Heterocycles in Organic Synthesis. Part 36.[1] An Alternative to the Gattermann Reaction for the Conversion of Anilines into Thiocyanates [2]

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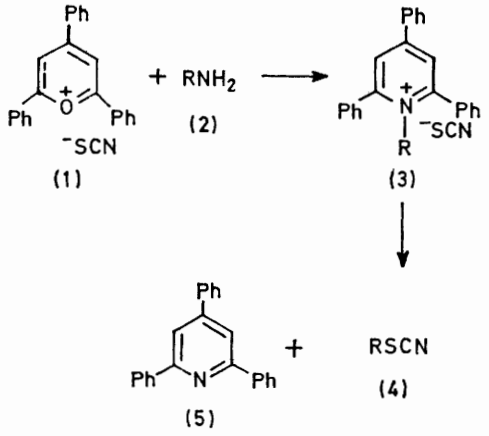
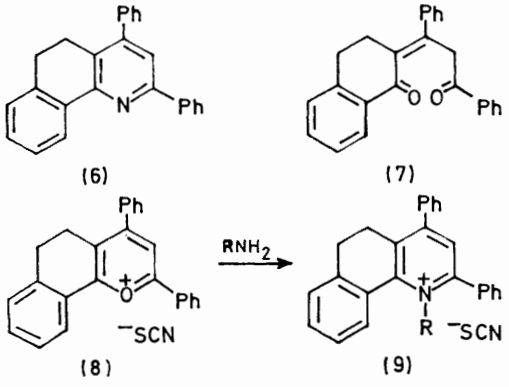
5,6-Dihydro-2,4-diphenylnaphtho[1,2-*b*]pyrylium thiocyanate is prepared in high yield. It reacts with primary arylamines to yield the corresponding fused pyridinium thiocyanates which when pyrolysed with a KNCS–NaCNS eutectic at *ca.* 220 °C give the aryl thiocyanates in yields averaging 80%.

In previous work we have prepared alkyl thiocyanates (4) from primary alkylamines (2) *via* the corresponding *N*-substituted-2,4,6-triphenylpyridinium thiocyanates (3).[3] However, although the pyrylium thiocyanate (1)



reacts readily with aromatic amines, the intermediates (3; R = aryl) are not sufficiently reactive and on pyrolysis only poor yields of the aromatic thiocyanates are formed.

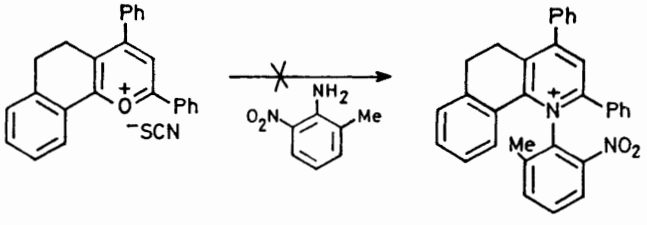


a; R = n-Butyl
b; R = Phenyl
c; R = *m*-Chlorophenyl
d; R = *p*-Chlorophenyl
e; R = *m*-Chloro-*p*-methylphenyl
f; R = *m*-Methylphenyl
g; R = *p*-Methylphenyl
h; R = *p*-Methoxyphenyl
i; R = 2-Pyridyl
j; R = 4-Pyridyl
k; R = Pyrimidin-2-yl
l; R = *m*-Nitrophenyl
m; R = *p*-Methylbenzyl
n; R = 2-Phenylethyl

The ease of thermal decomposition of an *N*-substituted pyridinium cation depends strongly on the steric requirements of the groups in the 2- and 6-positions of the pyridinium ring.[4] In particular 5,6-dihydro-2,4-diphenylnaphtho[1,2-*b*]pyridine (6) seems promising as a leaving group. Accordingly, 5,6-dihydro-2,4-diphenylnaphtho[1,2-*b*]pyrylium thiocyanate (8) was prepared from the corresponding pseudo-base (7) by the method used to get 2,4,6-triphenylpyrylium thiocyanate from 1,3,5-triphenylpent-2-ene-1,5-dione.[5]

RESULTS AND DISCUSSION

The tricyclic pyrylium thiocyanate (8) reacted readily with primary aliphatic and aromatic amines to yield the corresponding pyridinium thiocyanates (9) (Table 1). The more basic alkyl amines were more reactive towards the pyrylium thiocyanate and the pyridinium salts could be prepared at 20 °C, whereas the aryl derivatives required refluxing in absolute ethanol. Within the aromatic series the reaction time was dependent on the basicity of the amine: a *p*-methoxy-group facilitated the reaction, a *p*-nitro-group made it much more difficult, requiring the use of dimethylformamide as the solvent. Steric factors also play a dominant role in this reaction: 2-methyl-6-nitroaniline failed to react under a variety of reaction conditions.



The *para*-substituted arylpyridinium thiocyanates (*p*-Cl, *p*-Me) have higher melting points than the corresponding *meta*-derivatives, and all have much higher melting points than the alkyl derivatives. The *N*-arylpyridinium thiocyanates are much more stable than the alkyl derivative and can be refluxed in absolute ethanol without change.

The ^{1}H n.m.r. spectra of the tricyclic pyridinium thiocyanates are given in Table 2. Proton H_B is highly shielded in the 1-aryl derivatives, but not for the *N*-butyl compound, as expected. The pyridinium ring-proton H_A is deshielded due to the ring currents of the 2- and 4-phenyl groups but is relatively unaffected by the nature of the *N*-substituent. The CH_2CH_2 signal remains relatively constant for the aryl *N*-substituents [with the exception of compound (9a)]; an *N*-alkyl group shifts it upfield. In the pyridinium compound (9k),

TABLE 1

1-Substituted-5,6-dihydro-2,4-diphenylnaphtho[1,2-*b*]pyridinium thiocyanates

Compound	1-Substituent	M.p. (°C)	Yield (%)	Found (%) N	Found (%) S	Formula	Required (%) N	Required (%) S	Solvent	Crystal form
(9a)	n-Butyl	132—133	76	6.4	7.2	$C_{30}H_{28}N_2S$	6.2	7.1	MeCN	prisms
(9b)	Ph	283	98	6.0	6.8	$C_{32}H_{24}N_2S$	6.0	6.8	EtOH	prisms
(9c)	*m*-ClC_6H_4	181	94	5.5	6.5	$C_{32}H_{23}ClN_2S$	5.6	6.4	EtOH	needles
(9d)	*p*-ClC_6H_4	281—282	88	5.8	6.5	$C_{32}H_{23}ClN_2S$	5.6	6.4	EtOH	prisms
(9e)	*m*-Cl-*p*-MeC_6H_3	177—178	80	5.3	6.0	$C_{33}H_{25}ClN_2S$	5.4	6.2	EtOH	prisms
(9f)	*m*-MeC_6H_4 *	140—142	72	5.7	6.4	$C_{33}H_{26}N_2S$	5.8	6.6	EtOH	prisms
(9g)	*p*-MeC_6H_4	243	84	5.9	7.0	$C_{33}H_{26}N_2S$	5.8	6.6	EtOH	prisms
(9h)	*p*-$OMeC_6H_4$	192—193	96	5.7	6.7	$C_{33}H_{26}N_2OS$	5.6	6.4	EtOH	prisms
(9i)	2-Pyridyl	224—225	82	9.0	6.8	$C_{31}H_{23}N_3S$	9.0	6.8	EtOH	prisms
(9j)	4-Pyridyl *	185—189	90	9.0	6.8	$C_{31}H_{23}N_3S$	9.0	6.8	EtOH	prisms
(9k)	Pyrimidin-2-yl	291	85	12.2	6.8	$C_{30}H_{22}N_4S$	11.9	6.8	EtOH	prisms
(9l)	*m*-Nitrophenyl	193—195	60	8.1	6.3	$C_{32}H_{23}N_3O_2S$	8.2	6.3	EtOH	needles

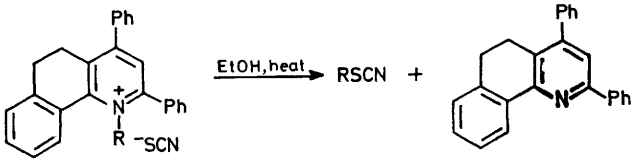
* Crystallisation solvent present as indicated by i.r. spectra.

proton H_B is also shifted to lower frequency, and a 2 H doublet appears at δ 8.45 for the 4,6-protons of the pyrimidine ring. Similarly the 3-proton in the 2-pyridyl derivative (9i) appears at δ 8.9.

The i.r. spectra of these pyridinium thiocyanates reflect their ionic structure. The spectra resemble those of other pyridinium salts with the same *N*-substituent but with a different anion (BF_4^-, $CF_3SO_3^-$), and in addition display the characteristic thiocyanate anion band near 2 060 cm^{-1} in bromoform, or near 2 040 cm^{-1} in Nujol.

As expected, the tricyclic pyridinium thiocyanates were more reactive than the corresponding 2,4,6-triphenylpyridinium thiocyanates. Although the n-butyl derivative (9a) was sufficiently stable to be crystallised from a low-boiling solvent, the *p*-methylbenzyl (9m) and phenethyl derivatives (9n) could only be isolated at low temperatures; recrystallisation from ethanol led to their decomposition to the alkyl thiocyanates and 5,6-dihydro-2,4-diphenylnaphtho[1,2-*b*]-pyridine (80%). G.l.c. analysis of the ethanolic solution indicated the substituted pyridine and the thiocyanate as the major products; a third small peak was assigned to the isomeric isothiocyanates.

The arylpyridinium thiocyanates were more stable. On heating alone above their melting points only polymeric material was formed. Previously, 2,4,6-triphenylpyridine was used as a flux to reduce the pyrolysis temperature for the synthesis of alkyl thiocyanates.[3] Use of this compound as a flux in the present synthesis required high reaction temperatures and led to contamination of the product by 2,4,6-triphenylpyridine. However, on heating with an eutectic mixture,[6] m.p. 123 °C,



(9m) or (9n) (6)

of sodium and potassium thiocyanate (1 : 3 w/w) the arylpyridinium thiocyanates smoothly converted into the pyridine and the aryl thiocyanate at *ca.* 220 °C (see Table 3). This provides a conversion of primary amines into the aromatic thiocyanates *via* pyridinium salts.

This method failed for heterocyclic thiocyanates: the corresponding 1-heteroarylpyridinium thiocyanates on pyrolysis gave complex oily mixtures, probably due to the decomposition of initially formed heteroaryl thiocyanates. A similar failure occurred for the *p*-methoxyphenyl derivative.

TABLE 2

N.m.r. data (δ/p.p.m.) for 1-substituted-5,6-dihydro-2,4-diphenylnaphtho[1,2-*b*]pyridinium thiocyanates (9)

Compound	1-Substituent	H_A [a]	Aromatic protons [b]	H_B [c]	CH_2CH_2	Alkyl substituents
(9a)	n-Butyl	7.9	7.8—7.0 (14 H, m)	*d*	2.8—2.4 (4 H, bs)	4.9—4.5 (2 H, t, first-CH_2), 1.1 (7H, m)
(9b)	Ph	8	7.7—6.6 (18 H, m)	4.2	3.3—2.9 (4 H)	
(9c)	*m*-ClC_6H_4	8	7.8—6.6 (17 H, m)	5.8	3.3—2.8 (4 H)	
(9d)	*p*-ClC_6H_4	8	7.7—6.5 (17 H, m)	5.7	3.4—2.8 (4 H)	
(9e)	*m*-Cl-*p*-MeC_6H_3	8	7.9—6.6 (17 H, m)	5.8	3.4—2.8 (4 H)	3.46 (3 H, s, Me)
(9f)	*m*-MeC_6H_4	8.0	7.8—6.6 (17 H, m)	5.8	3.3—2.8 (4 H)	2.25 (3 H, s, Me)
(9g)	*p*-MeC_6H_4	8.0	7.9—6.6 (17 H, m)	5.8	3.4—2.8 (4 H)	2.4 (3 H, s, Me)
(9h)	*p*-$OMeC_6H_4$	8.05	7.9—6.7 (17 H, m)	5.87	3.4—2.8 (4 H)	3.92 (3 H, s, OMe)
(9i)	2-Pyridyl	8.1	9.1—8.9 (1 H, d) [e] 8.0—6.6 (16 H, m)	5.85	3.5—3.0 (4 H)	
(9j)	4-Pyridyl	*d*	8.0—6.5 (19 H, m)	5.4	3.3—2.8 (4 H)	
(9k)	Pyrimidin-2-yl	8.36	8.45—8.25 (2 H, d) [f] 7.4—6.1 (14 H, m)	5.4	3.0—2.5 (4 H)	
(9l)	*m*-$NO_2C_6H_4$	8.1	8.5—8.15 (3 H, m) 7.9—6.6 (14 H, m)	5.8	3.4—2.8 (4 H)	

[a] All 1 H singlet signals. [b] All multiplets. [c] All 1 H multiplets. [d] Obscured by the aromatic region. [e] *J* 13.2 Hz. [f] *J* 12—13 Hz.

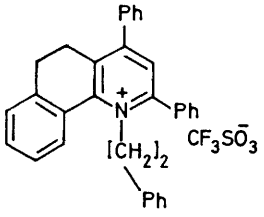
TABLE 3

Pyrolysis of 1-substituted-5,6-dihydro-2,4-diphenylnaphtho[1,2-*b*]pyridinium thiocyanates (9)

Materials			Conditions		Products			
Compound	Wt./g	Wt. of eutectic/g	Temperature (°C)	Time/h	Yield (%)	B.p. (°C)	Pressure (mmHg)	Lit. b.p/°C (mmHg)*
(9b)	3	6	200	0.75	67	71	2	103 (11)
(9c)	2.8	6	220	1.5	79	81	1.5	96 (3.6)
(9d)	2.8	6	200	1	75	98	3.5	80 (0.3)
(9e)	3.2	6	230	2	90	107	2	
(9f)	3	6	200	1	60	86	4	73 (2)
(9g)	3.5	6	260	2	43	78	2	73 (1.5)
(9l)	3.0	6	260	0.75	40	90—95	0.2	170—173 (11—13)
(10)	2.5	5.3	160	0.25	95			

* Ref. 9.

The method shows promise also for certain preparations of alkyl thiocyanates. The alkylpyridinium salts react very readily. Our previous method gave phenethyl thiocyanate contaminated with *ca.* 30% of the isothiocyanate.[3] As the 1-phenethyl tricyclic pyridinium thiocyanate could not be prepared pure (see above) we pyrolysed 5,6-dihydro-2,4-diphenyl-1-phenethylnaphtho[1,2-*b*]pyridinium trifluoromethanesulphonate (10)[7] with the eutectic mixture of potassium and sodium thiocyanates. Fifteen minutes at 160 °C gave β-phenethyl thiocyanate in 95% yield, uncontaminated by the isothiocyanate.



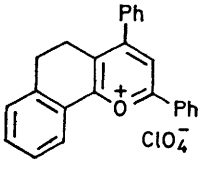
(10)

The thiocyanate group can directly replace a hydrogen atom in an aromatic ring: thus, thiocyanogen $(SCN)_2$ reacts with phenols, primary, secondary, and tertiary amines with free *ortho*- and/or *para*-positions.[8] Thiocyanogen chloride (ClSCN) is more active and can be used with aryl ethers and acylated aromatic amines.[9] Thiophenols react with ClCN to give thiocyanates in good yields.[10] The more widely applicable Gattermann reaction treats diazonium salts with aqueous thiocyanate and CuSCN to give the aryl thiocyanates. Aryl isothiocyanates may be formed as a by-product.[11] The advantage of our method is that the intermediate alkyl- and aryl-pyridinium salts are stable compounds, easily prepared and isolated. The products simply distil over from the eutectic mixture and can be easily isolated.

EXPERIMENTAL

M.p.s are uncorrected. ^1H N.m.r. spectra were recorded with a Perkin-Elmer R-12 spectrometer at 60 MHz using internal $SiMe_4$ as reference. I.r. spectra were obtained on a Perkin-Elmer 257 spectrophotometer. The ^1H n.m.r. spectra of pyrylium and pyridinium compounds were all run using CF_3CO_2H as the solvent.

Pseudo-base (7).—The pyrylium salt (11) [4a] (20 g, 0.047 mol) was suspended in boiling absolute EtOH (150 ml). NaOH (2 g, 0.047 mol) in water (10 ml) was added dropwise until a permanent colour change was observed. On cooling the 2-(1,3-diphenyl-3-oxopropylidene)-1-tetralone (7) separated out (16.4 g, 100%); it crystallised from absolute EtOH as plates, m.p. 138—139 °C (Found: C, 85.4; H, 5.8. $C_{25}H_{20}O_2$ requires C, 85.2; H, 5.7%); δ[$(CD_3)_2SO$] 8.2—7.8 (4 H, m), 7.8—7.2 (8 H, m), 3.45 (2 H, s), 3.1—2.7 (2 H, m), and 2.7—2.4 (2 H, m); $\nu_{max.}$ (Nujol) 1 675, 1 650, 1 325, 1 318, 1 292, 1 245, 1 220, 1 179, 1 153, 1 020, 1 000, 965, 932, 909, 805, 765, 745, 738, 718, 705, and 685 cm^{-1}.



(11)

5,6-*Dihydro*-2,4-*diphenylnaphtho*[1,2-b]*pyrylium Thiocyanate* (8).—Pseudo-base (7) (15 g, 0.04 mol) was stirred in boiling EtOH (100 ml) in a flask. H_2SO_4 (1N) (40 ml) was added to form a yellow product. Ammonium thiocyanate (5 g, 0.07 mol) in water (15 ml) was added. After cooling, the brick-red precipitate was filtered off and recrystallised from isopropyl alcohol (16.4 g, 98%) to give the thiocyanate as needles, m.p. 233—234 °C (Found: C, 79.2; H, 4.8; N, 3.6; S, 8.1. $C_{27}H_{19}NOS$ requires C, 79.4; H, 4.9; N, 3.6; S, 8.2%); δ(CF_3CO_2H) 8.6—8.2 (4 H, m), 8.0—7.4 (1 H, m), and 3.5—3.1 (4 H, m); $\nu_{max.}$ ($CHBr_3$) 2 070, 1 619, 1 600, 1 575, 1 495, 1 478, 1 449, 1 430, 1 425, 1 390, 1 300, 1 245, 1 213, 875, 822, 793, 778, 776, 750, 730, 700, and 675 cm^{-1}.

1-*n*-*Butyl*-5,6-*dihydro*-2,4-*diphenylnaphtho*[1,2-b]*pyridinium Thiocyanate* (9a).—The pyrylium salt (8) (2.4 g, 0.006 mol) was stirred with n-butylamine (0.43 g, 0.006 mol) in absolute EtOH (10 ml) at 20 °C for 12 h. The reaction mixture was diluted with Et_2O and left at 0 °C overnight. The separated *pyridinium salt* crystallised from MeCN as prisms (2.17 g, 76%), m.p. 132—133 °C; $\nu_{max.}$ ($CHBr_3$) 2 060, 1 610s, 1 600ms, 1 572w, 1 540, 1 500, 1 469, 1 420, 1 395, 1 203, 890, 790, 753, and 700 cm^{-1}.

General Procedure for Preparation of 1-*Aryl*-5,6-*dihydro*-2,4-*diphenylnaphtho*[1,2-b]*pyrylium Thiocyanates*.—5,6-Dihydro-2,4-diphenylnaphtho[1,2-*b*]pyrylium thiocyanate (4.0 g, 0.01 mol) was refluxed for 2—4 h in absolute EtOH (20

ml) with an equivalent amount of arylamine. After cooling to 20 °C and diluting with Et_2O (60 ml) the products obtained were filtered off and recrystallised from absolute EtOH (see Table 1).

Pyrolysis of 5,6-*Dihydro*-2,4-*diphenyl*-1-*phenethylnaphtho*-[1,2-b]*pyridinium Trifluoromethanesulphonate* (10) *with Sodium and Potassium Thiocyanate.*—Dry 5,6-dihydro-2,4-diphenyl-1-phenethylnaphtho[1,2-*b*]pyridinium trifluoromethanesulphonate (10) (2.5 g, 0.041 mol), mixed with anhydrous potassium thiocyanate (4 g), and sodium thiocyanate (1.3 g), was pyrolysed at 160 °C at 2 mmHg for 15 min to give β-phenethyl thiocyanate [3a] as a pale yellow liquid (liquid N_2 trap) (0.63 g, 95%); δ($CDCl_3$) 7.6—7.0 (5 H, s), and 3.15 (4 H, br s); $\nu_{max.}$ (film) 2 145, 2 043, 1 606, 1 545, 1 498, 1 457, 1 420, 1 275, 1 232, 1 075, 1 030, 915, 750, and 700 cm^{-1}.

General Procedure for Pyrolysis of 1-*Aryl*-5,6-*dihydro*-2,4-*diphenylnaphtho*[1,2-b]*pyridinium Thiocyanates.*—Compounds (9b—g) were dried over P_2O_5 at 10 mmHg for 24 h prior to pyrolysis. The given quantities were then mixed with the stated amount of eutectic and then pyrolysed at the melting point of the mixture, under vacuum (2 mmHg) for 1—2 h. The products were collected in a liquid N_2 trap. These were characterised by comparison of i.r. and ^1H n.m.r. spectral data.

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