine should yield the N-(2-pyridyl)formamidine; however, 2-amino-5-methylpyridine gave only N-(5-methylpyrid-2-yl)acetamide. It has been reported[9] that, when aniline hydrochloride was refluxed with formamide, N-phenylformamidine was formed readily. However, 2-amino-3-methylpyridine hydrochloride, on being heated with formamide, gave only the N-formyl derivative of 2-amino-3-methylpyridine.

As the availability of the fused ring system with various substituents at position 2 depends primarily on the synthesis of the appropriate amidine precursor, several unsuccessful attempts were made to prepare suitable substituted amidines.

Attempted synthesis of a diamidine from malononitrile and 2-aminopyridine in the presence of aluminum chloride resulted only in a vigorous reaction from which no product could be isolated. A convenient, synthetic route to 2-amino-s-triazolo[1,5-a]pyridine would be the oxidative cyclization of a pyrid-2-ylguanidine, but attempts to prepare 4-methylpyrid-2-ylguanidine from the reaction of 2-amino-4-methylpyridine hydrochloride and cyanamide in boiling water[10] were unsuccessful. 2-Pyridylurea, readily available from the fusion of 2-aminopyridine and urea,[11] failed to undergo cyclization to s-triazolo[1,5-a]pyridin-2-ol with lead tetraacetate or ferric chloride. An alternative ring closure product,[7] oxazolo[4,5-b]pyridine, was also not detected in the reaction mixture.

2-Alkyl- (or Aryl-) s-triazolo[1,5-a]pyridines.—Dehydrogenation of the N-(2-pyridyl)alkyl- (or aryl-) amidines with lead tetraacetate occurred readily in a refluxing anhydrous benzene solution with the formation of the bicyclic ring system 2. The products thus obtained are listed in Table II. A free-radical mechanism was most likely involved and can be represented as a two-step process as shown in Chart I.

It should be possible, if this mechanism were operative, to obtain dimeric products such as 6 from the resonance-stabilized, initial free radical (5). Although no such products have actually been identified, high-boiling residues always remained from the purification of the s-triazolo[1,5-a]pyridines, and these products are at present under investigation. The formation of this dimeric-type product would be analogous to the

(6) P. Oxley, M. W. Partridge, and W. F. Short, *J. Chem. Soc.*, 1110 (1947).

(7) J. Bernstein, B. Stearns, E. Shaw, and W. A. Lott, *J. Am. Chem. Soc.*, **69**, 1151 (1947).

(8) (a) For another unsuccessful attempt, see W. L. F. Armarego, *J. Chem. Soc.*, 2784 (1965); (b) E. C. Taylor and W. A. Ehrhart, *J. Am. Chem. Soc.*, **82**, 3140 (1960); E. C. Taylor and P. K. Loeffler, *ibid.*, **82**, 3247 (1960).

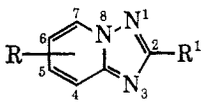
(9) C. C. Price and R. M. Roberts, *ibid.*, **68**, 1255 (1946).

(10) S. R. Safir, S. Kushner, L. M. Brancone, and Y. Subbarow, *J. Org. Chem.*, **13**, 924 (1948).

(11) G. A. Moersh, R. W. Gouley, H. T. Patterson, and H. S. Moshier, *J. Am. Chem. Soc.*, **69**, 2619 (1947).

TABLE II

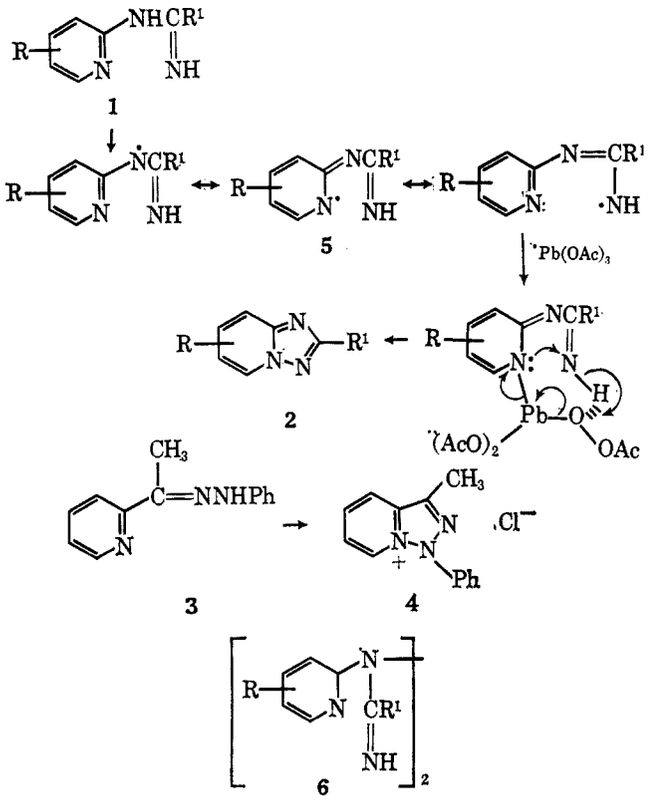
SUBSTITUTED *s*-TRIAZOLO[1,5-*a*]PYRIDINES



R	R¹	M.p. or b.p. (mm.); °C.	Method[a]	Yield, %	Solvent[b]	Form[c]	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
H	H	102–103	B	90	B	Needles	$C_6H_5N_3$	60.5	4.2	35.5	60.3	4.2	35.1
H	Et	60–62 (0.25)	A	78	..	Colorless oil	$C_8H_9N_3$	65.3	6.2	28.0	65.2	6.3	28.5
H	Ph	138	A, C	72	A	Plates	$C_{12}H_9N_3$	73.8	4.7	21.5	73.9	4.7	21.0
4-CH_3	H	51	B	60	B	Needles	$C_7H_7N_3$	63.1	5.3	31.6	63.2	5.2	31.5
4-CH_3	CH_3	56 (0.1)	A	62	..	Colorless oil	$C_8H_9N_3$	65.3	6.2	28.6	65.4	6.4	28.4
4-CH_3	Ph	97–98	A	67	A	Irreg. prisms	$C_{13}H_{11}N_3$	74.6	5.3	20.1	74.4	5.5	20.0
4-CH_3	Et	52–53	A	81	B	Needles	$C_9H_{11}N_3$	67.1	6.9	26.1	66.9	6.8	26.1
5-CH_3	H	79	B	60	B	Needles	$C_7H_7N_3$	63.1	5.3	31.6	63.35	5.4	31.4
5-CH_3	CH_3	51–52	A	25	C	Needles	$C_8H_9N_3$	65.3	6.2	28.6	65.2	6.2	28.6
5-CH_3	Ph	140	A, C	68, 80	A	Needles	$C_{13}H_{11}N_3$	74.6	5.3	20.1	74.9	5.0	20.4
6-CH_3	H	57–58	B	65	B	Needles	$C_7H_7N_3$	63.1	5.3	31.6	63.0	5.5	31.7
6-CH_3	CH_3	53–54	A	83	B	Needles	$C_8H_9N_3$	65.3	6.2	28.6	65.2	6.3	28.2
6-CH_3	Ph	120–121	A	78	A	Plates	$C_{12}H_{11}N_3$	74.6	5.3	20.1	74.8	5.3	20.2
7-CH_3	H	58–59	B	60	B	Needles	$C_7H_7N_3$	63.1	5.3	31.6	63.2	5.4	31.4
7-CH_3	CH_3	49–52 (0.02)	A	66	..	Colorless oil	$C_8H_9N_3$	65.3	6.3	28.6	65.3	6.1	28.5
7-CH_3	Ph	84–85	A	65	A	Irreg. prisms	$C_{13}H_{11}N_3$	74.6	5.3	20.1	74.4	5.4	19.9
5,7-$(CH_3)_2$	CH_3	44–46	A	75	C	Prisms	$C_9H_{11}N_3$	67.1	6.9	26.1	66.9	7.1	25.8
5,7-$(CH_3)_2$	Ph	153–156	A	79	A	Prisms	$C_{14}H_{13}N_3$	75.3	5.9	18.8	75.3	5.8	18.8

[a] See Experimental Section. [b] A = benzene, B = benzene–petroleum ether, and C = petroleum ether. [c] All crystalline products were colorless.

CHART I



formation of hydrazobenzene from aniline by lead tetraacetate oxidation.[12] It is interesting that a dehydrogenation agent such as 2,3-dichloro-5,6-dicyanobenzoquinone gave only tarry material when applied to this reaction system.

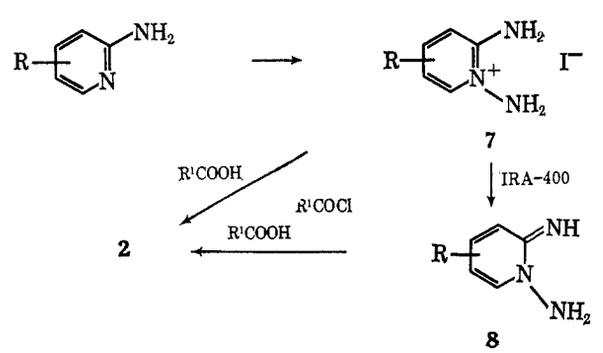
The majority of the 2-alkyl-*s*-triazolo[1,5-*a*]pyridines were purified by distillation *in vacuo* since the products were low-melting solids. It is of interest to note that three of the 2-alkyl-*s*-triazolo[1,5-*a*]pyridine derivatives are colorless liquids, which is indeed surprising since the corresponding, isomeric *s*-triazolo[4,3-*a*]-pyridines are solids. Especially surprising is the melting point of 102–103° of *s*-triazolo[1,5-*a*]pyridine itself. The products were obtained as colorless oils or colorless needles and all had a disagreeable odor, characteristic of nitrogenous bases, which could be detected even in the smallest quantities. This odor is not characteristic of the isomeric [4,3-*a*] series. Sublimation of the 2-phenyl derivatives was found to be the most efficient method of purification from nonvolatile by-products present in the crude reaction residue, and all the 2-phenyl-*s*-triazolo[1,5-*a*]pyridines crystallized from petroleum ether or benzene–petroleum ether as colorless plates (Table II).

Because of the limited applications of the above syntheses, particularly the synthesis of members unsubstituted in the 2-position, an alternative route was sought. A suitable intermediate would be a 1,2-diaminopyridinium salt (**7**), or the related free base, which would be expected to undergo a facile ring closure to the bicyclic system. 1-Aminopyridinium salts have been known for some time[13] and the recent, direct amination of tertiary amines to the correspond-

(12) K. H. Pausacker and J. G. Scroggie, *J. Chem. Soc.*, 4003 (1954).

(13) J. N. Ashley, G. L. Buchanan, and A. P. T. Easson, *ibid.*, 60, (1947); J. A. Moore, *J. Am. Chem. Soc.*, **77**, 3417 (1955); J. A. Moore and J. Binkert, *ibid.*, **81**, 6045 (1959); E. N. Shaw, "Pyridine and Its Derivatives," Part II, E. Klingsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1961, p. 143.

ing hydrazinium salts with hydroxylamine-O-sulfonic acid[14] suggested the application of this procedure to 2-aminopyridine. It was found that 2-aminopyridine and its ring-substituted methyl derivatives were aminated readily although the yields of purified products were only of the order of 30%. This appears to be more of an isolation problem rather than an unsatisfactory reaction, as these salts are exceedingly soluble in alcohol. Consistent yields of the amination product were dependent on purification of the commercial hydroxylamine-O-sulfonic acid, best achieved by washing with ether. Generation of the corresponding free bases (**8**) was carried out by passing an alcohol solution of the salt through a column of Amberlite IRA-400 ion-exchange resin. These bases were well-defined, crystalline products, very sensitive to moisture and readily reverted to their salts with mineral acids.



Those bases which were too sensitive to moisture for accurate combustion analysis were thoroughly characterized as their salts and through their ultraviolet, infrared, and n.m.r. spectral characteristics. At this time a short note appeared[15] describing the amination of 2-aminopyridine itself but no details of the procedure were given.

Cyclization of the 1,2-diaminopyridinium salts with aliphatic acids readily gave the corresponding 2-substituted *s*-triazolo[1,5-*a*]pyridines (**2**). Aliphatic or aromatic acid chlorides in the presence of pyridine were particularly useful in effecting this cyclization, and terephthaloyl chloride yielded the corresponding dicondensation product. Of particular interest are the ring closures of the free bases with formic acid in which yields of the cyclized products in excess of 90% were usually obtained. We are, at present, investigating the use of the free bases for the introduction of more diverse substituents into the 2-position of the bicyclic nucleus.

Oxidation of *s*-triazolo[1,5-*a*]pyridine with potassium permanganate resulted in the disruption of the pyridine ring and the formation of *s*-triazole-3-carboxylic acid. This reaction is analogous to that occurring in the *s*-triazolo[4,3-*a*]pyridine series. Bromination of the nucleus with bromine in methanol or acetic acid was not successful, *s*-triazolo[1,5-*a*]pyridine hydrobromide only being obtained. N-Bromosuccinimide likewise gave negative results and nitration of the nucleus was also unsuccessful.

(14) R. Gösl and A. Mewsen, *Chem. Ber.*, **92**, 2521 (1959); *Org. Syn.*, **43**, 1 (1963); H. F. Hodson, British Patent 926,249 (May 15, 1963); *Chem. Abstr.*, **59**, 11435*f* (1963). Other references of interest can be found in W. R. Hertler and M. S. Raasch, *J. Am. Chem. Soc.*, **86**, 3661 (1964).

(15) T. Okamoto, M. Hirobe, and Y. Tamai, *Chem. Pharm. Bull.* (Tokyo), **11**, 1089 (1963).

Experimental Section[16]

N-(2-Pyridyl)alkyl- (or aryl-) amidines. A. Aluminum Chloride Method.—The 2-aminopyridine 0.2 mole), aluminum chloride (0.2 mole), and the cyanide (alkyl cyanides, 0.3 mole; phenyl cyanide, 0.2 mole) were heated together at 170° for 15–30 min. after the initial, vigorous reaction had subsided. The intermediate complex was decomposed by the cautious addition of water and the reaction mixture was then made alkaline with sodium hydroxide solution, keeping the temperature at 0–5°. The above was repeated again and the aqueous solutions were combined. After extraction into ether (five 100-ml. portions) and drying (Na_2SO_4), the crude product was obtained as a viscous oil, which was fractionated under reduced pressure into the amidine (Table I) and unreacted amine.

B. Imino Ether Method.—Equimolar amounts of 2-amino-4,6-dimethylpyridine (6.1 g., 0.05 mole) and ethyl acetimidate hydrochloride (6.1 g., 0.05 mole) were stirred together in a dry pyridine solution (40 ml.) for 1 hr. The amidine hydrochloride separated and crystallized from methanol–ether as colorless needles, 7.2 g. (60%), m.p. 224–225°.

Anal. Calcd. for $C_9H_{14}ClN_3$: C, 54.1; H, 7.1; N, 21.1. Found: C, 54.0; H, 7.1; N, 20.9.

The free base was obtained from the hydrochloride by treating its aqueous solution with sodium hydroxide solution at 0°. It crystallized from benzene–petroleum ether as fine, colorless needles, 5.0 g. (85%), m.p. 124–125°, identical with the product prepared by method A.

1,2-Diaminopyridinium Iodides (Table III).—Hydroxylamine-O-sulfonic acid (11.3 g., 0.1 mole) was dissolved in water (64 ml.), 2-aminopyridine (14.1 g., 0.15 mole) was added, and the mixture was heated on a steam bath at 85–90° for 30 min. After cooling, potassium carbonate (13.8 g., 0.1 mole) was added with shaking. Water was then removed at 45–50° using a rotary evaporator, and the resulting mass was shaken with absolute alcohol (80 ml.). The potassium sulfate that separated was removed by filtration and the filtrate was treated with 57% hydriodic acid (14 ml.). The alcoholic filtrate was then kept below −20° for 1.5 hr. and crystallization was induced by rubbing. The colorless 1,2-diaminopyridinium iodide which separated crystallized from absolute alcohol (charcoal) as colorless needles (7.0 g., 30%), m.p. 160° dec.

Preparation of the 1-Amino-2-imino-1,2-dihydropyridines from Their Salts.—1,2-Diaminopyridinium iodide (1.2 g.) in methanol (20 ml.) was passed through a column (1 × 20 cm.) of Amberlite IRA-400 ion-exchange resin regenerated by passing 1 *N* NaOH solution. The eluate was evaporated and a gummy mass was obtained (0.5 g.) which after several crystallizations from benzene–petroleum ether was obtained as light yellow needles: m.p. 65–66°; $\lambda_{max}^{CH_3OH}$ 231, 306 mμ (log ε 3.93, 3.75); infrared ($CHCl_3$), strong bands at 3145, 1618, 1546 cm.$^{-1}$. The base was very hygroscopic, this property often interfering with an accurate melting point determination; it readily formed the quaternary hydroxide and with hydriodic acid regenerated the iodide.

Anal. Calcd. for $C_5H_7N_3$: C, 55.05; H, 6.4; N, 38.5. Found: C, 54.9; H, 6.5; N, 38.1.

The following bases were obtained in comparable yields in a similar fashion as cream needles from benzene–petroleum ether: 1-amino-2-imino-3-methyl-1,2-dihydropyridine: m.p. 62–63°; $\lambda_{max}^{CH_3OH}$ 233, 314 mμ (log ε 4.00, 3.78); infrared ($CHCl_3$), strong bands at 3125, 1613, 1527–1515 cm.$^{-1}$.

Anal. Calcd. for $C_6H_9N_3$: C, 58.5; H, 7.3; N, 34.1. Found: C, 58.3; H, 7.3; N, 34.1.

1-Amino-2-imino-4-methyl-1,2-dihydropyridine, m.p. 60°, consistently retained 1/3 mole of water: $\lambda_{max}^{CH_3OH}$ 233, 301 mμ (log ε 3.78, 3.69); infrared ($CHCl_3$), strong bands at 3145, 1639–1631, 1550 cm.$^{-1}$.

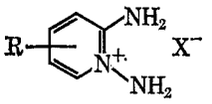
Anal. Calcd. for $C_6H_9N_3 \cdot 1/3H_2O$: C, 55.8; H, 7.5; N, 32.55. Found: C, 55.4; H, 7.0; N, 31.9.

1-Amino-2-imino-5-methyl-1,2-dihydropyridine, m.p. 75–77°, also tenaciously held about 0.5 mole of water: $\lambda_{max}^{CH_3OH}$ 233, 313 mμ (log ε 3.82, 3.50); infrared ($CHCl_3$), strong bands at 3145, 1634, 1550–1538 cm.$^{-1}$. 1-Amino-2-imino-6-methyl-1,2-

(16) Infrared spectra were measured with a Baird IR 2 spectrophotometer and with a Perkin-Elmer 421 spectrophotometer, and ultraviolet absorption spectra were determined using a Beckman DK2 spectrophotometer. Analyses were by Galbraith Laboratories, Knoxville, Tenn., and Drs. G. Weiler and F. B. Strauss, Oxford, England. Petroleum ether refers to the fraction b.p. 60–110°.

TABLE III

1,2-DIAMINOPYRIDINIUM SALTS[a]



R	X	M.p., °C. dec.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
H	I	160	$C_5H_8IN_3$	25.3	3.4	17.7	25.4	3.5	17.7
H	Cl	170–172	$C_5H_8ClN_3$			28.9			28.8
3-CH_3	I	172	$C_6H_{10}IN_3$	28.7	4.0	16.7	28.8	4.0	16.75
4-CH_3	I	119	$C_6H_{10}IN_3$	28.7	4.0	16.7	28.9	3.8	16.5
5-CH_3	I	161	$C_6H_{10}IN_3$	28.7	4.0	16.7	28.9	4.05	16.8
5-CH_3	Br	240	$C_6H_{10}BrN_3$	35.3	4.9	20.6	35.1	4.8	20.8
6-CH_3	I	206	$C_6H_{10}IN_3$	28.7	4.0	16.7	28.9	4.3	16.9

[a] All crystallized as colorless needles from ethanol.

dihydropyridine, m.p. 84°, behaved in a similar fashion in holding fractional amounts of water: $\lambda_{max}^{CH_3OH}$ 233, 311 mμ (log ε 3.95, 3.91); infrared ($CHCl_3$), strong bands at 3175, 1618, 1550–1538 cm.$^{-1}$.

s-Triazolo[1,5-a]pyridines. A.—The above amidines (0.05 mole) were dissolved in dry benzene (60 ml.) and a small amount of benzene was distilled to remove last traces of moisture. After cooling the solution to room temperature, dry lead tetraacetate (0.05 mole) was added and the mixture was heated under reflux for 30–60 min. The reaction mixture was extracted with 30% sodium hydroxide solution (three 30-ml. portions) and the benzene solution was then dried (Na_2SO_4) and evaporated under reduced pressure. The brown residue was usually purified by sublimation or by distillation *in vacuo* and then crystallization from benzene or from benzene–petroleum ether. These products are described in Table II.

B.—1,2-Diaminopyridinium iodide (5.9 g., 0.03 mole) was dissolved in pyridine (6 ml.) and 90% formic acid (6.5 ml.) was added and the mixture was refluxed for 8 hr. The excess reagents were removed under reduced pressure and the residue was extracted with hot benzene (50 ml., charcoal) and concentrated. The crystalline material that separated crystallized from benzene–petroleum ether as colorless needles (2.6 g., 88%), m.p. 102–103°. The identity of the product as *s*-triazolo[1,5-*a*]pyridine was established by mixture melting point determination and identical infrared and n.m.r. spectra with those of an authentic specimen.

The same product was obtained in 90% yield when the base from 1,2-diaminopyridinium iodide was refluxed with excess formic acid for 2 hr. and the reaction mixture was worked up essentially as described above.

C.—1,2-Diaminopyridinium iodide (0.005 mole) in pyridine (3 ml.) was heated with aliphatic or aromatic acid chlorides (0.01 mole) for 3 hr. and the excess reagents were subsequently removed under reduced pressure. The 3-methyl product was obtained by sublimation directly from the crude residue and was converted into its picrate in methanol, forming yellow needles, m.p. 176–178° dec. Its identity as 3-methyl-*s*-triazolo[1,5-*a*]-pyridine picrate was confirmed by direct comparison with an authentic sample of the picrate.

The 3-phenyl product was isolated from the reaction mixture by extraction with hot benzene (charcoal) and crystallized from benzene–petroleum ether as colorless needles, m.p. 137–138°. The melting point remained undepressed on admixture with an authentic sample, and the infrared spectra of the two products were superimposable.

3-Phenyl-5-methyl-*s*-triazolo[1,5-*a*]pyridine was prepared as above from 4-methyl-1,2-diaminopyridinium iodide, pyridine, and benzoyl chloride in 80% yield, m.p. 140°. The product was identical with an authentic sample of 3-phenyl-5-methyl-*s*-triazolo[1,5-*a*]pyridine in all respects.

***p*-Di(3-*s*-triazolo[1,5-*a*]pyridyl)benzene.**—1,2-Diaminopyridinium iodide (1.2 g., 0.005 mole) was refluxed in pyridine (5 ml.) with terephthaloyl chloride (0.5 g., 0.0025 mole) for 4 hr. The solid (0.45 g.) which separated on cooling was collected and found to be very sparingly soluble in most of the common organic solvents. It crystallized from dimethylformamide as a microcrystalline powder, m.p. >370°.

Anal. Calcd. for $C_{18}H_{12}N_6$: C, 69.2; H, 3.8; N, 26.9. Found: C, 69.0; H, 4.0; N, 26.7.

***s*-Triazolo[1,5-*a*]pyridine Hydrobromide. A.**—*s*-Triazolo-[1,5-*a*]pyridine (0.5 g., 0.06 mole) was dissolved in methanol (5 ml.), and bromine (2 ml.) in methanol (8 ml.) was added dropwise with shaking when a white solid separated. The mixture was kept at room temperature overnight and the excess reagents were subsequently removed under reduced pressure. The residue crystallized from methanol and then from methanol–ether as short, white needles (0.5 g.), m.p. 264° dec.

Anal. Calcd. for $C_6H_6BrN_3$: C, 36.0; H, 3.0; N, 21.0. Found: C, 36.1; H, 3.1; N, 21.2.

B.—*s*-Triazolo[1,5-*a*]pyridine (0.4 g.) was dissolved in absolute alcohol (5 ml.) and 48% hydrobromic acid (1 ml.) was added dropwise. The white solid that separated crystallized from methanol–ether as short, white needles (0.4 g.), m.p. 264° dec. The melting point remained undepressed when admixed with a sample prepared above and the infrared spectra of the two products were superimposable.

Potassium Permanganate Oxidation of *s*-Triazolo[1,5-*a*]-pyridine.—*s*-Triazolo[1,5-*a*]pyridine (0.5 g., 0.04 mole) was dissolved in water (100 ml.) and potassium permanganate (3.7 g.) was added with stirring. After the addition was complete, the mixture was kept at 50–60° on a steam bath for 1 hr. It was then filtered to remove the manganese dioxide and the filtrate was concentrated under reduced pressure to about 20 ml. and cooled. The cold solution was carefully acidified to pH 1 and the *s*-triazole-3-carboxylic acid that separated (0.3 g.) was collected, m.p. 125–127° dec. The melting point remained undepressed when mixed with an authentic specimen of the acid, and their infrared spectra were superimposable.

Attempted Synthesis of N-(2-Pyridyl)formamidines. A. From Formamide.—2-Amino-3-methylpyridine hydrochloride (14.4 g., 0.01 mole) was heated with formamide (3.5 g., 0.078 mole) at 160° for 3 hr. Water (30 ml.) was added to the reaction mixture and, after basification with ammonium hydroxide solution, the alkaline solution was extracted with benzene (two 75-ml. portions) and dried (Na_2SO_4). The benzene was removed and a yellow, viscous oil which crystallized after standing overnight was obtained. The crude product crystallized from benzene–petroleum ether as colorless needles, 11.0 g. (99%), m.p. 135–137°. Its mixture melting point and infrared spectrum were identical with those of N-(3-methylpyrid-2-yl)formamide (lit.[17] m.p. 138°).

B. From Triethyl Orthoformate.—2-Amino-5-methylpyridine (17.7 g., 0.16 mole), acetic anhydride (80 ml.), and triethyl orthoformate (80 ml.) were heated under reflux for 2 hr. Removal of the acetic anhydride and triethyl orthoformate under reduced pressure left a light brown residue which crystallized from benzene–petroleum ether as colorless needles, 10 g. (42%), m.p. 102–103°. This was identified by mixture melting point and infrared data as N-(5-methylpyrid-2-yl)acetamide (lit.[18] m.p. 103–104°).

Attempted Synthesis of N-[2-(4-Methylpyrid-2-yl)]guanidine.—2-Amino-4-methylpyridine hydrochloride (12.0 g., 0.083 mole) was stirred and heated in water (100 ml.). After reaching the boiling point, cyanamide (7.4 g. in 17 ml. of water) was added

(17) G. R. Clemo and G. A. Swan, *J. Chem. Soc.*, 603 (1945).

(18) J. Bernstein, B. Stearns, M. Dexter, and W. A. Lott, *J. Am. Chem. Soc.*, **69**, 1147 (1947).

dropwise over a period of 1 hr. and then refluxed with stirring an additional 15 min. On cooling to 0° in an ice bath, the solution was basified with concentrated sodium hydroxide solution and the resulting crude product was collected and recrystallized from petroleum ether from which 2-amino-4-methylpyridine separated as colorless plates, 7.7 g. (78%), m.p. 98°.

Attempted Synthesis of s-Triazolo[1,5-a]pyridin-2-ol by Oxidation of 2-Pyridylurea. A. With Lead Tetraacetate.—2-Pyridylurea (1.0 g., 0.007 mole) and glacial acetic acid (25 ml.) were heated under reflux for 1 hr. The reaction mixture was poured into water, and when no product crystallized, the aqueous solution was concentrated under reduced pressure to a dark brown oil. This residue could not be purified or characterized.

B. With Ferric Chloride.—2-Pyridylurea (4.0 g., 0.03 mole) was dissolved in water (100 ml.) and hydrochloric acid (10 ml.) and the resulting mixture was heated to reflux temperature. To the stirred solution, ferric chloride (16.2 g. in 100 ml. of water) was added dropwise, and after addition, the reaction mixture was stirred an additional 30 min. The contents were then cooled to 0° in an ice bath and sodium carbonate was added until the solution had pH 11. Sodium sulfide was added and the precipitated iron sulfide was removed. No identifiable products were isolated from the reaction mixture.

1,2,4-Triazoles. XIV. Reactions of the s-Triazolo[4,3-a]pyridine Ring System[1a,b]

K. T. POTTS,[1c] H. R. BURTON, AND S. K. ROY

Department of Chemistry, University of Louisville, Louisville, Kentucky 40208

Received July 26, 1965

s-Triazolo[4,3-a]pyridine was readily oxidized at room temperature with potassium permanganate to s-triazole-3-carboxylic acid and underwent rearrangement to s-triazolo[1,5-a]pyridine on treatment with hot base. This rearrangement occurred readily with a variety of 3-substituents. Bromination took place in the 3-position and only in the six-membered ring when it was activated by at least two methyl substituents. Other electrophilic substitution reactions were unsuccessful and the nucleus was also resistant to nucleophilic substitution. Under neutral conditions the 3-proton only was exchanged with deuterium. Dimethyl acetylenedicarboxylate and tetracyanoethylene did not form Diels–Alder adducts but yielded instead 3-substitution products. A 3-amino substituent readily formed benzal and benzoyl derivatives and, *via* the diazonium salt, was replaced with hydrogen and halogens. The diazonium salt coupled readily with 2-naphthol. 3-Halogen-substituted products were resistant to nucleophilic displacement reactions, did not form Grignard reagents, and were formed in poor yield from the corresponding s-triazolo[4,3-a]pyridin-3-ol. Protonation and salt formation occurred at N-1 except for the 3-amino product, where salt formation occurred at N-2. The salts were readily reduced with sodium borohydride, but the unprotonated nucleus itself was resistant to catalytic hydrogenation and reduction with metal hydrides. Methylation of s-triazolo[4,3-a]pyridin-3-ol with methyl sulfate and alkali and diazomethane gave 2-methyl-s-triazolo[4,3-a]pyrid-3-one, and under comparable conditions s-triazolo[4,3-a]pyridine-3-thiol yielded methyl 3-s-triazolo[4,3-a]pyridyl sulfide.

In an earlier publication,[2] synthetic sequences used to obtain representatives of the s-triazolo[4,3-a]-pyridine ring system were described and, as part of a program studying the properties of bicyclic heterocycles with bridgehead nitrogen atoms, we now report on the reactions and properties of the s-triazolo[4,3-a]pyridine system (**1**).

The behavior of the nucleus under oxidizing conditions is particularly interesting. In contrast to various indolizines which always yield substituted pyridine derivatives,[3] s-triazolo[4,3-a]pyridine (**1**, R = H) was readily oxidized by potassium permanganate (an exothermic reaction) at room temperature to s-triazole-3-carboxylic acid (**2**). The pyrazolo[1,5-a]-pyridine system is similarly oxidized to pyrazole-3-carboxylic acid,[4] and the additional nitrogen atoms in the five-membered ring apparently confer greater stability on that portion of the molecule. This ready oxidation caused us to examine in detail reactions that would give a qualitative estimation of the double bond character present in the pyridine portion of the nucleus, indicated by proton magnetic resonance studies.[5]

The greater stability of the s-triazole ring was again evidenced by the action of hot alkali on various 3-substituted s-triazolo[4,3-a]pyridines. Hot sodium hydroxide solution brought about an interesting rearrangement of the s-triazolo[4,3-a]pyridine nucleus to products that had identical analytical and molecular weight data with their precursors and which have been identified as isomeric s-triazolo[1,5-a]pyridines (**3**). This identity was initially indicated by the characteristic ultraviolet spectra already established for isomeric, fused-ring systems containing the s-triazole nucleus[6] and was confirmed by the various interrelationships and transformations shown in Chart I, as well as by comparison of the products with those of established structure. Thus 3-methyl-s-triazolo[4,3-a]pyridine (**1**, R = CH_3), when heated with 10% sodium hydroxide solution for 48 hr., gave 2-methyl-s-triazolo[1,5-a]-pyridine (**3**, R = CH_3), identical with a sample prepared[7] by the lead tetraacetate oxidation of N-2-pyridylacetamidine (**6**, R = CH_3). The rearrangement of 3-amino-s-triazolo[4,3-a]pyridine (**1**, R = NH_2) to 2-amino-s-triazolo[1,5-a]pyridine (**3**, R = NH_2) under these conditions provided a means of interrelating the isomeric products. Deamination of 2-amino-s-triazolo[1,5-a]pyridine using the diazonium salt and hypophosphorous acid gave s-triazolo[1,5-a]-

(1) (a) Support of this work by Public Health Service Research Grant CA-05973, 01-03, National Cancer Institute, is gratefully acknowledged. (b) Part of this material appeared as a preliminary communication: K. T. Potts and H. R. Burton, *Proc. Chem. Soc.*, 420 (1964). (c) To whom correspondence should be sent: Department of Chemistry, Rensselaer Polytechnic Institute, Troy, N. Y.

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(4) J. D. Bower and G. R. Ramage, *J. Chem. Soc.*, 4506 (1957).

(5) K. T. Potts, H. R. Burton, T. H. Crawford and S. W. Thomas, to be submitted. All these protons occur at lower field than in the unsubstituted product, a fact readily attributable to the 3-substituent.

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(7) K. T. Potts, H. R. Burton, and J. Bhattacharyya, *ibid.*, **31**, 260 (1966).