tilled at 136–156° (0.1 mm) and was shown by glpc to be a pure sample of the desired compound: nmr (neat) δ 0.3–1.2 (m, 7, C_2H_5–$SiCH_2$–), 1.4–2.1 (m, 2, $-CH_2-$), 2.6–3.2 (m, 2, NCH_2-).

Anal. Calcd for $C_{15}H_{33}N_3Si_3$: C, 53.10; H, 9.73; N, 12.39; Si, 24.77; mol wt, 399. Found: C, 52.97; H, 10.15; N, 11.86; Si, 25.13; mol wt, 339 (mass spectrometry).

Alcoholysis of Cyclotri(2-ethyl-1-aza-2-silacyclopentane).—Cyclotri(2-ethyl-1-aza-2-silacyclopentane) (0.81 g) was refluxed with excess anhydrous ethanol overnight. A fraction, 0.82 g (56%), distilled at 54° (0.1 mm) and was shown by glpc to be pure 3-aminopropyldiethoxylethylsilane: nmr (neat) δ 0.1–1.6 (m, 10.4, $SiCH_2CH_2-$, $SiCH_2CH_3$, and $-NH_2$), 0.95, (t, 6, OCH_2CH_3), 2.37 (t, 2, NCH_2-), 3.49 (q, 4, OCH_2).

Anal. Calcd for $C_9H_{23}NO_2Si$: C, 52.68; H, 11.22; N, 6.83; mol wt, 205. Found: C, 53.08, 53.14; H, 11.54, 11.69; N, 6.91, 6.88; mol wt, 205 (mass spectrometry).

Registry No.—1-(Triphenylsilyl)-2,2-diethoxy-1-aza-2-silacyclopentane, 32284-27-8; 1-(ethoxydimethylsilyl)-2,2-diethoxy-1-aza-2-silacyclopentane, 32284-28-9; trimer D, 32974-82-6; $(C_2H_5O)_2SiC_3H_6NSi(CH_3)_2OSi(CH_3)_2(OC_2H_5)$, 32974-83-7; cyclotri(2-ethoxy-1-aza-2-silacyclopentane, 32974-84-8; cyclotri(2-phenyl-1-aza-2-silacyclopentane, 32974-85-9; 3-aminopropyldiethoxyphenylsilane, 32974-86-0; $[NH_2C_3H_6(C_6H_5)SiO]_n$, 33029-43-5; cyclotri(2-ethyl-1-aza-2-silacyclopentane), 32974-87-1; 3-aminopropyldiethoxylethylsilane, 20723-29-9.

Acknowledgment.—We wish to thank Dr. Daniel S. Dyer, Mr. Lee D. Smithson, and Miss M. T. Ryan, Analytical Branch, Materials Physics Division, Air Force Materials Laboratory, for the nmr and mass spectral measurements, and Dr. Harold Rosenberg of this laboratory for assisting in the revisions of this manuscript.

The Preparation and Reactions of Some 2-Keto-2*H*-pyrido[1,2-*a*]pyrimidines

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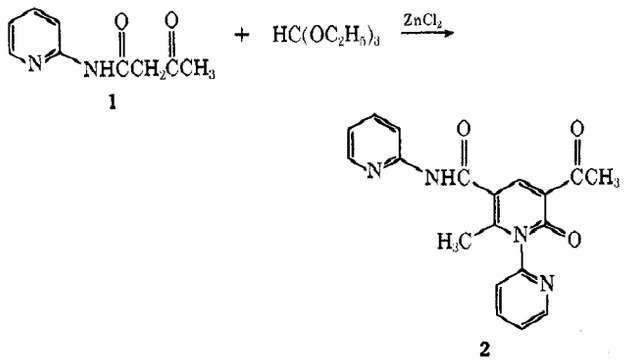
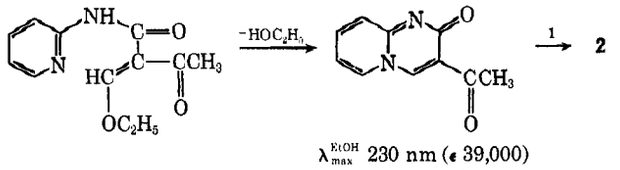
The title compounds are obtained by the reaction of 2-acetoacetylaminopyridines with dimethylformamide dimethyl acetal yielding *N*-(2-pyridyl)-2-acetyl-3-dimethylaminoacrylamides, followed by ring closure with acetic anhydride. The title compounds revert to the starting acrylamides on reaction with dimethylamine; other amines also react with ring opening. The zinc chloride catalyzed reaction with acetoacetamides and the base-catalyzed reaction with acetoacetic esters yield substituted 2-pyridones.

Recently[1] we found that the reaction of 2-acetoacetylaminopyridines (*e.g.*, **1**) with triethyl orthoformate and zinc chloride yields substituted 2-pyridones such as **2**. To explain this result we proposed a mechanism



which involved the formation of a 2-keto-2*H*-pyrido[1,2-*a*]pyrimidine (**3**) as an intermediate. If **3** really

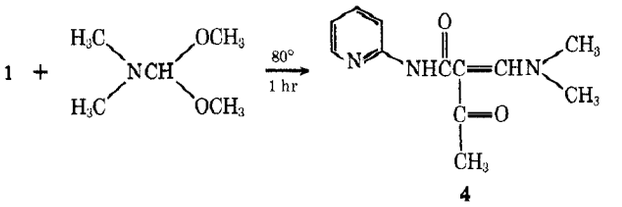


λ_{max}^{EtOH} 230 nm (ε 39,000)
355 (4500)

3

is an intermediate in the formation of products such as **2**, it should be quite reactive and form **2** on reaction with **1**. The present work was undertaken to prove this point by isolating **3**.

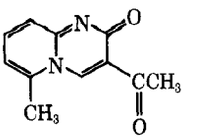
Since the reaction of **1** with triethyl orthoformate does not yield the expected ethoxymethylene derivative, the reaction of **1** with dimethylformamided imethyl acetal was used to obtain **4** in 59% yield. Similar



4

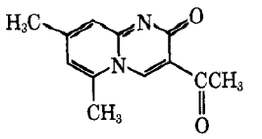
results were obtained with other acetoacetylaminopyridines and a carbethoxyacetylaminopyridine (see Table I).

Brief boiling of **4** in acetic anhydride gave an 89% yield of **3** which crystallized out of the hot reaction mixture. A total of five (see Table II) 2-keto-2*H*-pyrido[1,2-*a*]pyrimidines were prepared. Of these, **5** and **6** are of special interest, since they are the product

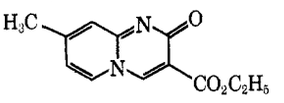


λ_{max}^{EtOH} 226 nm (ε 29,000), 363 (3800)

5



6



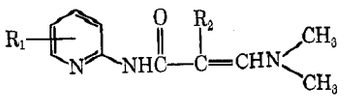
λ_{max}^{EtOH} 231 nm (ε 55,000), 341 (5100)

7

(1) M. C. Seidel, G. C. Van Tuyle, and W. D. Weir, *J. Org. Chem.*, **35**, 1475 (1970).

TABLE I[a]

N-(2-PYRIDYL)-3-DIMETHYLAMINOACRYLAMIDES

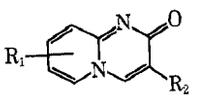


Compd	R_1	R_2	Yield, %	Mp, °C
4	H	$-C(=O)-CH_3$	59	172–174
12	4-CH_3	$-CO_2C_2H_5$	70	84–86
22	6-CH_3	$-C(=O)-CH_3$	47	148–148.5
23	5-Cl	$-C(=O)-CH_3$	54	172.5–173.5
24	4,6-$(CH_3)_2$	$-C(=O)CH_3$	68	159–161

[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all compounds in this table: Ed.

TABLE II[a]

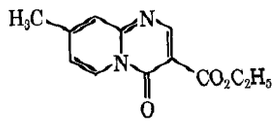
2-KETO-2*H*-PYRIDO[1,2-*a*]PYRIMIDINES



Compd	R_1	R_2	Yield, %	Mp, °C
3	H	$-C(=O)-CH_3$	89	221–222 dec
5	6-CH_3	$-C(=O)-CH_3$	49	194–196 dec
6	6,8-$(CH_3)_2$	$-C(=O)CH_3$	32	188–189 dec
7	8-CH_3	$-CO_2C_2H_5$	66	220–223 dec
25	7-Cl	$-C(=O)-CH_3$	60	231–232 dec

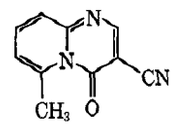
[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all compounds in this table. Ed.

of a ring closure onto a pyridine ring nitrogen in the presence of a 6 substituent (for some of the few other examples see ref 2–4). A compound with structure **7** has already been described in the literature[3] as having a melting point (164°) different from that of our sample (220–223° dec). The present assignment, however, is supported by the fact that **7** was converted back to the starting acrylamide (*i.e.*, 4-CH_3 **4**) by mild treatment with dimethylamine. Antaki's compound most probably was the isomeric 4-keto compound **8**, mp 172°.[5] Comparison of uv spectra lends support to this view. The spectra of **8** (prepared according to Lappin[5]) and **9** (reported by Antaki[3]) are similar in shape and relative height of the peaks. The spectra



λ_{max}^{EtOH} 216 nm (ε 30,000)
364 (31,000)

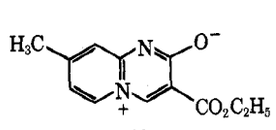
8



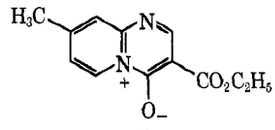
λ_{max}^{EtOH} 220 nm (ε 12,000)
365 (20,000)

9

of the 2-keto compounds **3**, **5**, and **7** are different in that the absorption at 341–365 nm is much weaker. This band can be considered evidence[6] for the contribution of the zwitterionic structures **10** and **11** corresponding



10

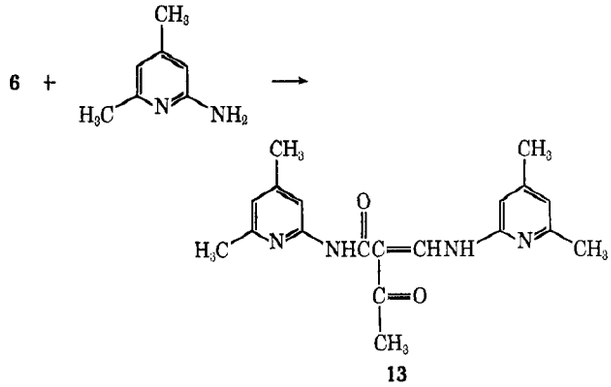


11

to **7** and **8**. The contribution of **10** to the ground state of **7** can be assumed to be less than that of **11** to the ground state of **8** since the charge separation energy should be greater for **10**. Thus, the band at 341–365 nm should be weaker in the spectra of the 2-keto compounds, which was found to be the case.

The 2-keto-2*H*-pyrido[1,2-*a*]pyrimidines (such as **3**) react with amines with ring opening. Dimethylamine yields the starting acrylamides (such as **4**) in yields of 85–96%.

The reaction of 2-amino-4,6-dimethylpyridine with **6** yielded **13**. As pointed out above, the 2-keto-2*H*-



13

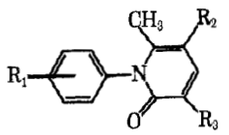
pyrido[1,2-*a*]pyrimidines were thought to be intermediates in the reaction of 2-acetoacetylaminopyridines with triethyl orthoformate and $ZnCl_2$.[1] In order to test this postulate, the 2-keto-2*H*-pyrido[1,2-*a*]pyrimidines were allowed to react with 2-acetoacetylaminopyridines in ethanol with $ZnCl_2$ as catalyst.

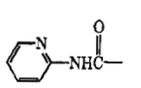
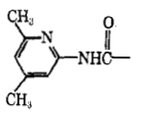
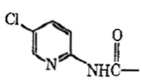
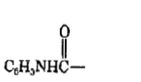
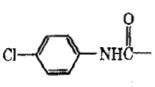
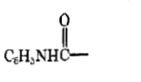
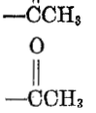
This reaction yielded the same condensed products (type **2**, **15**, and **16**; see Table III) as in our previous work[1] except in better yields, with shorter reaction times (1 hr *vs.* 3 hr), and in higher purity. By comparison, the reaction of **14** with triethyl orthoformate and $ZnCl_2$ had given a mixture of **13** and **15** in poor yields.[1]

(2) M. Shur and S. S. Israelstam, *J. Org. Chem.*, **33**, 3015 (1968).
(3) H. Antaki, *J. Amer. Chem. Soc.*, **80**, 3066 (1958).
(4) G. R. Lappin, *J. Org. Chem.*, **26**, 2350 (1961).
(5) G. R. Lappin, *J. Amer. Chem. Soc.*, **70**, 3348 (1948).
(6) R. Adams and I. J. Pachter, *ibid.*, **74**, 5491 (1952).

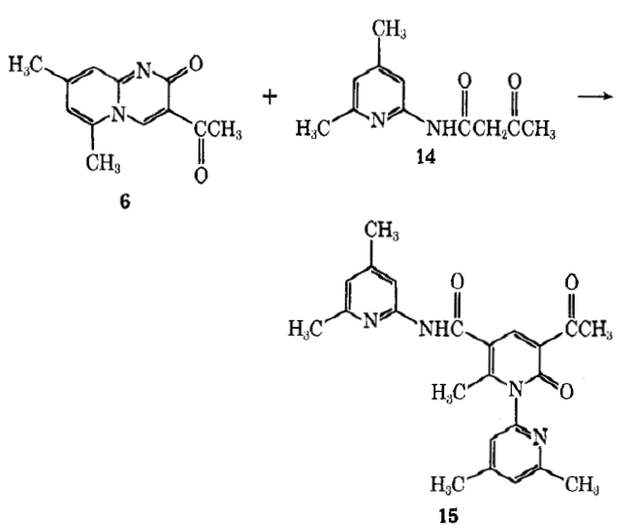
TABLE III[a]

1-PYRIDYL-2-PYRIDONES



Compd	R_1	R_2	R_3	Yield, %	Mp, °C
2	H			100	228–230
15	4,6-$(CH_3)_2$			89	248–252
16	H			90	232–234
17	H			80	233.9
18	6-CH_3			86	229.5–231.5
19	4-CH_3		$C_2H_5O_2C$—	72	260–261
20	H	*tert*-$C_4H_9O_2C$–		95	172–173.5
21	H	$C_2H_5O_2C$–		87	152.7

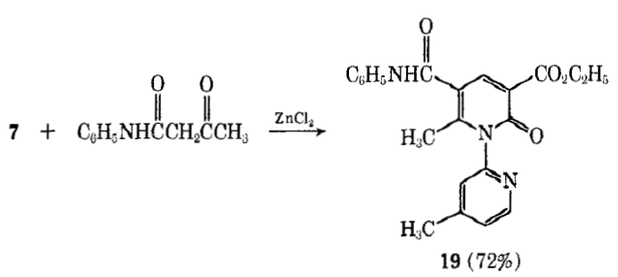
[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all compounds in the table except **2**, **15**, **17**, and **18**: Ed. The latter were shown by mixture melting point determination and comparison of the ir spectra to be identical with compounds of the same structure referred to in ref 1.



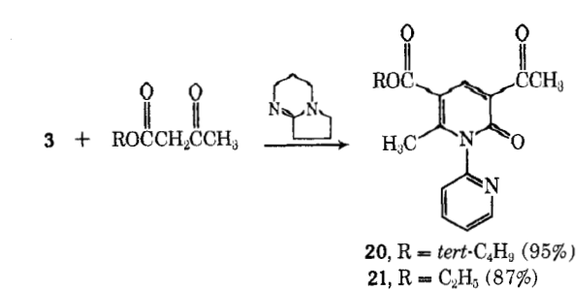
6 + **14** → **15**

Mixed condensed products were obtained in equally high yields in the reaction of 2-keto-2*H*-pyrido[1,2-*a*]-pyrimidines with acetoacetanilides (see also compounds **17** and **18** in Table III). Similarly high yields were obtained in base-catalyzed reactions with acetoacetic esters.

Compound **20** was used to independently synthesize **17**. Acid hydrolysis of **20** yielded the corresponding carboxylic acid, which without isolation was transformed into the mixed anhydride with triethylamine and ethyl chloroformate. Reaction of the crude mixed anhydride with aniline gave **17** in 43% overall yield.



7 + $C_6H_5NHCCH_2CCH_3$ $\xrightarrow{ZnCl_2}$ **19** (72%)



3 + $ROCCH_2CCH_3$ → **20**, R = *tert*-C_4H_9 (95%); **21**, R = C_2H_5 (87%)

Experimental Section

All melting points are uncorrected; those given as a single value were taken on a Mettler FPI apparatus. The microanalyses were carried out by Mr. C. W. Nash and his associates. For the preparation of the acetoacetylaminopyridines see ref 1.

2-Carbethoxyacetylamino-4-methylpyridine (26).—To an ice-cooled solution of 39 g (0.36 mol) of 2-amino-4-methylpyridine and 36 g (0.36 mol) of triethylamine in 250 ml of toluene was added 54 g (0.36 mol) of carbethoxyacetyl chloride, slowly and with stirring. After standing overnight, the reaction mixture was washed with water and the organic layer was dried and evaporated. The residue was recrystallized from methylcyclohexane to yield 42 g (52%) of **26**, mp 89.5°.

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.46; H, 6.35; N, 12.61. Found: C, 59.17; H, 6.54; N, 12.70.

***N*-(4-Methyl-2-pyridyl)-2-carbethoxy-3-dimethylaminoacrylamide (12).**—See also Table I; the other compounds in this table were prepared in analogous fashion.

A solution of 40 g (0.172 mol) of **26** and 36 g (0.3 mol) of dimethylformamide dimethyl acetal in 200 ml of 1,2-dimethoxyethane was refluxed for 1.5 hr. The solvent was then removed on a rotatory evaporator and the residue was recrystallized from methylcyclohexane, yield of **12** 33 g.

2-Keto-3-acetyl-2*H*-pyrido[1,2-*a*]pyrimidine (3).—See also Table II; the other compounds in Table II were prepared similarly.

A slurry of 10 g (0.045 mol) of **4** in 70 ml of acetic anhydride was quickly heated to a boil and kept gently boiling for 10 min, during which time the starting material dissolved and, later, the product precipitated. After cooling, the product was separated, washed with 2-propanol, and dried, yield 7.5 g of **3**. All the compounds in Table II were appreciably soluble in water.

1-(2-Pyridyl)-3-acetyl-6-methyl-2-pyridone-5-(5-chloro-2-pyridyl)carboxamide (16).—See also Table III; compounds **2**, **15**, **17**, **18**, and **19** in this table were prepared in analogous fashion.

A mixture of 4.7 g (0.025 mol) of **3**, 10.6 g (0.05 mol) of 2-acetoacetylamino-5-chloropyridine,[1] and 200 mg of $ZnCl_2$ in 150 ml of ethanol was refluxed for 1 hr. The starting materials soon dissolved and the product began to crystallize. The mixture was cooled, and the product was filtered and recrystallized from methylcellosolve, yield 8.6 g of **16**.

***N*-(4,6-Dimethyl-2-pyridyl)-2-acetyl-3-(4,6-dimethyl-2-pyridyl)-aminoacrylamide (13).**—A solution of 3 g (0.014 mol) of **6** and 2.4 g (0.02 mol) of 2-amino-4,6-dimethylpyridine in 100 ml of ethanol was refluxed for 1 hr. The mixture was then cooled, and the product was filtered off and dried, yield 3.5 g (74%) of **13**, mp 226–227°. By mixture melting point and ir spectra, this material was identical with compound **7** of ref 1.

1-(2-Pyridyl)-3-acetyl-5-carbo-*tert*-butoxy-6-methyl-2-pyridone (20).—See also Table III; compound **21** in this table was prepared in the same way.

A slurry of 9.4 g (0.05 mol) of **3**, 16 g (0.1 mol) of *tert*-butyl acetoacetate, and 0.5 g of 1,5-diazabicyclo[4.3.0]-5-nonene in 200 ml of dimethylformamide was stirred at room temperature for 30 min. The starting material had dissolved to form a red solution. The solution was poured into excess water, and the product was filtered off, washed with water, and dried, yield 15.5 g of **20**. Recrystallization from 2-propanol did not raise the melting point.

1-(2-Pyridyl)-3-acetyl-6-methyl-2-pyridone-5-carboxylic Acid Anilide (17). Independent Synthesis.—A solution of 8.0 g (0.024 mol) of **20** in 50 ml of 6 *N* HCl was heated on a steam bath for 15 min and then left standing at room temperature for 1 hr. The solvent was then removed in a rotatory evaporator and the product was dried, yielding 5.5 g (0.02 mol) of the HCl salt of the carboxylic acid corresponding to **20**. This material was slurried in 100 ml of benzene, and 6 g (0.06 mol) of triethylamine was added. Most of the solid dissolved. Then, while applying ice cooling, 2.2 g (0.02 mol) of ethyl chloroformate was added. After 30 min at room temperature, 1.86 g (0.02 mol) of aniline was added and the mixture was refluxed for 30 min. Then water was added, and the benzene layer was separated, dried, and evaporated. The residue was recrystallized from ethanol, yield 3 g (43%), mp 235.1°; on admixture of **17**, the material melted at 235.2°. The ir spectra were identical.

Registry No.—**2**, 23600-24-0; **3**, 33068-07-4; **4**, 33015-41-7; **5**, 33015-42-8; **6**, 33015-43-9; **7**, 33015-44-0; **12**, 33068-08-5; **15**, 23600-27-3; **16**, 33015-46-2; **17**, 23600-41-1; **18**, 23646-60-8; **19**, 33015-49-5; **20**, 33015-50-8; **21**, 33015-51-9; **22**, 33015-52-0; **23**, 33068-09-6; **24**, 33015-53-1; **25**, 33015-54-2; **26**, 33015-56-4.

Acknowledgment.—I should like to gratefully acknowledge the encouragement of this work by Dr. C. L. Levesque, Rohm and Haas Company.

Relative Rates of N-Methylation of Ortho-Substituted Pyridines. Steric and Electronic Effects

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Relative rates of N-methylation of eleven 2-substituted and two 2,6-disubstituted pyridines by methyl iodide in DMSO at 23° were obtained by nmr methods. Rate constants relative to pyridine for the monosubstituted compounds are NH_2, 1.23; CH_3, 0.38; C_2H_5, 0.17; $C_6H_5CH_2$, 0.081; CO_2CH_3, 0.0084; CH_3CONH, 0.0082; Cl, 0.0039; Br, 0.0039; 2-C_5H_4N, 0.0026; and CN, 0.0022. Results for the disubstituted pyridines are CH_3,NH_2, 0.050; and $(CH_3)_2$, 0.023. Kinetic results are only poorly correlated with pK_a values. It is suggested that steric effects are superimposed on electronic effects in the N-methylation reactions and that steric effects can be surprisingly constant.

Our understanding of the effects of ortho substituents on chemical equilibria and reactivity has undergone a recent and profound change. It was long held that steric effects could and often did influence reactions at ortho positions in a nonadditive way. However, in the absence of steric and hydrogen-bonding factors, electronic effects of ortho groups were expected to be proportional to those of para substituents.[2,3]

Charton has challenged this view. He has employed a multiparameter equation to correlate all the known sets of ortho substituent constants.[4] Except for some very bulky groups and those capable of intramolecular hydrogen bonding, previously defined ortho substituent constants have been expressed in terms of inductive and resonance components which often are not related to those for para or even meta groups. Steric effects were said to be absent or constant.[4]

Of the series of compounds statistically examined by Charton, all are monosubstituted and nearly all have the geometry given by I where G is the ortho substituent and Y is a reactive center such as CO_2R, CN, OH, and NH_3^+.

(1) On leave from LaTrobe University, Melbourne, Australia.

(2) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1940, pp 204–207.

(3) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 13.

(4) For a list of references, see M. Charton, *J. Org. Chem.*, **36**, 882 (1971); *Prog. Phys. Org. Chem.*, **8**, 235 (1971).