The Conversion of Pyridinium-2-carboxylates into 2-Thioxo-1,2-dihydropyridines (Pyridine-2-thiones)

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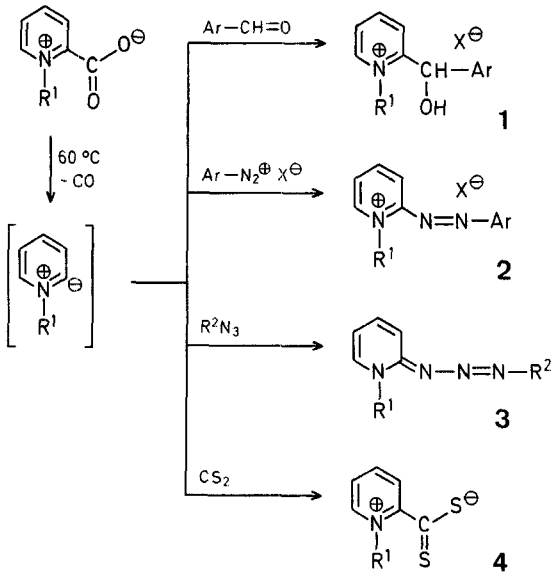
1-Substituted pyridinium-[1,2,3] and quinolinium-2-carboxylates[2] lose carbon dioxide at 60 °C to form intermediate ylids, which are protonated in protic solvents[4], but which in aprotic solvents can be trapped by electrophiles: e.g. aldehydes give alcohols **1**[2], diazonium ions give azo compounds **2**[2], azides give triazenes **3**[2], and carbon disulphide gives dithioacids **4**[5] (Scheme **A**).



Scheme **A**

Pyridine-2-thiones have been prepared from the corresponding pyridones and phosphorus pentasulphide[6,7,8], from 2-thiopyrones with primary amines[9], and by ring synthesis[10]. There

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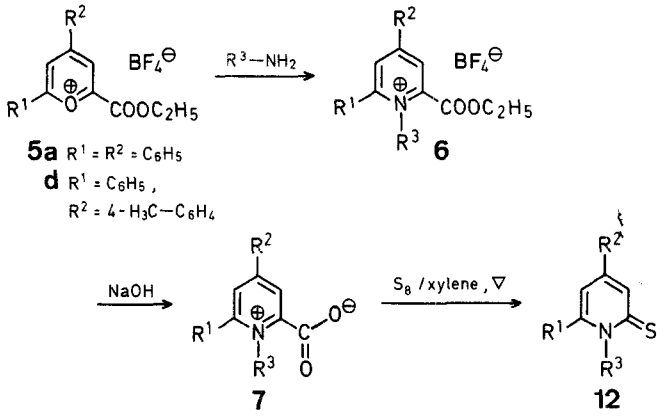
have been scattered reports only of their preparation by the action of sulphur on a preformed pyridine ring: from pyridine 1-oxides on successive treatment with butyllithium and sulphur[11], and from picolinic acid 1-oxide and sulphur at 110–120 °C[12].

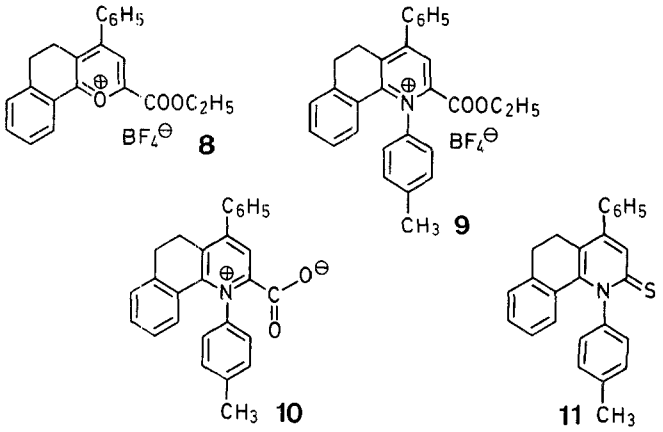
We now describe an apparently general method for the conversion of pyridinium-2-carboxylates into pyridine-2-thiones. 2-Ethoxycarbonyl-4,6-diphenylpyrylium tetrafluoroborate **(5a)**[13] on reaction with primary amines gave the pyridinium salts **6a–c** which were hydrolysed to the betaines **7a–c**[4,5,14]. 2-Ethoxycarbonyl-4-(4-methylphenyl)-6-phenylpyrylium tetrafluoroborate[15] **(5d)** and 5,6-dihydro-2-(ethoxycarbonyl)-4-phenylbenzo[*h*]chromenylium tetrafluoroborate **(8)** similarly gave the esters **6d** and **9** and the hygroscopic betaines **7d** and **10** which were characterised spectroscopically (see experimental). The betaines **7e** and **7f** were prepared from picolinic acid[16,17]. Pyridinium betaines **7a–f** and **10** were each smoothly converted by sulphur in xylene at 140 °C into the corresponding pyridine-2-thiones **(11** and **12a–f)** (Schemes B and C and Table).

Infrared spectra of the pyridine-2-thiones show a characteristic[8,18] strong thiocarbonyl absorption at 1150–1170 cm^{-1} and absence of the carbonyl absorption found in **7** at 1650 cm^{-1}. In the ^{1}H-N.M.R. spectra of the pyridine-2-thiones (Table), the H—C-3 and H—C-5 doublets appear at $\delta = 7.90$–8.20 and $\delta = 6.85$–6.95 ppm, respectively. The latter is significantly deshielded with respect to its position in the pyridine-2-carboxylates **7** which show signals for H—C-3 at $\delta = 8.05$–8.15 and for H—C-5 at $\delta = 7.85$–7.95 ppm.



6,7,12	R¹	R²	R³
a	C6H5	C6H5	C6H5
b	C6H5	C6H5	H3C—C6H4
c	C6H5	C6H5	C5H4N
d	C6H5	H3C—C6H4	H3C—C6H4
e	H	H	C2H5
f	H	H	CH3

Scheme **B**



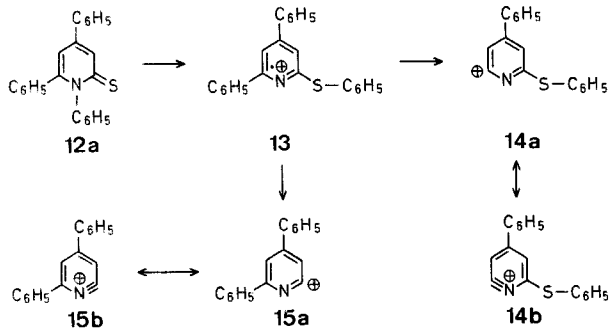
Scheme **C**

The mass spectrum of the 1,4,6-triphenylpyridine-2-thione **(12a)** is rationalised in terms of an initial isomerisation into a thioether (Scheme **D**). This process **12** → **13** could take place thermally in the probe of the mass spectrometer or alternatively it may be activated by electron impact. We have demonstrated similar thermal rearrangements of 4,6-diphenyl-1-(4-methylphenyl)-pyridine-2-thione[8]. The pyridinethione **12a** shows an intense molecular ion peak ($m/e = 339$) but (in contrast to the spectra of other thione derivatives[8]) only weak fragment ion peaks (~1.5%) corresponding to loss of SH and CS. The molecular ion **13** loses phenyl and 4-H_3C—C_6H_4—S fragments to give daughter ions at $m/e = 262$ and $m/e = 230$, respectively.

Table. Pyridine-2-thiones prepared

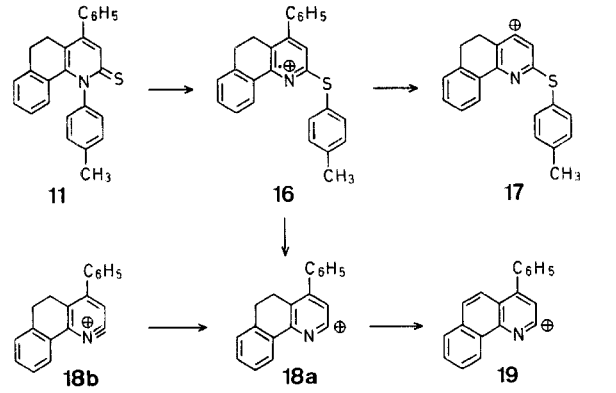
Product	Yield [%]	m.p. [°C] or b.p. [°C]/torr	Solvent (Crystal Form)	Molecular Formula[a] or Lit. m.p. or b.p./torr	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
11	72	270°	CH_3OH/C_6H_6 (prisms)	$C_{26}H_{21}NS$ (379.5)	2.30 (s, 3H, CH_3); 2.6–2.8 (m, 4H, CH_2CH_2); 7.0–7.6 (m, 13 H_{arom}); 7.95 (d, 1H, $J = 2$ Hz, 3-H)
12a	50	193°	CH_3OH (prisms)	$C_{23}H_{17}NS$ (339.5)	6.85 (d, 1H, $J = 2$ Hz, 5-H); 7.05–7.85 (m, 15 H_{arom}); 8.15 (d, 1H, $J = 2$ Hz, 3-H)
12b	64	231°	CH_3OH/ether (prisms)	229–231°[8]	2.20 (s, 3H, CH_3); 6.90 (d, 1H, $J = 2$ Hz, 5-H); 7.0–7.85 (m, 14 H_{arom}); 8.20 (d, 1H, $J = 2$ Hz, 3-H)
12c	35	155°	CH_3OH (prisms)	154–156°[8]	6.9–8.8 (m, 16 H_{arom})
12d	55	245°	CH_3OH (needles)	$C_{25}H_{21}NS$ (367.5)	2.30 (s, 3H, CH_3); 2.45 (s, 3H, CH_3); 6.95 (d, 1H, $J = 2$ Hz, 5-H); 7.05–8.0 (m, 13 H_{arom}); 8.15 (d, 1H, $J = 2$ Hz, 3-H)
12e	60	189°/15	—	188°/15[18]	1.45 (t, 3H, $J = 4$ Hz, CH_3); 4.65 (q, 2H, $J = 4$ Hz, CH_2); 6.80 (t, 1H, $J = 4$ Hz, 5-H); 7.30 (t, 1H, $J = 4$ Hz, 4-H); 7.75 (d, 1H, $J = 2$ Hz, 6-H); 7.95 (d, 1H, $J = 4$ Hz, 3-H)
12f	65	90	CH_3OH (needles)	89°[18]	2.30 (s, 3H, CH_3); 6.80 (t, 1H, $J = 4$ Hz, 5-H); 6.90 (t, 1H, $J = 4$ Hz, 4-H); 7.60 (d, 1H, $J = 4$ Hz, 6-H); 7.85 (d, 1H, $J = 4$ Hz, 3-H)

[a] Satisfactory microanalyses obtained: C ±0.31, H ±0.07, N ±0.10.



Scheme **D**

The mass spectrum of the pyridinethione **11** can be rationalised similarly. The molecular ion **16** ($m/e = 379$) loses a phenyl radical to give the intense cation **17** ($m/e = 302$) and 4-H_3C—C_6H_4—S to give the cation **18** ($m/e = 256$) which in turn eliminates a molecule of hydrogen to give the cation **19** at $m/e = 254$ (Scheme **E**).



Scheme **E**

^{1}H-N.M.R. spectra were recorded with a Varian EM 360L spectrometer using TMS as internal standard. I.R. spectra were obtained using NaCl plates on a Perkin-Elmer 297 spectrophotometer as solutions in $CHBr_3$. Mass spectra were recorded on a Kratos MS 30. Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected.

The following compounds **7** were prepared using literature methods: **7a** (m.p. 152 °C; Lit.[4], m.p. 150 °C); **7b** (m.p. 162–164 °C; Lit.[5], m.p. 163 °C); **7c** (m.p. 130 °C; Lit.[14], m.p. 130 °C); **7e** (m.p. 55 °C; Lit.[16], m.p. 54–55 °C); and **7f** (m.p. 130–140 °C; Lit.[17], m.p. 130–140 °C).

2-Ethoxycarbonyl-1,4-bis[4-methylphenyl]-6-phenylpyridinium Tetrafluoroborate (6d):

A suspension of 2-ethoxycarbonyl-4-(4-methylphenyl)-6-phenylpyrylium tetrafluoroborate[15] (**5d**; 2.4 g, 3 mmol) in dichloromethane (30 ml) is stirred with 4-methylaniline (0.7 g, 3.3 mmol) for 8 h at 25 °C. After concentration, the residue is triturated with ether (~ 100 ml) to give white crystals which are filtered and recrystallised from ethanol (95%) as needles; yield: 2.26 g (89%); m.p. 190 °C.

$C_{28}H_{26}BF_4NO_2$	calc.	C 67.89	H 5.29	N 2.82
(495.3)	found	68.00	5.30	2.81

I.R. ($CHBr_3$): $\nu = 1740$ (C=O); 1620 (C=N); 1050 cm^{-1} ($BF_4^{\ominus}$).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.10$ (t, 3H, $J = 4$ Hz); 2.35 (s, 3H); 2.40 (q, 2H, $J = 4$ Hz); 2.48 (s, 3H); 7.0–7.6 (m, 13H_{arom}); 8.25 (d, 1H, $J = 2$ Hz); 8.52 ppm (d, 1H, $J = 2$ Hz).

Pyridinium Betaines 7d and 10:

A suspension of the pyridinium salt **6d** or **9** (10 mmol) in water is stirred with aqueous sodium hydroxide (17.5 mmol) for 24 h. The white solid is filtered off and washed with water (100 ml) and ether (50 ml) to give the betaine as microcrystals (satisfactory analysis was not obtained due to decomposition during crystallisation).

1,4-Bis[4-methylphenyl]-2-phenylpyridinium-2-carboxylate **(7d)**; yield: 74%; m.p. 148 °C.

I.R. ($CHBr_3$): $\nu = 1650$ (C=O); 1620 cm^{-1} (C=N).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 2.25$ (s, 3H); 2.40 (s, 3H); 7.0–7.5 (m, 13H_{arom}); 8.00 (d, 1H, $J = 2$ Hz); 8.30 ppm (d, 1H, $J = 2$ Hz).

1-(4-Methylphenyl)-4-phenyl-5,6-dihydrobenzo[*h*]quinolinium-2-carboxylate **(10)**; yield: 68%; m.p. 195 °C.

I.R. ($CHBr_3$): $\nu = 1650$ (C=O); 1615 cm^{-1} (C=N).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 2.40$ (s, 3H); 2.7–3.1 (m, 4H); 6.85–7.8 (m, 13H_{arom}); 7.90 ppm (s, 1H).

Pyridine-2-thiones 11 and 12a–f; General Procedure:

The betaine **7a–f** or **10** (5 mmol) in xylene (50 ml) is refluxed with sulphur (10 mmol) for 2 h. After washing with 10% aqueous ammonium sulphide (50 ml), water (50 ml), and drying with sodium sulphate followed by evaporation of the solvent, the residue is boiled with a mixture of methanol (30 ml) and ether (20 ml), the pyridine-2-thiones separate out and are recrystallised from the appropriate solvent (Table).

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[1] H. Quast, E. Frankenfeld, *Angew. Chem.* **77**, 680 (1965); *Angew. Chem. Int. Ed. Engl.* **4**, 691 (1965).
[2] H. Quast, E. Schmitt, *Liebigs Ann. Chem.* **732**, 43 (1970).
[3] H. Quast, A. Geller, *Liebigs Ann. Chem.* **1975**, 992.
[4] A. R. Katritzky, R. Awartani, R. C. Patel, *J. Org. Chem.* **47**, 498 (1982).
[5] A. J. Cozens, *M. Sc. Thesis*, University of East Anglia, Norwich, England, 1980.
[6] M. J. Renault, *C. R. Acad. Sci. Ser. C* **77**, 232 (1951).
[7] M. J. Renault, *Bull. Soc. Chim. Fr.* **20**, 1001 (1953).
[8] A. S. Afridi, A. R. Katritzky, C. A. Ramsden, *J. Chem. Soc. Perkin Trans. 1* **1977**, 1436.
[9] I. El-Kholy, F. K. Rafla, G. Soliman, *J. Chem. Soc.* **1961**, 4490.
[10] V. G. Zhiryakov, P. I. Abramenko, *Khim. Geterotsikl. Soedin. Akad. Nauk Latv. SSR* **1965**, 334; *C. A.* **63**, 13231 (1965).
[11] R. A. Abramovitch, E. E. Knaus, *J. Heterocyclic Chem.* **6**, 989 (1969).
[12] R. A. Damico, *U. S. Patent* 3583999 (1971); *C. A.* **75**, 76623 (1971).
[13] A. R. Katritzky, A. Chermprapai, R. C. Patel, A. Tarraga-Tomas, *J. Org. Chem.* **47**, 492 (1982).
[14] A. R. Katritzky, B. J. Agha, R. Awartani, R. C. Patel, in preparation.
[15] T. Siddiqui, *Ph. D. Thesis*, University of East Anglia, Norwich, England, 1981.
[16] H. Mayer, *Monatsh. Chem.* **24**, 199 (1903).
[17] H. Quast, E. Schmitt, *Liebigs Ann. Chem.* **732**, 64 (1970).
[18] R. Lawrence, E. S. Waight, *J. Chem. Soc.* [B] **1968**, 1.

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