

Pyridinium-1-thioacylaminides

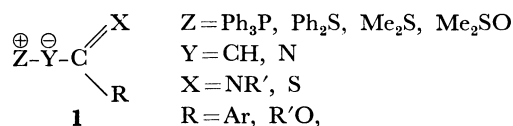
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Synopsis. Pyridinium-, 2-methylpyridinium-, and 2,6-dimethylpyridinium-1-thioacylaminides (**5**—**7**) were prepared from the corresponding unsubstituted pyridinium-1-aminides and methyl dithiocarboxylates in fairly good yields. The alkylation reaction of **5**—**7** took place exclusively on the thiocarbonyl sulfur, yielding pyridinium salts in quantitative yields. The NMR spectroscopic studies indicated that *E* and *Z* forms existed for these pyridinium salts. The thermal decomposition of **5**—**7** yielded the corresponding pyridine, nitrile, and sulfur in good yields.

Recently a number of heterocyclic aminides have been prepared, and their physical and chemical properties have been clarified.¹⁻⁴ In a continuation of our previous studies of the *P*- and *S*-ylides and aminides⁵ with C=S or C=N groups as substituents such as **1**, we have become interested in the chemistry of pyridinium-1-thioacylaminides **5**, **6**, and **7**:



Some pyridinium-1-aminides with thioacyl groups as substituents have been previously prepared. 2,4,6-Triphenylpyridinium perchlorate reacts with thioacylhydrazine to give the rather unstable 1-thioamidotriphenylpyridinium perchlorate, which then decomposes on attempted deprotonation.² Isothiocyanate reacts with free pyridinium-1-aminides **2**—**4** to yield thiourea derivatives.³ 2-Methylpyridinium-1-[(methylthio)thiocarbonylaminide](**6c**) has been prepared from free aminide **3**, carbon disulfide, and an alkylating reagent in a 59% yield.⁴

The action of methyl dithiocarboxylates to **2**, **3**, or **4**, generated from the corresponding 1-aminopyridinium mesitylene-sulfonates⁶ and potassium carbonate in ethanol, yielded the expected pyridinium-1-thioacylaminides **5**, **6**, or **7** in good yields, as are listed in Table 1. The structure of the products was elucidated on the basis of their elemental analyses, ¹H-NMR spectra, alkylation reaction, and thermal-decomposition reaction.

The alkylation of the oxygen analogues of **5**, **6**, or **7** takes place on the aminide nitrogen, not on the acyl oxygen.^{1b)} In contrast, the alkylation of **5**, **6**, and **7** with various alkylating reagents (R'X) takes place exclusively on the sulfur, very easily at room temperature, to give the corresponding pyridinium salts **5**, **6**, and **7**(R'X) in fairly good yields.

Pyridinium 1-methoxythiocarbonylaminides **5d**, **6b**, and **7b** reacted with methyl iodide to give the corresponding (methylthio)carbonylaminides **8**, **9**, and **10** as final products in quantitative yields. The reaction with methyl benzenesulfonate yielded the expected salts **5d**, **6b**, and **7b**(MeOSO₂Ph).

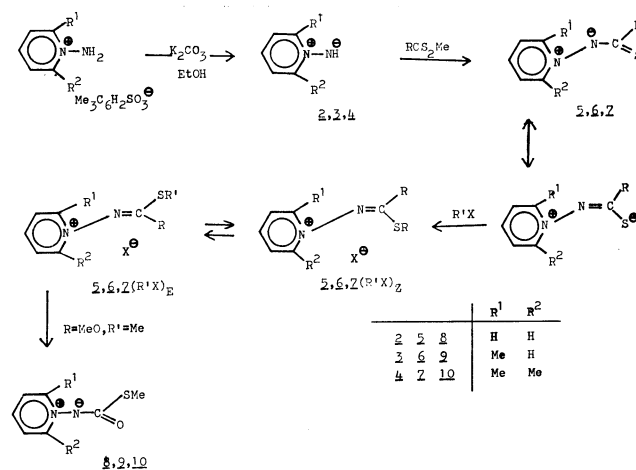
The stereochemistry of the salts was assigned on

the basis of the fact that the R' groups cis to the pyridine ring are shielded by the ring and that they appear at the higher field than the R' trans to the ring.⁷⁾

Alkylation and isomerization reaction of **5**—**7** were studied by means of NMR spectroscopy. On heating at 70 °C for 2 h in CDCl₃ **5**(R'X)₂ and **6**(R'X)₂ were easily isomerized to give equilibrium mixtures; in contrast, **7**(R'X)₂ showed no isomerization on heating for 10—20 h, indicating the retardation of rotation around the C=N bond due to the steric hindrance.

The stereochemistry of the C=N bond with alkyl, aryl, alkoxy, alkylthio, or amino groups as substituents has been widely studied.⁸⁾ A number of factors seem to govern the *E*—*Z* equilibrium ratios for this system.⁸⁾ Table 2 seems to indicate that *E*-forms are furnished for the **5**(R'X) and **6**(R'X) salts, in this order with respect to the substituent R':phenyl, alkylthio, and alkoxy. The steric effect seems to be a dominant factor for the salts with alkylthio groups as substituents **5f**(EtI, PhCH₂Br, PhCOCH₂Br), while interorbital repulsion⁹⁾ seems to control the stereochemistry of the salts with alkoxy groups [**5d**, **5e**, and **7b**(MeOSO₂Ph)].

The conformations of the initial alkylation products **5**, **6**, and **7**(R'X)₂ seem to show that the starting aminides **5**—**7** were of the *Z*-form, indicating the importance of the delocalization of the aminide electrons through the thiocarbonyl groups of **5**—**7**, as is shown in Scheme 1.



Scheme 1.

Although **5**—**7** were stable in a refrigerator, on heating at 80—120 °C in a solvent (benzene or toluene) a smooth decomposition was observed, yielding nitrile, pyridine, and sulfur in good yields.

Trapping experiments to find an intermediate, nitrile sulfide,^{5b)} for the thermolysis of **5**—**7** failed. On heating, a mixture of **5**, **6**, or **7** and dimethyl acetylenedicarboxylate in tarry mass, from which no crystalline compound was isolated.

Experimental

Preparation of 5–7. A mixture of 1-amino-, 1-amino-2-methyl-, or 1-amino-2,6-dimethylpyridinium mesitylene-sulfonate⁶⁾ (1.1 mmol), potassium carbonate (3 mmol), and methyl dithiocarboxylate (1 mmol) in ethanol (25 cm³) was stirred for 2.5 h at room temperature. The solvent was then removed *in vacuo* at room temperature; the subsequent separation of the chloroform-soluble product yielded crystalline pyridinium-1-thioacylamines **5–7**. The physical properties are collected in Table 1.

Alkylation of 5–7. To a solution of **5**, **6**, or **7** in benzene we added a 2-fold excess amount of an alkylation reagent (R'X) at room temperature. The reaction was checked by TLC (silica gel) until the starting material was reacted completely. The precipitated salt **5**, **6**, or **7**(R'X) was washed with dry benzene and dried *in vacuo* (Table 2). The isomerization and the determination of the equilibrium ratios in CDCl₃ were studied by means of NMR spectroscopy.

The Reaction of 5d, 6b, and 7b with Methyl Iodide. To a solution of **5d**, **6b**, or **7b** (1 mmol) in chloroform (5 cm³) we added methyl iodide (2 mmol) in one portion. The solution was then kept standing at room temperature for 12 h. The evaporation of the solvent and recrystallization from benzene gave **8**, **9**, or **10** in a quantitative yield. The NMR spectroscopic studies in CDCl₃ indicated that the initially formed salts showed the same spectra as those from the reaction with methyl benzenesulfonate. **8**: mp

TABLE 1. THE PREPARATION OF PYRIDINIUM-1-AMINIDES, **5–7**

R	Yield %	Mp θ _m /°C	NMR (δ in CDCl ₃) ^{a)}	Found(Calcd) (%)		
				C	H	N
5a 4-MeC ₆ H ₄	75	170–173	2.40(Me)	68.52 (68.39)	5.11 (5.30)	12.55 (12.27)
5b Ph	88	167–169		67.01 (67.26)	4.63 (4.70)	13.24 (13.07)
5c 4-MeOC ₆ H ₄	74	162–164	3.88(OMe)	63.92 (63.91)	5.02 (4.95)	11.81 (11.47)
5d MeO	73	130–131	4.40(OMe)	49.63 (49.98)	4.67 (4.79)	16.80 (16.65)
5e EtO	85	130–131	1.40(t, J=7 Hz, Me), 4.50(q, CH ₂)	52.90 (52.73)	5.48 (5.53)	15.19 (15.37)
5f MeS	81	124–126	2.53(SMe)	45.29 (45.63)	4.36 (4.38)	15.37 (15.20)
5g EtS	89	127	1.38(t, J=7 Hz, Me), 3.20(q, CH ₂)	48.30 (48.46)	5.14 (5.08)	14.45 (14.13)
6a Ph	79	133–135	2.61(2-Me)	48.22 (48.39)	5.77 (5.30)	12.48 (12.27)
6b MeO	83	108–109	2.67(2-Me), 4.05(OMe)	53.02 (52.73)	5.50 (5.53)	15.16 (15.37)
6c^{b)} MeS	80	141–143	2.58(SMe), 2.65(2-Me)	48.25 (48.46)	5.22 (5.08)	14.04 (14.13)
7a 4-MeOC ₆ H ₄	89	156	2.65(2,6-Me ₂), 3.88(OMe)	65.92 (66.16)	5.87 (5.92)	10.63 (10.29)
7b MeO	84	139–141	2.68(2,6-Me ₂), 4.06(OMe)	55.21 (55.08)	6.03 (6.16)	14.61 (14.27)
7c EtO	93	114–116	1.41(t, J=7 Hz), 2.68(2,6-Me ₂), 4.51(q, CH ₂)	56.83 (57.12)	6.64 (6.71)	13.72 (13.32)
7d MeS	81	152–153	2.60(SMe), 2.68(2,6-Me ₂)	51.08 (50.91)	5.89 (5.70)	13.01 (13.19)
7e EtS	87	140–141	1.40(t, J=7 Hz, Me), 2.67(2,6-Me ₂), 3.18(q, CH ₂)	53.17 (53.06)	6.01 (6.23)	12.04 (12.38)

a) Aryl protons were observed at δ 7.4–8.2. b) Lit.⁹⁾ mp 128–129 °C; NMR (CDCl₃) δ=2.57(SMe) and 2.64(2-Me).

TABLE 2. PROPERTIES OF PYRIDINIUM SALTS **5–7**(R'X)

5–7 (R'X)	Mp θ _m /°C	NMR(δ in CDCl ₃) SMe		Z/E
		5–7 (R'X) _Z	5–7 (R'X) _E	
5b (MeI)	Oil	2.34	2.78	36 : 64
5c (MeI)	136–138	2.37	2.75	30 : 70
5d (MeOSO ₂ Ph)	Oil	2.43	2.60	83 : 17
5e (MeBr)	115–117	2.39	2.63	83 : 17
5f (MeI)	Oil	2.68, 2.75	—	—
	(EtI)	137–139	2.73	47 : 53
	(PhCH ₂ Br)	130–132	2.74	45 : 55
	(PhCOCH ₂ Br)	Oil	2.70	31 : 69
5g (MeI)	135–137	2.65	2.73	53 : 47
6b (MeOSO ₂ Ph)	Oil	2.46	2.64	80 : 20
6c (MeI)	150	2.73, 2.82	—	—
	(EtI)	97–99	2.69	45 : 55
7a (MeI)	179–181	2.46	—	—
7b (MeOSO ₂ Ph)	Oil	2.59	—	—
7c (MeOSO ₂ Ph)	Oil	2.47	—	—
7d (MeI)	180–183	2.75, 2.85	—	—
	(EtI)	142–144	2.85	—
7e (MeI)	157–159	2.74	—	—

131–132 °C; NMR(CDCl₃) δ=2.33(SMe) and 7.6–8.8 (m, Ar). Found: C, 49.88; H, 4.73; N, 16.59%. Calcd for C₇H₈N₂OS: C, 49.98; H, 4.79; N, 16.65%. **9**: mp 116 °C; NMR(CDCl₃) δ=2.35 (SMe), 2.71 (2-Me), and 7.6–8.8 (m, Ar). Found: C, 52.41; H, 5.64; N, 15.11%. Calcd for C₈H₁₀N₂OS: C, 52.73; H, 5.53; N, 15.37%. **10**: mp 142–143 °C; NMR(CDCl₃) δ=2.34 (SMe), 2.67 (2,6-Me), and 7.7–8.8 (m, Ar). Found: C, 55.43; H, 6.02; N, 14.13%. Calcd for C₉H₁₂N₂OS: C, 55.08; H, 6.16; N, 14.27%.

Thermal Decomposition of 5–7. A solution of **5**, **6**, or **7** in benzene or toluene (100 mg in 3 cm³) was heated until the starting material had reacted completely. The products were confirmed by comparisons of their NMR spectra or VPC with those of authentic samples.

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