Carbon–Sulfur and Carbon–Selenium Double Bond Formation Through Thiolysis and Selenolysis of 4-Methylsulfanyl-Substituted Pyridinium and Quinolinium Halides

Jocelyne Levillain,[a] Daniel Paquer,[b] Aboubacary Sene,[c] Michel Vazeux*[a]

[a] Laboratoire de Chimie Moléculaire et Thioorgarnique, UMR 6507 ISMRA, Université de Caen, 6 Bd Maréchal Juin, F-14050 Caen Cedex, France
[b] Laboratoire de Chimie Organique, Université de Metz, Ile du Saulcy, F-57045 Metz Cedex, France
[c] Faculté des Sciences et techniques, Université Cheikh Anta DIOP, Dakar, Sénégal

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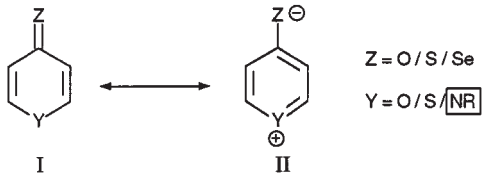
4-Methylsulfanylpyridinium and -quinolinium salts **3** and **4** with alkyl groups such as methyl, allyl, benzyl, ethoxycarbonylmethyl, benzoylmethyl on the nitrogen atom were prepared by the Menschutkin-type reaction and some of them caused to react under either the thiolysis or selenolysis reaction conditions. *N*-Substituted pyridine-4-thiones **5a–c** and quinoline-4-thiones **6a–e** were formed at different rates in high isolated yield. On the other hand, two *N*-alkyl-4-selenopyridones **7a,b** together with three 4-selenoquinolones **8a,b,c** were also produced in high chemical purity and characterized spectroscopically. In addition, 4-sulfanylpyridone **12** and 4-selenopyridone **13** with a *N*-*tert*-butyl group were obtained via Zincke's salt **9**. The overall process provides a useful alternative to the otherwise difficult direct *N*-alkylation of thioxo- and selenoxopyridine systems.

The 4-pyrone and its sulfur- and nitrogen-containing ring systems are important constituents of many molecules with biological significance.[1] Thiocarbonyl and selenocarbonyl derivatives, as members of this interesting family, are also of particular importance. Spectroscopic[2] and electrochemical[3] studies have been reported for a number of these species, as well as for their mono and dibenzo counterparts. They have also been shown to act as efficient traps[4] for a variety of free radicals. The great interest of such closely related molecules lies in the variety of reactions available to them and can be understood in terms of a more or less efficient electron delocalization between the C=O/S/Se π-bond and the nonbonding electron pair(s) on the heterocyclic heteroatom. Compounds of the pyridone class are obviously the more challenging and promising targets because of the additional functionality on the nitrogen atom. They exhibit a marked amphoteric character, as suggested by a significant contribution of the dipolar formula II to the resonance hybride. Besides reactions involving Diels–Alder cycloadditions[5] and conjugate additions,[6] they also undergo tandem elec-trophilic–nucleophilic additions, the combination of these two types of reactions has been used in a number of syntheses of nitrogen-containing heptafulvenes[7] and dihydropyridone derivatives.[8] Members of the 2- and 4-series have recently found many applications in the field of cyanin dyes,[9] β-lactamic antibiotics[10] and sugar nucleosides,[11] with much emphasis being placed on the thiocarbonyl chromophore. Specific important uses of the 2-pyridinethiones are as synthetic intermediates[12] and in heterocyclic synthesis.[13] In connection with our studies on the alkylidenation of suitably 4-sulfanyl-functionalized pyridinium and quinolinium cations via the sulfur contraction process,[14] and in view of the possibilities of employing thiocarbonyl and selenocarbonyl pyridine systems as potential radical scavengers and as chemical intermediates, we have undertaken a study of their preparation.

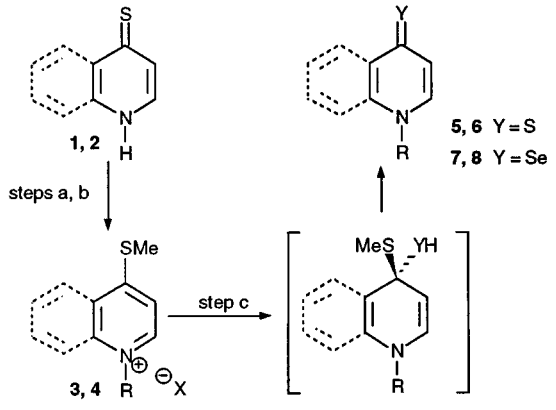


I II

Nitrogen–carbon bond forming reactions[15] from 4-sulfanylpyridine and ring transformations[16] apart, synthetic ways to *N*-substituted-4-pyridinethiones, including their benzo-analogues, can be classified into two major routes. The first path is best illustrated by the selective *N*-alkylation of ambident anions of 4(1*H*)-pyridone itself[17] followed by the thionation of the resulting *N*-alkyl-4-pyridones with phosphorus(V) based reagents.[18] This classical approach, however, may suffer from the requisite high selectivity of the first step and the rather drastic reaction conditions of the second which may preclude the introduction of sensitive functional groups on the nitrogen side chain. The second pathway may be viewed as being able to somewhat overcome these disadvantages. The thiolysis with sodium hydrogen sulfide or thiourea of preformed pyridinium salts[19] having nucleofugal substituents, usually halogeno and to a lesser extent oxygen, sulfur- and nitrogen-containing groups at the 4-position, provides an alternative method to the thiation procedure and may be the preferred route. With regard to the synthesis of selenoamides, this seems particularly true for the selenolysis method if compared to the selenation approach.[20] Mechanistically, these two types of reactions are nucleophilic substitution and occur via a two-stage process involving addition and elimination through the intermediary of a so-called σ-adduct.[21] The ease with which 4-methylsulfanylpyridinium cations can be prepared, together with their long shelf life and their inherent high reactivity towards heteronucleophiles, made us feel confident that the second procedure could satisfy our goal. It is believed that a methylsulfanyl substituent possessing electron-donating properties and having a high leaving group ability would facilitate both the Menschutkin and the chalcogenolysis reactions.

The overall process developed for the synthesis of some sulfanyl- and selenocarbonyl derivatives in the 4-pyridine and quinoline series is outlined in Scheme 1 and uses 4-methylsulfanylpyridinium and -quinolinium halides as key synthetic intermediates. These simple saIts are almost quantitatively prepared by a three-step sequence of reactions commencing from the corresponding and readily

available (1*H*)-4-thioxopyridine and -quinoline **1** and **2** themselves. The transformation includes in succession *S*-methylation with methyl iodide in ethanolic solution, dehydroiodination of the resulting *N*-protonated azinium iodides under aqueous basic conditions[22] and quaternization of the 4-methylsulfanylpyridine and -quinoline base intermediates with reactive halides in acetonitrile. The pale yellow coloured pyridinium and quinolinium salts **3a–c** and **4a–e** precipitated from the solution and were collected and purified (Table 1). In most cases, however, the reaction mixture was concentrated to dryness and the solid residue, first free from soluble materials in diethyl ether, was in sufficient purity for further reaction. This very simple procedure allows the use of an excess of halide to drive the Menschutkin reaction[23] to completion.



step a : CH_3I / EtOH, 40°C, 1h. then aq. NaOH, 15 mn, quant[20].
b : CH_3I or R-Br / CH_3CN, 50 °C, 1-12 h., 65-95%;
step c : 2 eq NaSH / EtOH-H_2O, 5 mn-2 h, 25 °C, 53-97 %
or 2 eq " NaSeH" / EtOH, 2 h, 25 °C

Class	P	Q
Cpd	1, 3, 5, 7	2, 4, 6, 8

P= pyridine Q= Quinoline

R	CH_3	$CH_2CH{=}CH_2$	CH_2CO_2Et	$CH_2C_6H_5$	$CH_2COC_6H_5$
Series	a	b	c	d	e

Scheme 1

When 4-methylsulfanylquinolinium halides **4a–e** were stirred with 2 molar equivalents of sodium hydrogen sulfide in a mixture ethanol–water (1:1) at room temperature, the thiolysis reaction proceeded rapidly to produce the corresponding *N*-substituted-quinoline-4-thiones **6a–e** in high chemical yield as shown in Table 2. In a similar manner, the pyridine-4-thiones **5a–c** were formed albeit in a longer reaction time. As has been observed already for the reaction of *N*-methyl salts **3a** and **4a** with hydroxide ions,[24] this strongly suggests that annelation with a benzene ring weakens the S–C(4) bond thus making attraction between the cationic substrate and the anionic nucleophile more efficient. Moreover, the consumption of 2 moles of sodium hydrogen sulfide per mole of salt favors regular kinetics for the reaction.[25]

On the other hand, some 4-methylsulfanylpyridinium and -quinolinium salts were found to undergo nucleophilic displacement with the sodium hydrogen selenide reagent, produced in situ from a degassed ethanolic solution of $NaBH_4$ with powdered Se according to the procedure developed by Klayman and Griffin.[26] Related reactions leading to simple *N*-alkyl γ-selenolutidones and selenoacridones from the corresponding chloro azinium cations as well as the selenolysis of 4-methoxy and 4-methylsulfanyl (thia)pyrilium salts were earlier reported.[27] As far as we are aware, however, little is known about the isolation of *N*-substituted selenopyridones and -quinolones[28] and there are virtually no reports of NMR analysis on these types of compounds. A direct extension of these studies is provided by the results collected in Table 5. Thus, the reactions of *N*-methyl and *N*-allyl pyridinium and quinolinium cations **3a,b** and **4a,b** with 2 equimolar amounts of "NaSeH" under nitrogen atmosphere at 25 °C for 2 hours followed by an aqueous workup gave the desired selenocarbonyl derivatives **7a,b** and **8a,b**, respectively. These heterocyclic vinylogous selenoamides, as reddish orange compounds, are produced in high chemical purity as judged by ^1H NMR. In an analogous fashion, *N*-ethoxycarbonylmethylquinoline-4-selenone (**8c**) was also obtained from salt **4c**. Besides prevailing **8c**, however, ethyl 1-(1,2-dihydro-4-methylsulfanylquinolyl)acetate was formed as a byproduct to some extent, its formation being in part prevented by not exceeding the amount of $NaBH_4$ necessary for the generation in situ of 2 molar equivalents of hydrogen selenide anion. The *N*-substituted γ-selenopyridones and -quinolones thus obtained can be stored in a refrigerator for extended periods of time under nitrogen atmosphere but, on exposure to the air, they undergo slow oxidation to the corresponding carbonyl derivatives and selenium. The ^1H and ^{13}C NMR spectra of these selenocarbonyl compounds are also summarized in Table 5 and may be compared to those of their thiocarbonyl analogs in Table 4. As a general trend, the ring β-protons and β-carbons upon substitution of C=S by C=Se are significantly shifted downfield and this can be attributed in part to an enhanced electron delocalisation round the selenium atom. A parallel but much higher effect is also produced by replacement of a C=O by a C=S group.[2]

In an effort to make the synthetic pathway outlined in Scheme 1 more attractive, we have developed, via the Zinckes reaction, a practical entry to the previously unknown pyridine systems functionalized with a 4-C=Y group (Y = O, S, Se) in which a *tert*-butyl substituent is linked to the ring nitrogen atom. According to Scheme 2, treatment of 4-methylsulfanylpyridine base with 1.2 equiv of 1-chloro-2,4-dinitrobenzene afforded the Zinckes salt **9** (*N*-DNB) in 73% isolated yield. Previous reports[29] have pointed out that the pyridinium nucleus with a strong electron-withdrawing group on the nitrogen atom is prone to be nucleophilically attacked in sequence at the C-2 and C-6 position by a primary amine thus allowing exchanges of the amine moiety in the pyridinium ring. As another example, salt **9** was easily converted into 1-*tert*-butyl-4-methylsulfanylpyridinium chloride (**10**) by reaction with *tert*-butylamine in refluxing dichloromethane. The main NMR features in DMSO-d_6 of **10** are close to those of **9**,

Table 1. 4-Methylsulfanylpyridinium and 4-Methylsulfanylquinolinium Halides Prepared

Salt[a]	Yield[b] (%)	mp (°C) (solvent)	Molecular[c] Formula	IR (KBr) ν cm^{-1}
3a	95	182–184 (185–186[25]) (EtOH)	$C_7H_{10}INS$	3100–2900, 1620, 1540, 1490, 1450, 1105
3b	95	124–125[d]	$C_9H_{12}BrNS$	3100–2900, 1620, 1540, 1460, 1100
3c	65	193 (EtOH)	$C_{10}H_{14}BrNO_2S$	3000–2940, 1740, 1625, 1120, 1100, 1020
4a	92	252–253 (247–248[24]) (EtOH)	$C_{11}H_{12}INS$	1610, 1600, 1550, 1525, 1420, 1380, 1210
4b	91	210 (CH_3CN/EtOAc)	$C_{13}H_{14}BrNS$	1610, 1595, 1555, 1530, 1390, 1245, 1205, 1160
4c	88	194 (CH_3CN/EtOAc)	$C_{14}H_{16}BrNO_2S$	3070–2850, 1736, 1598, 1552, 1390, 1262, 1248, 1208
4d	95	226 (EtOH)	$C_{17}H_{16}BrNS$	3064–2978, 1654, 1610, 1596, 1554, 1530, 1488, 1396
4e	92	222 (EtOH)	$C_{18}H_{16}BrNOS$	3022–2950, 1694, 1602, 1578, 1552, 1532, 1480, 1448, 1392, 1340, 1216
10[e]	55	111 (decomp.) (EtOAc/Et_2O)	$C_{10}H_{16}ClNS$	3483–3408, 3104–2984, 1622, 1558, 1540, 1493, 1478, 1456, 1446, 1406, 1376, 1318

[a] Salts as bromides except **3a, 4a** as iodides and **10** as chloride.
[b] All yields were based on isolated product.
[c] Satisfactory microanalysis were obtained **3b,c, 4e:** C±0.34; H±0.16; N±0.14; O±0.21; S±0.41; for **4b–d** and **10:** S±0.36.
[d] This salt was not recrystallyzed.
[e] Overall yield via the Zincke's salt **9.**

Table 2. *N*-Substituted Pyridine-4-thiones **5a–c, 12** and Quinoline-4-thiones **6a–e** Prepared

Product	Yield[a] (%)	mp (°C) (solvent)	Molecular[b] Formula	MS (70 eV) *m/z* (%)	IR (KBr) ν (cm^{-1})
5a	86	159–l61 (161–162[18a]) (EtOH)	C_6H_7NS	125 (M^+, 100), 81 (50), 42 (34)	2940, 1630, 1514, 1466, 1414, 1208, 1110, 1024
5b	97	64–65 (Toluene/light petroleum)	C_8H_9NS	151 (M^+, 100), 119 (13), 102 (24)	1616, 1508, 1466, 1420, 1282, 1206, 1108, 1026
5c[c]	53	122	$C_9H_{11}NO_2S$		3070–2852, 1736, 1598, 1552, 1528, 1390, 1262, 1248, 1012
6a	91	210–211 (209–11,[22] 210–212[30]) (CH_3CN/isopropyl ether)	$C_{10}H_9NS$	175 (M^+, 100), 131 (45), 130 (47)	1595, 1530, 1515, 1370, 1150, 1095
6b	86	97 (Toluene/light petroleum)	$C_{12}H_{11}NS$	201 (M^+, 61), 160 (10), 89 (21), 41 (100)	3070–2850, 1590, 1533, 1390, 1235, 1158, 1131
6c	92	169 (EtOAc/light petroleum)	$C_{13}H_{13}NO_2S$	247 (M^+, 21, 219 (10), 174 (30), 84 (64), 73 (7), 49 (100)	3070–2852, 1736, 1598, 1552, 1528, 1390, 1362, 1262, 1248, 1208
6d	92	157 (Toluene/light petroleum)	$C_{16}H_{13}NS$	251 (M^+, 10), 160 (7), 91 (30), 55 (100)	3000, 1614, 1606, 1538, 1508, 1386, 1228, 1162
6e	89	168 (Toluene/light petroleum)	$C_{17}H_{13}NOS$		2922, 1684, 1596, 1540, 1386, 1228, 1164
12	65	148 (decomp.) (Toluene/light petroleum)	$C_9H_{13}NS$	167 (M^+, 10), 166 (50), 151 (12), 111 (100), 110 (14), 57 (72)	3102–2968, 1622, 1610, 1458, 1192, 1140, 1132, 1088

[a] All yields were based on isolated product.
[b] The microanalyses were in satisfactory agreement with the calculated values: for **5b, 6b, c** and **12:** C±0.44; H±0.22; H±0.24; S±0.32; for compounds **5c, 6d:** S±0.33; for **5c** and **6e** HRMS: ±0.0045.
[c] Isolated by chromatography.

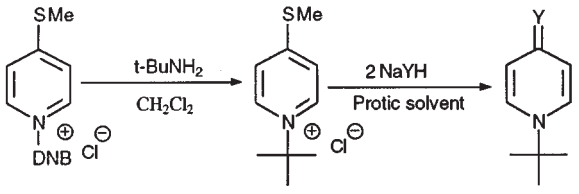
in particular the chemical shift of heterocyclic carbons (C2,6 at δ = 139.8, C3,5 at δ = 122.6 and C4 at δ = 162.6 for **10**; C2,6 at δ = 142.6, C3,5 at δ = 122.0 and C4 at δ = 167.8 for **9**). Submitted to the thiolysis and selenolysis standard conditions, cation **10** was found to deliver the sulfanyl- and selenocarbonyl derivatives **12** and **13**, respectively, in a very satisfactory manner. Hydrolytic cleavage of the C–S bond also proceeded smoothly in aqueous sodium hydroxide at 40 °C to give after usual workup 1-*tert*-butyl-4-pyridone (**11**) in 71% yield (experimental section).

A very convenient and high-yielding four-step reaction sequence which includes a blocking and deblocking pro-

Table 3. ^{1}H NMR and ^{13}C NMR Spectral Data of Selected 4-Methylsulfanylpyridinium and -quinolinium Salts ($CDCl_3$/TMS)

Salt	^{1}H NMR δ *J* (Hz)	^{13}C NMR δ
3b	2.7 (3 H, s), 5.5 (3 H, m), 5.62 (1 H, d, *J* = 16.8), 6.12 (1H, ddt, *J* = 16.8, 10.1, 6.5), 7.8 (2H, d, *J* = 7.1), 9.15 (2 H, d, *J* = 7.1)	s: 164.6 d: 122.7, 130.4, 142.6 t: 61.9, 123.8 q: 15.1
3c	1.3 (3 H, t, *J* = 7.1), 2.78 (3 H, s), 4.3 (2 H, q, *J* = 7.1), 6.0 (2 H, s), 7.76 (2 H, d, *J* = 7.2), 9.03 (2 H, d, *J* = 7.2)	s: 165.5, 166.3 d: 121.9, 144.0 t: 59.7, 63.3 q: 14.2, 15.0
4b	2.87 (3 H, s), 5.38 (1 H, d, *J* = 17.4), 5.45 (1 H, d, *J* = 10.7), 5.87 (2 H, d, *J* = 5.5), 6.15 (1 H, m), 7.87 (1 H, ddt, *J* = 17.4, 10.7, 5.5), 7.94 (1 H, d, *J* = 6.7), 8.09 (1 H, ddd, *J* = 8.5, 6.7, 1.5), 8.4 (2 H, m), 10.35 (1 H, d, *J* = 6.7)	s: 126.5, 135.8, 165.2 d: 115.8, 119.8, 125.4, 129.5, 130.1, 135.8, 147.3 t: 58.8, 121.4 q: 15.4
4c	1.3 (3 H, t, *J* = 7.1), 2.89 (3 H, s), 4.39 (2 H, q, *J* = 7.1), 6.35 (2 H, s), 7.7–7.8 (2 H, m), 8.0–8.2 (2 H, m), 8.4 (1 H, m), 10.18 (1 H, d, *J* = 6.8)	s: 125.5, 135.7, 165.8, 166.3 d: 115.2, 118.4, 126.3, 136.2, 136.6 t: 56.9, 63.2 q: 14.1, 15.3
4d[a]	2.94 (3 H, s), 6.26 (2 H, s), 7.3 (5 H, m), 7.95 (1 H, m), 8.04 (1 H, d, *J* = 6.7), 8.15 (1 H, m), 8.4 (2 H, m), 9.5 (1 H, d, *J* = 6.7)	s: 126.2, 134.2, 146.9, 164.9 d: 115.9, 120.1, 125.1, 127.1, 128.6, 129.1, 129.7, 134.4, 135.4 t: 58.7 q: 14.6
4e[a]	2.95 (3 H, s), 6.9 (2 H, s), 7.65 (2 H, m), 7.78 (1 H, m), 7.9–8.0 (2 H, m), 8.0 (1 H, d, *J* = 6.7), 8.07 (1 H, m), 8.16 (1 H, dd, *J* = 7.2, 1.3), 8.31 (1 H, d, *J* = 8.8), 8.47 (1 H, d, *J* = 8.4), 9.3 (1 H, d, *J* = 6.7)	s: 125.8, 133.6, 136.4, 165.6, 190.5 d: 115.3, 119.7, 124.7, 128.5, 128.8, 129.3, 134.5, 135.2, 147.2 t: 61.9 q: 14.8
10	1.47 (9 H, s), 2.74 (3 H, s), 7.92 (2 H, d, *J* = 7.1), 9.13 (2 H, d, *J* = 7.1)	s: 52.7, 164.3 d: 123.2, 139.7 q: 15.0, 27.8

[a] In DMSO-d_6.



Y	O	S	Se
Cpd	11	12	13

Scheme 2

cess and allows the introduction of functionalized carbon side chains on the nitrogen atom of (1*H*)-pyridine-4-thione and its mono-benzoanalogue has been developed. It was further applied to the syntheses of some *N*-substituted-4-selenopyridones and -quinolones. Although the reducing conditions of the thiolysis and selenolysis step could be a limiting factor, the synthetic versatility of the *N*-quarternization reaction is believed to make this procedure reliable for the synthesis of varied *N*-functionalized sulfanyl- and selenocarbonyl pyridine and quinoline derivatives in the 4- but also in the 2-series.

Melting points were determined with a Gallenkamp apparatus and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brucker AC 250 instrument operating at 250.13 MHz for ^{1}H, 62.89 for ^{13}C. IR spectra were taken with a Perkin-Elmer 16 PC FTIR spectrophotometer. Mass spectra were performed with a Nermag Riber Rl0 spectrometer (70 eV). HRMS were recorded on a DM 300 GEOL (70 eV) spectrometer. Microanalyses were obtained from the "Laboratoire central de microanalyse du CNRS" (Lyon). Analyses of sulfur were performed at Caen following Debal and Levy's method (*Bull. Chem. Soc. Fr.*, **1968**, 426), TLC plastic sheets silica gel 60 F_{254} (0.2 mm layer thickness) and PLC plates silica gel 60 F_{254} (1 mm layer thickness) were used for chromatography.

All commercially available bromides and MeI were used as received from the suppliers. Purification of solvents was effected according to standards methods. All reactions were conducted under N_2. (1*H*)-Pyridine-4-thione (**1**) and (1*H*)-quinoline-4-thione (**2**) were prepared by the procedure developed by Albert and Barlin.[22] The syntheses of 4-methylsulfanylpyridine and -quinoline bases and their methiodides **3a** and **4a** were also described by these authors.

***N*-Alkylation of 4-Methylsulfanylpyridine and -quinoline; General Procedure:**

The appropriate α-activated bromide (1.5 mmol) was added in one aliquot to a solution of 4-methylsulfanylpyridine or 4-methylsulfanylquinoline (1 mmol) in anhyd MeCN (5 mL). The mixture was stirred at r.t. or at 50 °C, respectively. The reaction was monitored by TLC (elution with CH_2Cl_2). After completion, the precipitate was filtered off and washed well with anhyd Et_2O. The pyridinium and quinolinium bromides were obtained in almost quantitative yields and were of sufficient purity for further reactions. For analysis, these salts were recrystallized as pale yellow needles (solvents given in Table 1). Salt **4e** was isolated as purple squares.

Thiolysis of 4-Methylsulfanylpyridinium and -quinolinium Halides; General Procedure:

To a solution of sodium hydrogen sulfide (0.12 g, 2.1 mmol) in EtOH/H_2O (5 mL, 1/1 : v/v) was added pyridinium or quinolinium salts (1 mmol). The mixture was stirred at r.t. for 5–10 min (quinoline series) or 1–2 h (pyridine series). The resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined CH_2Cl_2 layers were

Table 4. ^{1}H NMR and ^{13}C NMR Spectral Data of Selected *N*-Substituted Pyridine-4-thiones and Quinoline-4-thiones ($CDCl_3$/TMS)

Product	^{1}H NMR δ, J (Hz)	^{13}C NMR δ
5b	4.47 (2 H, d, *J* = 5.8), 5.3 (1 H, d, *J* = 16.9), 5.45 (1 H, d, *J* = 10.3), 5.94 (1 H, ddt, *J* = 16.9, 10.3, 5.8), 7.13 (2 H, d, *J* = 7.1), 7.46 (2 H, d, *J* = 7.1)	s: 191.8 d: 130.8, 131.7, 134.6 t: 59.8, 121.4
5c	1.24 (3 H, t, *J* = 7.1), 4.22 (2 H, q, *J* = 7.1), 4.44 (2 H, s), 6.92 (2 H, d, *J* = 7.1), 7.31 (2 H, d, *J* = 7.1)	s: 165.8, 184.1 d: 131.6, 135.1 t: 57.5, 63.l q: 14.2
6b	4.75 (2 H, d, *J* = 5.7), 5.07 (1 H, d, *J* = 17.2), 5.26 (1 H, d, *J* = 10.5), 5.91 (1 H, ddt, *J* = 17.2, 10.5, 5.7), 7.2 (1 H, d, *J* = 7.1), 7.3–7.4 (3 H, m), 7.6 (1 H, m), 8.9 (1 H, m)	s: 125.6, 133.9, 194.7 d: 116.7, 125.5, 130.5, 130.6, 132.7, 136.0, 136.1 t: 56.0, 119.2
6c	1.26 (3 h, t, *J* = 7.1), 4.27 (2 H, q, *J* = 7.1), 4.85 (2 H, s), 7.22 (1 H, d, *J* = 7.2), 7.28 (1 H, m), 7.47 (1 H, d, *J* = 7.2), 7.5 (1 H, m), 7.7 (1 H, m), 9.02 (1 H, dd, *J* = 8.3, 1.5)	s: 125.9, 134.0, 164.5, 186.5 d: 115.3, 125.8, 131.2, 133.3, 136.2, 136.3 t: 54.9, 62.8 q: 14.2
6e	5.6 (2 H, s), 7.03 (1 H, d, *J* = 8.4), 7.27 (1 H, d, *J* = 6.9), 7.3–7.7 (6 H, m), 7.99 (2 H, dd, *J* = 7.8, 1.4), 8.94 (1 H, d, *J* = 8.3)	
12	1.61 (9 H, s), 7.41 (2 H, d, *J* = 7.5), 7.49 (2 H, d, *J* = 7.5)	s: 62.5, 190.3 d: 131.2, 131.6 q: 29.9

Table 5. ^{1}H NMR and ^{13}C NMR Spectral Data of *N*-Substituted Pyridine-4-Selenones **7a, b, 13** and Quinoline-4-Selenones **8a–c** ($CDCl_3$/TMS)

Product	Chemical Purity[a]	Molecular[c] Formula	^{1}H NMR δ, J (Hz)	^{13}C NMR δ
7a	95%	C_6H_7NSe	4.35 (3 H, s), 7.19 (2 H, d, *J* = 7.0), 7.77 (2 H, d, *J* = 7.0)	s: 184.8 d: 135.3, 136.8 q: 45.5
7b	94%	C_8H_9NSe	4.45 (2 H, d, *J* = 5.1), 5.40 (1 H, d, *J* = 10.0), 5.52 (1 H, d, *J* = 17,1), 6,01 (1 H, m), 7.20 (2 H, d, *J* = 7.0), 7.82 (2 H, d, *J* = 7.0)	s: 186.5 d: 130.3, 132.6, 136.5 t: 60.0, 121.8
8a	94%	$C_{10}H_9NSe$	3.82 (3 H, s), 7.31 (1 H, d, *J* = 6.8), 7.5 (2 H, m), 7.78 (1 H, m), 7.97 (1 H, d, *J* = 6.8), 9.09 (1 H, m)	s: 126.8, 128.9, 194.4 d: 116.2, 131.0, 131.7, 133.4, 134.2, 135.4, q: 42.5
8b	85%	$C_{12}H_{11}NSe$	4.8 (2 H, d, *J* = 5.1), 5.15 (1 H, *J* = 17.1), 5.35 (1 H, d, *J* = 10.0), 6.01 (1 H, m), 7.38 (1 H, d, *J* = 6.9), 7.6 (1 H, m), 7.7–7.8 (2 H, m), 7.97 (1 H, d, *J* = 6.9), 9.06 (1 H, m)	
8c[b]	70%	$C_{13}H_{13}NO_2Se$	1.25 (3 H, t, *J* = 7.1), 4.26 (2 H, q, *J* = 7.1), 4.8 (2 H, s), 7.35 (1 H, d, *J* = 7.0), 9.00 (1 H, m)	
13	> 95%	$C_9H_{13}NSe$	1.56 (9 H, s), 7.37 (2 H, d, *J* = 7.2), 7.82 (2 H, d, *J* = 7.2)	s: 62.1, 184.5 d: 129.6, 135.4 q: 28.7

[a] Estimated from ^{1}H NMR Spectra.
[b] Significant amount of ethyl 1-(1,2-dihydro-4-methylsulfanylquinolyl)acetate is present.
[c] The HRMS were in satisfactory agreement with the calculated values: ± 0.0033 except for **8c**.

washed with brine and dried ($MgSO_4$). The removal of the solvent under reduced pressure yielded the desired yellow thiocarbonyl derivatives which was further recrystallized (solvents given in Table 2).

Selenolysis of 4-Methylsulfanylpyridinium and -quinolinium Halides; General Procedure:
A nearly colorless ethanolic solution of sodium hydrogen selenide was first prepared according to Klayman and Griffin:[26] Deoxygenated absolute EtOH (3 mL) was added with magnetic stirring to gray powder selenium (0.08 g, 1 mmol) and anhyd $NaBH_4$ (0.04 g, 1.05 mmol) cooled in an ice bath. After being stirred for 10–30 min, pyridinium or quinolinium halide (0.5 mmol) was carefully added and the reaction was allowed to stand at r.t. for ca. 2 h. N_2 was bubbled through the mixture for 1 h to remove H_2Se (bleach trap) and deoxygenated H_2O (3 mL) was added. The solution was extracted with oxygen free CH_2Cl_2 (3 × 5 mL). The combined CH_2Cl_2 layer was dried ($MgSO_4$) and concentrated under reduced pressure, giving an orange crude solid which was analyzed by spectroscopic means (Table 5).

Synthesis and Hydrolysis of 1-*tert*-Butyl-4-methylsulfanylpyridinium Chloride (10):
A solution of 4-methylsulfanylpyridine (0.625 g, 5 mmol) and freshly distilled 1-chloro-2,4-dinitrobenzene (1.21 g, 6 mmol) in MeOH (3 mL) was refluxed for 24 h with stirring. After removal of the solvent under reduced pressure, Et_2O (10 mL) was added. Salt **9** was ob-

tained by filtration and washing with Et_2O (3 × 5 mL) as white crystals (1.20 g, 3.65 mmol, 73 %, mp = 211 °C).
^{1}H NMR (DMSO-d_6 / TMS): δ = 3.34 (3 H, s), 8.19 (2 H, d, J = 7.1 Hz), 8.37 (1 H, d, J = 8.7 Hz), 8.92 (1 H, dd, J = 8.7, 2.5 Hz), 9.07 (2 H, d, J = 7.1 Hz), 9.09 (1 H, d, J = 2.5 Hz).
^{13}C NMR (DMSO-d_6 / TMS): δ = 14.5 (q), 121.5 (d), 122.0 (d), 130.2 (d), 132.2 (d), 138.5 (s), 142.6 (d), 143.4 (s), 148.9 (s), 167.8 (s)
tert-Butylamine (200 μL, 2.5 mmol) was added dropwise to a stirred suspension of **9** (0.66 g, 2 mmol) in anhyd CH_2Cl_2 (5 mL). The mixture was stirred 1 h at r.t. and turned to a deep red color. After the solution was refluxed for 36 h, the solvent was removed under reduced pressure and the crude product was dissolved in a mixture of H_2O and EtOAc (l/1 v/v). The aqueous layer was separated and the EtOAc layer was washed twice with H_2O. The H_2O extracts were combined, washed with CH_2Cl_2, and concentrated in vacuo to give salt **10** (0.32 g, 1.5 mmol, 75 %) as a pale yellow solid. White crystals were obtained from anhyd EtOAc–Et_2O (Table 1).
Hydrolysis of salt **10** (0.22 g, 1 mmol) was performed in 1M aq NaOH (2 mL) with stirring at 40 °C for 2h. After cooling to r.t., the mixture was acidified to pH 6–7 by sat. aq NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined extracts were washed with brine and then dried ($MgSO_4$). Removal of the solvent yielded a brown oil which was identified as 1-*tert*-butylpyridin-4-one (1.1 g, 71 %).
^{1}H NMR ($CDCl_3$/TMS): δ = 1.59 (9 H, s), 6.41 (2 H, d, J = 7.9 Hz), 7.59 (2 H, d, J = 7.9 Hz).

(1) Smith, D. M. in "*Comprehensive Organic Chemistry*"; Ed. Sammes, P. G., Pergamon: Oxford, 1979; vol. 4, part 16.1 See also J. Staunton in the same book, part.18.1, 2, 3 and 5.
(2) Martin, R. H.; Defay, N.; Geerts Evrard, F.; Given, P. H.; Jones, J. R.; Wedel, R. W. *Tetrahedron* **1965**, *21*, 1833.
Smitherman, H. C.; Ferguson, L. N. *Tetrahedron* **1968**, *24*, 923.
Still, I. W. J.; Plavac, N.; McKinnon, D. M.; Chauhan, M. S. *Can. J. Chem*. **1976**, *54*, 280.
(3) Bock, H.; Brühler, G.; Tabatabai, A.; Semkow, A.; Gleiter, R. *Angew Chem*. **1977**, *Angew Chem., Int. Ed. Engl*. **1977**, *10*, 724.
Russel, G. A.; Malatesta, V.; Morita, T.; Osuch, C.; Blankespoor, R. L.; Trahanovsky, K. D.; Goettert, E. *J. Am. Chem. Soc*. **1979**, *101*, 2112.
(4) Alberti, A.; Benaglia, M.; Depew, M. C.; Mc Gimpsey, W. G.; Pedulli, G. F.; Wan, J. K. S. *Tetrahedron* **1988**, *44*, 3693.
(5) Nakano, H.; Tomisawa, H.; Hongo, H. *J. Chem. Soc., Chem. Commun*. **1990**, 1775.
(6) Seebach, D.; Boes, M.; Naef, R.; Scheizer, W. B. *J. Am. Chem. Soc*. **1983**, *105*, 5390.
(7) Belsky, H.; Dodiuk, H.; Shvo, Y. *J. Org. Chem*. **1974**, *39*, 989.
Tomisawa, H.; Tambara, T.; Kato, H.; Hongo, H.; Fujita, R. *Heterocycles* **1981**, *15*, 277.
(8) Roduit, J. P.; Wyler, H. *Helv. Chim. Acta* **1985**, *68*, 403, and references therein.
Comins, D. L.; Goehring, R. R.; Joseph, S. P.; O'Connor, S. *J. Org. Chem*. **1990**, *55*, 2574.
Griera, R.; Rigat, L.; Alvarez, M.; Joule, J. A. *J. Chem. Soc. Perkin Trans* 1 **1992**, 1223.
(9) Liepins, R.; Walker, C. *Ind. Eng. Chem. Prod. Res. Develop*. **1971**, *10*, 401; *Chem. Abstr*. **1972**, *76*, 073 698.
Sogulyaev, Y. A.; Mushakalo, I. L.; Tolmacher, A. I., *Ukr. Khim*. Zh. **1991**, *57*, 426; *Chem. Abstr*. **1992**, *117*, 251 217.
(10) Katano, K.; Ogino, H.; Iwamatsu, K.; Nakabayashi, S.; Yoshida, T.; Komiya, I.; Tsuruoka, T.; Inouye S.; Kondo, S. *J. Antibiot*. **1990**, *43*, 1150.
Hamashima, Y.; Minami, K.; Ishikura, K.; Ishitobi, H.; Onoe, H. Jpn Patent 05148272, 1993; *Chem. Abstr*. **1994**, *120*, 134 140.
(11) Vorbrüggen, H.; Bennua, B. *Chem. Ber*. **1981**, *114*, 1279.
Seela, F.; Bindig, U. *Liebigs Ann. Chem*. **1989**, 895.
(12) Yamada, M.; Watabe, Y.; Sakakibara T.; Sudoh, R. *J. Chem. Soc., Chem. Commun*. **1979**, 179.
See also Yamada, M.; Watabe, Y.; Sakakibara T.; Sudoh, R. *Bull. Chem. Soc. Jpn*. **1988**, *61*, 247.
Kato, S.; Masumoto H.; Ikeda, S. I.; Itoh, M.; Murai, T.; Ishihara, H. *Z. Chem*. **1990**, *30*, 67.
(13) Blank, B.; DiTullio, N. W.; Krog, A. J.; Saunders, H. L. *J. Med. Chem*. **1971**, *21*, 489.
Molina, P.; Alajarin, M.; Vilaplana, M. J.; Katritzky, A. R. *Tetrahedron Lett*. **1985**, *26*, 467.
(14) Levillain, J.; Vazeux, M. *Synthesis*, **1995**, 56.
Levillain, J. Ph. D. *Thesis*, 20–l2-1994, University of Caen.
(15) Effenberger, F.; Muck, A. O. Bessey, E. *Chem. Ber*. **1980**, 113, 2086.
Pervez, H.; Onyriuka, S. O.; Rees, L.; Rooney, J. R.; Suckling, C. J. *Tetrahedron*, **1988**, *44*, 4555.
(16) Whittingham, W. G. in "*Comprehensive Organic Functional Group Transformation*", Ed. Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W., Pergamon, 1995, vol. 3, 329 and references cited p 357–358.
(17) Izzo, P. T.; Lee, V. J. *J. Heterocycl. Chem*. **1988**, *25*, 289.
Johnson, B. L.; Kitahara, Y.; Weakley, T. J. R.; Kenna, J. F. W. *Tetrahedron Lett*. **1993**, *34*, 5555.
(18) Jones, R. A.; Katritzky, A. R. *J. Chem. Soc*. **1958**, 3610.
Cava, M. P.; Levinson, M. I. *Tetrahedron* **1985**, *41*, 5061.
(19) Ogawa, A.; Sonoda, S. in "*Comprehensive Organic Synthesis*", Ed. Winterfeldt, E., Pergamon: Oxford, 1991, vol. 6, 461.
(20) Collin, P. Dell in "*Comprehensive Organic Functional Group Transformation*", Ed. Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W., Pergamon, 1995, vol. 5, p 629.
(21) Chupakhin, O. N.; Charushin, V. N.; Van der Plas, H. C. *Tetrahedron*, **1988**, *44*, 1.
(22) Albert, A.; Barlin, G. B. *J. Chem. Soc*. **1959**, 2384.
(23) Duffin, G. F. in "*Advances in Heterocyclic Chemistry*", Ed. Katritzky, A. R. Academic: 1964, vol. 3, 1.
(24) Barlin, G. B.; Benbow, J. A. *J. Chem. Soc. Perkin Trans. 2*, **1975**, 298.
(25) Barlin, G. B.; Benbow, J. A. *J. Chem. Soc. Perkin Trans 2*, **1974**, 790.
(26) Klayman, D. L.; Griffin, T. S. *J. Am. Chem. Soc*. **1973**, *95*, 197.
(27) Silverman R. B. in "*Organic Selenium Compounds: Their Chemistry and Biology*", Ed. Klayman D. L., Günther H. H., 1973, 257.
(28) Mautner, H. G.; Chu, S. H.; Lee, C. M. *J. Org. Chem*. **1962**, *27*, 3671.
(29) Matsumura, E.; Kobayashi, H.; Nishikawa, T.; Ariga, M.; Tohda, Y.; Kawashima, T. *Bull. Chem. Soc. Jpn*. **1984**, *57*, 1961.
Génisson, Y.; Marazano, C.; Das, B. C. *J. Org. Chem*. **1993**, *58*, 2052.
(30) Alvarez, M.; Salas, M.; Rigat, L.; De Veciana, A.; Joule, J. A. *J. Chem. Soc. Perkin Trans. 1* **1992**, 351.