5-Oxo-4,5-dihydro-1H-pyrrolo[3,2-b]pyridine (34).—5-Methoxy-4-azaindole (19) (1 g) was dissolved in 20 ml of 48% hydrobromic acid, and the mixture was heated under reflux for 2.5 hr. It was then evaporated to dryness; the residue was dissolved in 4 ml of water; and the solution was adjusted to pH 7 with solid sodium carbonate. The precipitate was filtered, dried, crystallized from methanol, and sublimed at 220° (1 μ), giving 825 mg (96%): mp 280–289°; uv max 330 mμ (ϵ 12,700).

Anal. Calcd for $C_7H_6ON_2$: C, 62.7; H, 4.5; N, 20.9. Found: C, 62.4; H, 4.5; N, 20.9.

3-Dimethylaminomethyl-5-methoxy-4-azaindole (36).—5-Methoxy-4-azaindole (19) (1 g) was dissolved in 60 ml of 1-butanol; 400 mg of paraformaldehyde and 1 g of dimethylamine hydrochloride were added; and the mixture was heated at reflux for 30 min and evaporated to dryness *in vacuo*. The residue was dissolved in 50 ml of 4 *N* hydrochloric acid, washed twice with 100 ml of ether, alkalized with solid potassium carbonate, and extracted several times with chloroform. The dried (Na_2SO_4) chloroform extracts were evaporated *in vacuo*, and the oily residue was dissolved in 50 ml of ethanol and precipitated as a dipicrate. The dipicrate was centrifuged, washed twice with 20 ml of cold ethanol, and recrystallized from methanol to yield 3.3 g (75%), mp 174–176°.

Anal. Calcd for $C_{23}H_{21}O_{15}N_9$: C, 41.6; H, 3.1; N, 19.0. Found: C, 41.4; H, 3.0; N, 18.9.

The free base was recovered by dissolution of the dipicrate in 90% aqueous acetone and passage through an IRA-400 (HCO_3) ion-exchange resin[26] column: nmr (D_2O), δ 3.1 [s, $N(CH_3)_2$], 4.8 (s, CH_2), 8.3 (s, C-2 H).

3-Formyl-5-methoxy-4-azaindole (35).—5-Methoxy-4-azaindole (15) (200 mg, 1.2 mmol) dissolved in 0.1 ml of dimethylformamide was added to a mixture of 0.12 ml (1.3 mmol) of phosphorous oxychloride and 0.4 ml of dimethylformamide cooled at 0°; the solution was heated at 70° for 2 hr and was cooled. Then 2 ml of ice water was added. The crystalline precipitate was centrifuged, dried, and crystallized from ethanol giving 85 mg (40%) of **35**: mp 145–147°; ir, 1720 cm^{-1} (CHO).

Anal. Calcd for $C_9H_8N_2O_2$: C, 61.3; H, 4.5; N, 15.9. Found: C, 61.6; H, 4.7; N, 16.2.

Registry No.—**2**, 17288-26-5; **3** monopicrate, 17288-27-6; **4**, 17288-28-7; **5**, 17288-29-8; **6**, 17288-30-1; **7**, 17322-90-6; **8**, 17288-31-2; **9**, 17288-32-3; **10**, 17288-33-4; **11**, 17288-34-5; **12**, 17288-35-6; **15**, 17288-36-7; **16**, 17288-37-8; **17**, 17288-38-9; **18**, 17288-39-0; **19**, 17288-40-3; **20**, 17288-41-4; **21**, 272-49-1; **22**, 17288-43-6; **23**, 17288-44-7; **24**, 17288-45-8; **25**, 17288-46-9; **26**, 17288-47-0; **27**, 17288-48-1; **28**, 17288-49-2; **29**, 17288-50-5; **30**, 17288-51-6; **31**, 17288-52-7; **32**, 17288-53-8; **33**, 17288-54-9; **34**, 17322-91-7; **35**, 17288-55-0; **36** dipicrate, 17288-56-1.

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Bridgehead Nitrogen Heterocycles. I. A Convenient Synthesis of Pyrazolo[1,5-*a*]pyridines[1]

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Cyclization of 2-alkyl-1-aminopyridinium salts (2) with acyl or aroyl chlorides in pyridine solution provides a convenient synthesis of derivatives of the title ring system (3). With 1-amino-2-methyl- and 1-amino-2,6-dimethylpyridinium iodides and benzoyl chloride, intermediate pyridinium betaines (6) were isolated unless prolonged reaction times were employed. Acylation at the 3 position occurs extremely readily in this ring system. Spectral data for derivatives of this ring system are described.

The direct amination of tertiary amines with hydroxylamine-O-sulfonic acid to yield the corresponding hydrazinium salts[2] has been applied to the preparation of 1,2-diaminopyridinium salts which underwent an extremely facile cyclization with aliphatic acids or acid chlorides to *s*-triazolo[1,5-*a*]pyridine derivatives.[3] The ease of amination of 2-alkylpyridines (1) to 2-alkyl-1-aminopyridinium salts (2) with hydroxylamine-O-sulfonic acid[2] suggested that cyclization of these salts with acyl chlorides might provide an extremely simple and direct synthesis of the pyrazolo[1,5-*a*]pyridine ring system (3). In this communication we describe the successful synthesis of this ring system by this route which now makes it readily available.

Pyrazolo[1,5-*a*]pyridine and its 2-phenyl derivative have been prepared previously[4a] by potassium ferricyanide oxidative ring closure of the corresponding 2-(2-aminoethyl)pyridines. Oxidation of pyrazolo[1,5-*a*]pyridine with potassium permanganate was shown to give pyrazole-3-carboxylic acid,[4a] clearly establishing that ring closure had occurred in the oxidation process. This was also indicated by the uv absorption spectrum of the system.[4b] A more complex substituted derivative has also been reported,[4c] and, by 1,3 dipolar addition type reactions to azomethine imines, fused[4d] and reduced[4e] pyrazolo[1,5-*a*]pyridine derivatives have been obtained. This last route has recently been used[4f] for the preparation of a variety of pyrazolo-[1,5-*a*]pyridine derivatives and is an effective complement to the synthetic procedures described below. In this present study several alkylpyridine derivatives were aminated at position 1 in moderately good yield, either with hydroxylamine-O-sulfonic acid or with its potassium salt.[2] The resulting 1-aminopyridinium salts (2) (Table I) were found to be extremely reactive toward acetyl chloride in pyridine, and cyclization occurred in a very short time. The 1-amino-2-methylpyridinium salts failed to give cyclic products with benzoyl chloride unless prolonged reaction times (24 hr) were used. With shorter reaction periods, pyridinium betaines were isolated as the sole products from the reaction mixtures. Moreover, the 1-amino-2-methylpyridinium salts always resulted in cyclic products which were acylated (acetyl or benzoyl group) in the 3 position. At no time was it possible to obtain a

(1) Support of this work by U. S. Public Health Service Research Grant CA 08495-01, 02 National Cancer Institute, is gratefully acknowledged.

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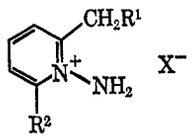
TABLE I

SOME 1-AMINOPYRIDINIUM SALTS[a]

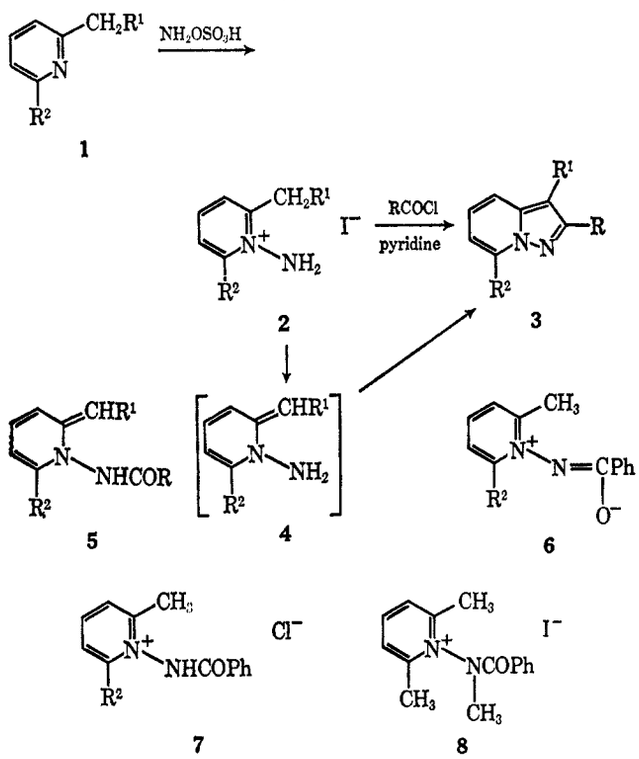


R¹	R²	X	Mp, °C	Yield, %	Formula[d]	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Uv data, $\lambda_{max}^{CH_3OH}$, mμ (log ε)
H	H	I	152	60	$C_6H_9IN_2$	30.5	3.8	11.9	30.7	3.8	11.9	208 (4.19), 224 (4.19), 260[b] (3.80), 270[b] (3.74)
H	H	Br	174–175	60	$C_6H_9BrN_2$	37.6	4.8	14.8	37.8	4.6	14.6	206 (3.92), 250 (3.87), 265[b] (3.76)
CH_3	H	I	102–103	30	$C_7H_{11}IN_2$	33.6	4.4	11.2	33.7	4.5	11.0	206 (3.93), 224 (4.09), 259[b] (3.73), 270[b] (3.65)
H	C_2H_5[c]	I	162	30	$C_8H_{13}IN_2$	36.4	4.9	10.6	36.3	5.0	10.7	208 (4.21), 220 (4.19), 275 (3.84)
H	CH_3	Br	228	40	$C_7H_{11}BrN_2$	41.4	5.4	13.8	41.25	5.4	13.9	206 (3.92), 250 (3.87), 265[b] (3.76)

[a] Colorless needles from absolute ethanol. [b] Shoulder. [c] Hygroscopic. [d] Respective registry numbers follow: 7583-90-6; 17414-45-8; 14613-36-6; 17408-27-4; 17408-28-5.

pyrazolo[1,5-*a*]pyridine derivative unsubstituted in the 3 position. (See Scheme I.)

SCHEME I



That cyclization of the pyridine salts to the bicyclic system had occurred was evident on the basis of analytical data (Table II) together with ir, nmr, and mass spectral data, as well as correlation of uv spectral data with that reported in the literature.[4b] Thus, the compound (**3**, R = R¹ = R² = CH_3) obtained when 1-amino-2-ethyl-6-methylpyridinium iodide was treated with acetyl chloride showed no –NH– and carbonyl absorption in its ir spectrum. Its mass spectrum[5] indicated a molecular weight of 160 [*m/e* 160 (M^+) (20%)], and its nmr spectrum (Table III) was consistent with what one would expect for a methyl-substituted pyrazolo[1,5-*a*]pyridine on the basis of data available for the parent nucleus.[6] Ready characterization of these products was effected by their conversion into picrates and hydrochlorides (Table II). These data quickly eliminated consideration of the uncyclized amide structure (**5**).

As mentioned above, reactions aimed at obtaining the fused system (**3**) unsubstituted in the 3 position were unsuccessful. Thus, when 1-amino-2-methylpyridinium iodide was treated with acetyl chloride, 3-acetyl-2-methylpyrazolo[1,5-*a*]pyridine (**3**, R = CH_3; R¹ = $COCH_3$; R² = H) was obtained instead of the anticipated 2-methylpyrazolo[1,5-*a*]pyridine (**3**, R¹ = R² = H; R = CH_3). The 3-acetyl product showed a carbonyl absorption at 1660 cm^{-1} in carbon tetrachloride solution, indicating that there must be some resonance contribution from the form involving the lone pair on the bridgehead nitrogen atom; *i.e.*, they do have some of the character of a vinylogous amide. Attempts to form 2,4-dinitrophenylhydrazones were unsuccessful, and the reduced basicity of the system was clearly shown by their inability to form salts with hydrochloric or picric acid, though it was possible to prepare the methiodide of 3-acetyl-2-methylpyrazolo[1,5-*a*]-pyridine (**3**, R = CH_3; R¹ = $COCH_3$; R² = H). That acetylation had taken place at the 3 position was evident from the nmr spectrum of the products (see Table III and Experimental Section). The bromination of pyrazolo[1,5-*a*]pyridine has also been shown[7] to occur in the 3 position and Hückel MO calculations[7] indicate that a high degree of π-electron localization is to be expected at this position. The fact that acetylation occurred in this position under such mild reaction conditions provides additional experimental support for these theoretical predictions and is reminiscent of the reactivity of the 3 position of the indolizine nucleus.

Reduction of the carbonyl group in 3-acetyl-2-methylpyrazolo[1,5-*a*]pyridine (**3**, R = CH_3; R¹ = $COCH_3$; R² = H) was effected with lithium aluminum hydride. The corresponding alcohol (**3**, R = CH_3; R¹ = $CHOHCH_3$; R² = H) was the sole product instead of the expected 3-ethyl-2-methylpyrazolo[1,5-*a*]-pyridine (**3**, R = CH_3; R¹ = CH_2CH_3; R² = H). No change in the reaction product was obtained when $LiAlH_4$–$AlCl_3$ was used as the reducing agent. The structure of the alcohol was established from its ir spectrum and by the characterization of its picrate.

As the cyclization of a 1-amino-2-ethylpyridinium salt occurred much more readily with benzoyl chloride

(5) Mass spectra were obtained with the direct inlet technique using a Hitachi Perkin-Elmer RMU-6E mass spectrometer.

(6) P. J. Black, M. L. Hefferman, L. M. Jackman, Q. N. Porter, and G. R. Underwood, *Aust. J. Chem.*, **17**, 1128 (1964).

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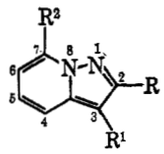
TABLE II

SOME PYRAZOLO[1,5-*a*]PYRIDINES



R	R¹	R²	Mp, °C	Formula[f]	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Uv data, $\lambda_{max}^{CH_3OH}$, mμ (log ε)
CH_3	$COCH_3$	H	90	$C_{10}H_{10}N_2O$[a]	69.0	5.7	16.1	68.9	5.9	15.9	223[b] (4.63), 226 (4.66), 252[b] (4.08), 260 (4.10), 310[b] (4.15)
CH_3	$COCH_3$	CH_3	110	$C_{11}H_{12}N_2O$	70.2	6.4	14.9	70.4	6.5	14.9	227 (4.43), 250[b] (3.72), 260[b] (3.72), 322 (4.20), 332[b] (4.11)
CH_3	CH_3	H	185	$C_9H_{11}N_2Cl$[c,d]	59.2	6.0	15.3	59.3	6.0	15.2	227 (4.68), 234 (4.65), 287 (3.80), 298 (3.83), 320 (3.43)
C_6H_5	CH_3	H	100	$C_{14}H_{12}N_2$[e]	80.7	5.8	13.45	80.5	5.95	13.5	208 (4.32), 238 (4.52), 258 (4.44), 296[b] (3.92), 310[b] (3.88)
CH_3	CH_3	CH_3	52	$C_{10}H_{12}N_2$[f]	75.0	7.55	17.5	74.7	7.75	17.2	229 (4.53), 294[b] (3.62), 301 (3.63)
C_6H_5	CH_3	CH_3	135–140[g] (0.1 mm)	$C_{15}H_{14}N_2$[h]	81.05	6.35	12.6	81.1	6.5	12.8	208 (4.16), 235 (4.51), 256 (4.36), 305 (3.89), 315[b] (3.84)
CH_3	$COCH_3$	C_2H_5	93	$C_{12}H_{14}N_2O$	71.3	7.0	13.85	71.05	7.0	13.8	226 (4.51), 250[b] (3.76), 260 (3.79), 320 (4.29), 332[b] (4.19)
Ph	COPh	H	110	$C_{20}H_{14}N_2O$	80.5	4.7	9.4	80.7	4.8	9.5	204 (4.47), 237[b] (4.50), 245 (4.52), 328 (4.09), 337[b] (4.03)
Ph	COPh	CH_3	125	$C_{21}H_{16}N_2O$	80.75	5.2	9.0	80.95	5.2	9.1	204 (4.58), 238 (4.56), 247[b] (4.54), 331 (4.20), 341[b] (4.17)

[a] Periodide, mp 165° dec. *Anal.* Calcd for $C_{11}H_{13}N_2I_4O$: C, 19.2; H, 1.9; N, 4.1. Found: C, 19.5; H, 2.5; N, 4.1. [b] Shoulder. [c] Free base, bp 160–165° (70 mm), darkens rapidly in air [$\lambda_{max}^{CH_3OH}$ mμ (log ε); 228 (4.55), 233 (4.55), 298 (3.57), 325[b] (3.21), 250[b] (3.72)]; picrate, mp 195° dec. *Anal.* Calcd for $C_{15}H_{13}N_5O_7$: C, 48.0; H, 3.5; N, 18.7. Found: C, 48.3; H, 3.7; N, 18.7. [d] Hydrochloride. [e] Picrate: mp 118°; registry number, 17408-33-2. *Anal.* Calcd for $C_{20}H_{15}N_5O_7$: C, 54.9; H, 3.5; N, 16.0. Found: C, 54.9; H, 3.5; N, 16.0. [f] Picrate: mp 165°; registry number, 17408-35-4. *Anal.* Calcd for $C_{16}H_{15}N_5O_7$: N, 18.0. Found: N, 18.3. [g] Boiling point. [h] Picrate: mp 112°; registry number, 17408-37-6. *Anal.* Calcd for $C_{21}H_{17}N_5O_7$: N, 15.5. Found: N, 16.0. [i] Respective registry numbers follow: 17408-29-6; 17408-30-9; 17408-31-0; 17408-32-1; 17408-34-3; 17408-36-5; 17408-38-7; 17408-39-8; 17408-40-1.

TABLE III

NMR DATA[a] FOR SOME PYRAZOLO[1,5-*a*]PYRIDINE DERIVATIVES[b]

Compound R	Compound R¹	Compound R²	Chemical shift, τ (ppm) τ2	τ3	τ4	τ5	τ6	τ7	Coupling constants, J (cps) $J_{4,5}$	$J_{4,6}$	$J_{4,7}$	$J_{5,6}$	$J_{5,7}$	$J_{6,7}$
CH_3	CH_3	H	*7.63*	*7.85*	2.74	3.08	3.48	1.74	8.90	1.17	1.02	6.79	1.00	6.93
CH_3	CH_3	7-CH_3	*7.57*	*7.80*	2.75	3.07	3.57	*7.33*	8.72	1.20		6.95		
CH_3	$COCH_3$	7-CH_3	*7.28*	*7.45*	1.87	2.67	3.24	*7.28*	9.02	1.51		7.01		
CH_3	$COCH_3$	H	*7.34*	*7.47*	1.82	2.59	3.14	1.60	9.12	1.52	1.54	7.10	1.00	6.79

[a] Methyl protons *in italics*. [b] Determined in $CDCl_3$.

than the cyclization of a 1-amino-2-methylpyridinium salt, the course of cyclization with a pyridinium salt containing both an ethyl and a methyl group in the appropriate positions in the same molecule was of particular interest. Thus, when 1-amino-2-ethyl-6-methylpyridinium iodide was treated with acetyl chloride, 2,3,7-trimethylpyrazolo[1,5-*a*]pyridine (**3**, R = R¹ = R² = CH_3) and 3-acetyl-2-methyl-7-ethylpyrazolo[1,5-*a*]pyridine (**3**, R = CH_3; R¹ = $COCH_3$; R² = C_2H_5) were isolated in approximately equal amounts. However, with benzoyl chloride only the sole product of ring closure involving the ethyl group, 3,7-dimethyl-2-phenylpyrazolo[1,5-*a*]pyridine (**3**, R = Ph; R¹ = R² = CH_3), was obtained.

Aliphatic acids did not react with the pyridinium salts either in the presence or the absence of pyridine and over extended reaction periods. When methanolic solutions of the salts were passed through Amberlite IRA-400 ion-exchange resin, a deep violet solution from which no pure product could be isolated was obtained. These strongly alkaline solutions regenerated the corresponding pyridinium salts when treated with a mineral or carboxylic acid. Again, the free base (**4**) generated from 1-amino-2-ethylpyridinium iodide (**2**, R¹ = CH_3; R² = H) reacted with benzoyl chloride in pyridine to give 3-methyl-2-phenylpyrazolo-[1,5-*a*]pyridine (**3**, R = Ph; R¹ = CH_3; R² = H) which was obtained from the salt and benzoyl chloride in the usual way.

The products obtained when 1-amino-2-methylpyridinium salts were treated with benzoyl chloride for moderate reaction periods are particularly interesting and indicate the probable course of the cyclization reaction. From 1-amino-2-methylpyridinium iodide the betaine 1-benzamido-2-methylpyridinium N-betaine (**6**, R² = H) was isolated instead of the anticipated pyrazolo[1,5-*a*]pyridine (**3**, R = Ph; R¹ = R² = H, or **3**, R = Ph; R¹ = COPh; R² = H). Similarly, 1-benzamido-2,6-dimethylpyridinium N-betaine (**6**, R² = CH_3) was the sole product isolated when 1-amino-2,-6-dimethylpyridinium iodide (**2**, R¹ = H; R² = CH_3) was treated with benzoyl chloride. These pyridinium betaines were quite stable, and their structures were established on the basis of their spectral characteristics and their chemical reactions.[8] Their ir spectra were devoid of –NH– and carbonyl absorptions. The nmr,

(8) J. A. Moore and J. Binkert [*J. Amer. Chem. Soc.*, **81**, 6045 (1959)] have characterized several N-acylaminopyridinium betaines in a similar way.

uv, and mass spectral data were consistent with the assigned structures (see Experimental Section). Moreover, when these pyridinium betaines were treated with dry HCl in methanol, the hydrochlorides obtained (**7**, R^2 = H or CH_3) showed absorption bands due to the imino and carbonyl groups in their infrared spectra. Similarly, when 1-benzamido-2,6-dimethylpyridinium N-betaine (**6**, R^2 = CH_3) was treated with methyl iodide in dry acetone, it readily gave a methiodide, assigned structure **8** on the basis of its ir ($\nu_{C=O}$ 1660 cm^{-1}) and nmr spectra (τ 6.00, N–CH_3), as well as analytical data. The pyridinium betaines, when exposed to the above reaction conditions for prolonged periods, underwent cyclization to the fused system.

It is most likely that the initial reaction is acylation of the 1-amino group, followed by removal of a proton from the 2-alkyl substituent by pyridine. The transient carbanion derived from a 2-ethyl group would be expected to be more reactive than its counterpart derived from a methyl substituent, and consequently cyclization would be expected to occur more readily for the former products. Moreover, with benzoyl chloride, acylation of the amino group results in a benzamido intermediate with a subsequent decrease in the positive character of the carbonyl carbon atom. Taking into account these two features, the isolation of the pyridinium betaines and the prolonged reaction times required to effect cyclization with 1-amino-2-methylpyridinium salts and benzoyl chloride are not unexpected.

Spectral Characteristics.—Uv absorption spectral data are described in Table II. All show long wavelength absorption attributable to n → π^* transitions, and the spectra are consistent with those of similar ring systems. The infrared spectra of the products showed >C=N– absorption in the range 1630–1660 cm^{-1} and >C=C< absorption at 1590–1600. The nmr spectra of these bicyclic systems were in agreement with the assigned structures and consistent with those described earlier for pyrazolo[1,5-*a*]pyridine[6] and its 3-bromo derivative.[7] The variety of substituents present in the compounds obtained in this present study provides a useful confirmation of the earlier assignments. Our data for several of these products are listed in Table III.

Experimental Section[9]

1-Aminopyridinium salts.—The general procedure found most satisfactory is illustrated below. Hydroxylamine-O-sulfonic acid (11.3 g, 0.1 mol) in water (60 ml) and 2-ethylpyridine (32.1 g, 0.3 mol) were heated with stirring at 80–90° for 30 min. Potassium carbonate (13.8 g, 0.1 mol) was added to the cooled reaction mixture, and water was then removed at 40–50° using a rotary evaporator. The resulting dry residue was shaken with anhydrous ethanol (100 ml), and the potassium sulfate was filtered. The dark brown filtrate was treated with 57% hydriodic acid (14 ml), and the mixture was kept below −15° for 30 min when 1-amino-2-ethylpyridinium iodide separated. After recrystallization from anhydrous ethanol (charcoal), the salt separated as colorless needles (7.5 g). The salts prepared by this procedure are described in Table I. The corresponding bromides were obtained by using 48% hydrobromic acid in the above work-up procedure.

2,3-Dimethylpyrazolo[1,5-*a*]pyridine.—This preparation illustrates the general procedure used. 1-Amino-2-ethylpyridinium iodide (7.5 g) was treated in pyridine (15 ml) at 0° with acetyl chloride (6.0 ml), and the mixture was allowed to attain room temperature when a vigorous, exothermic reaction set in. The mixture was refluxed for 10 min, and then the excess reagents were removed under reduced pressure. The residual dark mass was treated with water (100 ml), cooled, basified (pH 8–9), and extracted thoroughly with chloroform. The chloroform extract was washed with a little water, dried (Na_2SO_4), and distilled. The dark gummy residue was taken up in benzene and chromatographed on alumina. The benzene eluate yielded a brown oil which, after purification by preparative glpc, was obtained as a colorless oil, 0.85 g (20%), which rapidly turned yellow in air. The base readily gave a picrate which crystallized from methanol as yellow needles and also a hydrochloride which crystallized from methanol–ether as colorless needles. These products are described in Table II.

3-Acetyl-2-methylpyrazolo[1,5-*a*]pyridine.—1-Amino-2-methylpyridinium iodide (4.2 g) in dry pyridine (4 ml) at 0° was treated slowly with acetyl chloride (2.5 ml) with stirring, and the reaction mixture was then allowed to warm to room temperature. An exothermic reaction took place, and the product was heated under reflux for 15 min. After the excess solvent was removed under reduced pressure, the residual mass was treated with ice water (25 ml), basified (pH 7.5) with sodium hydroxide solution, and extracted thoroughly with chloroform. The organic layer was washed and dried (Na_2SO_4), and the chloroform was distilled. The residue was chromatographed in benzene on alumina. The product obtained crystallized from benzene–petroleum ether (bp 35–60°) as short, colorless needles: 0.60 g (20%); mp 90°; ir (CCl_4) 1660 cm^{-1} (C=O).

Reduction of 3-Acetyl-2-methylpyrazolo[1,5-*a*]pyridine.—Dried, powdered 3-acetyl-2-methylpyrazolo[1,5-*a*]pyridine (0.5 g) was added in small portions to a solution of lithium aluminum hydride (0.6 g) in anhydrous tetrahydrofuran (50 ml). Marked effervescence occurred, and the solution turned a fluorescent, pale green. The mixture was stirred under reflux for 24 hr in an atmosphere of nitrogen. Water was then added to the cooled reaction mixture, and the precipitated inorganic material was removed by filtration under nitrogen. The pale yellow filtrate was extracted several times with chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and then concentrated. The red oil remaining was absorbed on a column of neutral alumina (2 × 24 cm) and eluted with petroleum ether (bp 35–60°)–benzene (5:1) mixture. Evaporation of the fraction gave a colorless oil: 0.25 g (50%); ir (film) 3325 cm^{-1} (OH). It readily formed a picrate which separated from methanol as yellow needles, mp 165°.

Anal. Calcd for $C_{16}H_{15}N_3O_8$: C, 47.4; H, 3.7; N, 17.3. Found: C, 47.2; H, 3.6; N, 17.5.

3-Acetyl-2-methyl-7-ethylpyrazolo[1,5-*a*]pyridine and 2,3,7-Trimethylpyrazolo[1,5-*a*]pyridine.—From 1-amino-2-methyl-6-ethylpyridinium iodide (3.3 g), pyridine (5 ml), and acetyl chloride (1.25 ml), allowed to react in the above way, a crude product was obtained that was chromatograhed in benzene–petroleum ether (bp 35–60°) (1:1) on neutral alumina. The first fraction (400 ml) yielded 2,3,7-trimethylpyrazolo[1,5-*a*]pyridine as a low-melting colorless solid: 0.16 g (8.0%); mp 52°. It readily formed a picrate which is described in Table II.

Subsequent fractions (200 ml) from the chromatogram on evaporation gave 3-acetyl-2-methyl-7-ethylpyrazolo[1,5-*a*]pyridine: 0.15 g (6.0%); mp 93°; ir (Nujol), 1650 cm^{-1} (C=O); nmr ($CDCl_3$), τ 8.74, 8.62, 8.49 (t, 3, J = 7.2 cps CH_3 of ethyl group), 7.45 (s, 3, $COCH_3$), 7.29 (s, 3, CH_3), 7.02, 6.89, 6.77, 6.65 (Qu, 2, J = 7.20 $-CH_2-$), 3.47, 3.35 (d, 1, J = 7.00, 2.64 (m, 1), 1.93, 1.81 (d, 1, J = 7.00).

3-Methyl-2-phenylpyrazolo[1,5-*a*]pyridine.—From 1-amino-2-ethylpyridinium iodide (5.0 g), pyridine (10 ml), and benzoyl chloride (4.0 ml), allowed to react in the above way, a crude product was obtained which was chromatographed on neutral alumina using benzene as eluent. 3-Methyl-2-phenylpyrazolo-[1,5-*a*]pyridine was obtained as colorless needles from benzene–petroleum ether (bp 35–60°): 1.20 g (30%); mp 100°; nmr ($CDCl_3$), τ 7.50 (s, 3, CH_3), 3.38–2.04 (m, 9, aromatics).

1-Benzamido-2,6-dimethylpyridinium N-Betaine (6, R^2 = CH_3).—From 1-amino-2,6-dimethylpyridinium iodide (5.0 g), pyridine (10 ml), and benzoyl chloride (3.0 ml), allowed to react in the

(9) All evaporations were done under reduced pressure using a Rotavap. Ir spectra were determined on Perkin-Elmer 421 and 337 spectrophotometers and uv spectra on a Cary Model 14 spectrophotometer. Nmr data were obtained using a Varian A-60 instrument in deuteriochloroform solution with TMS as internal standard. Melting points were determined in capillaries and chromatography was carried out using Woelm neutral alumina, activity I, on a column 20 cm × 2.5 cm. Microanalyses were by Galbraith Laboratories, Inc., Knoxville, Tenn.

above way, a crude product was obtained which was chromatographed on neutral alumina using benzene as eluent. 1-Benzamido-2,6-dimethylpyridinium N-betaine was obtained as colorless, irregular needles: 1.80 g (43.5%); mp 150°; nmr ($CDCl_3$), τ 7.35 (s, 6, CH_3), 2.55 (m, 5, phenyl), 2.35 2.25 (d, J = 6.00 cps), 2.22, 2.09 (d, J = 6.00), one aromatic proton, and 1.76 (m, 2, aromatic); $\lambda_{max}^{CH_3OH}$, mμ (log ϵ), 206 (4.22), 230 (4.19), 271 (4.10), 306 sh (3.28); mass spectrum (70 eV) *m/e* (relative intensity), 226 (36), 211 (100), 181 (12), 149 (59.5), 122 (73.5), 107 (70), 105 (52), 93 (45), 77 (96).

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.3; H, 6.2; N, 12.3. Found: C, 74.55; H, 6.2; N, 12.3.

1-Benzamido-2,6-dimethylpyridinium chloride (**7**, R^2 = CH_3) was prepared by passing dry HCl gas into a methanolic solution of the pyridinium betaine (**6**, R^2 = CH_3). The hydrochloride was isolated as colorless, irregular prisms which decomposed over 265°: nmr ($CDCl_3$), τ 7.13 (s, 6, CH_3) and 2.45–1.75 (m, 8, aromatic); the peak due the imino proton could not be discerned in the spectrum; ir (Nujol), 3350 (NH), 1675 cm^{-1} (C=O); $\lambda_{max}^{CH_3OH}$, mμ (log ϵ), 206 (4.38), 230 (4.26), 271 (4.02), 306 sh (3.21).

Anal. Calcd for $C_{14}H_{14}N_2O \cdot HCl$: C, 64.4; H, 5.85; N, 10.65. Found: C, 64.6; H, 5.8; N, 10.5.

The methiodide of 1-benzamido-2,6-dimethylpyridinium N-betaine was also prepared by standard methods using dry acetone as a solvent. The methiodide (**8**) crystallized from methanol–ether as pale yellow needles: mp 203° dec; ir (Nujol), 1660 cm^{-1} (C=O); nmr ($CDCl_3$), τ 7.07 (s, 6, CH_3), 6.00 (s, 3, N-CH_3), 2.35–1.87 (m, 8, aromatic protons).

Anal. Calcd for $C_{15}H_{17}IN_2O$: C, 48.9; H, 4.6; N, 7.6. Found: C, 48.9; H, 4.6; N, 7.4.

1-Benzamido-2-methylpyridinium N-Betaine.—From 1-amino-2-methylpyridinium iodide (9.0 g), pyridine (15 ml), and benzoyl chloride (5.0 ml), allowed to react in the above way, a crude product was obtained which was chromatographed on neutral alumina using benzene as eluent. 1-Benzamido-2-methylpyridinium N-betaine was obtained as colorless needles: 2.30 g (32%); mp 116°; nmr ($CDCl_3$), τ 7.25 (s, 3, CH_3), 2.50 (m, 5, phenyl protons), 2.30, 2.20 (d, 2, J = 6.00 cps), and 1.76 (m, 2), aromatic protons; $\lambda_{max}^{CH_3OH}$, mμ (log ϵ), 202 (4.47), 233 (4.20), 268 (3.91), 313 sh (3.48); mass spectrum (70 eV) *m/e* (relative intensity), 212 (53), 197 (100), 170 (17.5), 135 (77.5), 107 (35), 105 (43), 93 (70), 77 (62).

Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.6; H, 5.7; N, 13.2. Found: C, 73.3; H, 5.9; N, 13.6.

1-Benzamido-2-methylpyridinium chloride (**7**, R^2 = H) was prepared as above: mp 208°; ir (Nujol), 3350 (NH), 1660 cm^{-1} (C=O); nmr ($CDCl_3$), τ 7.12 (s, 3, CH_3), 2.41 (m, 5, phenyl protons), 2.06, 1.94 (d, 2, J = 7.00 cps), 1.67 (m, 2) aromatic protons; the peak due to the imino proton was not visible in the spectrum; $\lambda_{max}^{CH_3OH}$, mμ (log ϵ), 202 (4.36), 233 (4.18), 268 (3.96), 313 sh (3.27).

Anal. Calcd for $C_{13}H_{12}N_2O \cdot HCl$: C, 62.8; H, 5.2; N, 11.3. Found: C, 62.6; H, 5.2; N, 11.1.

Registry No.—3-α-Hydroxyethyl-2-methylpyrazolo[1,5-*a*]pyridine, 17408-41-2; 3-α-hydroxyethyl-2-methylpyrazolo[1,5-*a*]pyridine picrate, 17408-42-3; **6** (R^2 = Me), 17408-43-4; **7** (R^2 = Me), 17408-44-5; **7** (R^2 = H), 17408-46-7; **8**, 17408-45-6; 1-benzamido-2-methylpyridinium N-betaine, 17408-47-8.

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1-Alkyl-2,5-diphenyl-1,4-dithiinium Salts and Their Ambident Behavior toward Bases[1]

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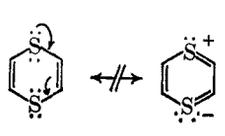
Alkylation of 2,5-diphenyl-1,4-dithiin (**5**) by methyl, methyl-d_3, and ethyl iodides in the presence of silver 2,4,6-trinitrobenzenesulfonate, mercuric iodide, silver perchlorate, or silver tetrafluoroborate gave high yields of the 1-alkyl-2,5-diphenyl-1,4-dithiinium salts (**6a–g**), while 3-bromo-2,5-diphenyl-1,4-dithiin (**14**) was similarly methylated at the S-1 site. 1-Methyl-2,5-diphenyl-1,4-dithiinium tetrafluoroborate (**6d**) was readily demethylated by common nucleophiles, including dimethyl sulfide and piperidine, and was further attacked at S-4 by *n*-butyllithium with ring scission to form 1-butylthio-2-methylthio-1-phenylethylene (**8**), which was also synthesized by an unambiguous route. Sodium hydride selectively abstracted H-3 of **6d** to yield quantitatively the ring-cleavage product, 1-phenylethynylthio-2-methylthio-1-phenylethylene (**13a**), and the methyl-d_3 analog (**6e**) behaved similarly. The nmr spectra of the salts (*e.g.*, **6a**) revealed that H-3 of the dithiinium ring is strongly deshielded (δ 8.75) *via* d-orbital conjugation of the sulfonium sulfur, while H-6 remains more normally olefinic (δ 6.90) suggesting a lack of cyclic conjugation.

Among heterocyclic sulfur compounds of modern vintage Parham's 1,4-dithiin (1,4-dithiadiene) (**1**)[2,3] was of early interest because of possible sulfur d-orbital participation resulting in valence shell expanded forms such as **2**. However, single crystal X-ray analysis showed that 1,4-dithiin exists in a boat form, and its chemical properties were found to be predominantly olefinic.[3] LCAO–MO calculations by Kreevoy,[4] neglecting d-orbital participation, were in essential agreement with the observed properties of **1**, indicating virtually no contributions from structures such as **2**. This conclusion is hardly surprising, since, as Jaffé and others[5] have argued on theoretical grounds, *a sulfur atom may expand its valence shell only if, in the singly bonded structure, it bears a positive charge.* Hence, it appeared probable to us that 3d–π bonding would be more likely for S-1 of a 1-alkyl-1,4-dithiinium ion (**3**), in which the sulfonium requirement would be fulfilled



1 **2**

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