HETEROCYCLES, Vol 16, No 7, 1981

STANNYLATION-IODINATION REACTION ON PYRIDINE NUCLEI. A FACILE METHOD FOR SYNTHESIS OF IODOPYRIDINES AND IODOQUINOLINES.

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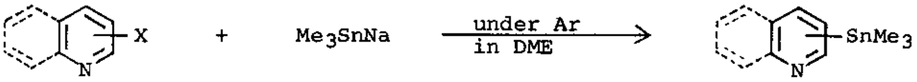
Abstract — Pyridines and quinolines bearing trimethylstannyl substituent at 2-, 3-, or 4-position were synthesized by the reaction of the respective chloro or bromo derivatives with trimethylstannyl sodium, generated *in situ* from chlorotrimethylstannane and sodium, in the range of 61-88% yields. Upon treatment with iodine, these trimethylstannyl derivatives smoothly underwent iododemetallation to give the corresponding iodo derivatives of pyridine and quinoline in satisfactory yields.

It is well known that organostannyl groups as well as organosilyl groups have widely been useful as synthetic tools. In the area of N-heteroaromatics, however, little attention has been devoted to application of such organometallic groups. Our interest was in the preparation of trimethylstannyl derivatives of pyridine and quinoline, and in the investigation of the behavior of the stannyl group. This communication is the subject of trimethylstannylation-iodination reaction in the pyridine and quinoline ring systems.

SYNTHESIS OF TRIMETHYLSTANNYL-PYRIDINES AND -QUINOLINES:

So far there has been only an example of synthesis of organostannyl substituted N-heteroaromatic in the literature: 2-trimethylstannylpyridine (**3d**) was prepared in 12% yield from 2-chloropyridine and chlorotrimethylstannane in the presence of magnesium.[1] In our study the reaction of chloro or bromo derivatives (**1**) of pyridine and quinoline with trimethylstannyl sodium was used to prepare the respective trimethylstannyl derivatives (**3**). Preparation of 2-trimethylstannylquinoline (**3a**) is representatively described. A solution of 2-chloroquinoline (**1a**, 38.0 g, 232 mmol) in 1,2-dimethoxyethane (DME, 100 ml) was added dropwise with stirring in ice-salt bath to a solution of trimethylstannyl sodium (**2**) in DME (250 ml), which was prepared from chlorotrimethylstannane (53.4 g, 268 mmol) and metallic sodium (18.5 g, 0.8 g atom) according to Kuivila's method.[2]

After being stirred at an ambient temperature for 3 hr, the solvent was evaporated at reduced pressure, and the residue was extracted with ether. Distillation of the extracts afforded 2-trimethylstannylquinoline (3a, 54.3 g) as colorless liquid in 80% yield. Evidence for the structural assignment of 3a was obtained from the spectral and analytical data, which are summarized in Table 1. Similarly, 3- and 4-trimethylstannylquinolines (3b,c), 2- and 3-trimethylstannylpyridines (3d,e), and 2-methyl-4-trimethylstannylpyridine (3f) were prepared. The experimental and spectral data are summarized in Table 1.



1a-f 2 3a-f

1a : 2-Cl-Q.
b : 3-Br-Q.
c : 4-Br-Q.
d : 2-Cl-Py.
e : 3-Br-Py.
f : 4-Cl-2-Me-Py.

3a : 2-TMSn-Q.
b : 3-TMSn-Q.
c : 4-TMSn-Q.
d : 2-TMSn-Py.
e : 3-TMSn-Py.
f : 2-Me-4-TMSn-Py.

Py. = pyridine ; Q. = quinoline ; TMSn = trimethylstannyl

Scheme 1

Table 1. Experimental and Spectral Data of Trimethylstannyl Derivatives 3.

Product No.	Yield (%)	Bp(°C)/torr (mp °C)	IR (neat) cm^{-1}	NMR (CCl_4) ppm	Mass *m/e*	Elemental Analysis Calcd. (Found) C	H	N
3a	80	124-126/1.0	1580 (C=N) 770, 750 ($SnMe_3$)	0.37(9H,s) 7.1-8.2(6H,m)	292(M^+)	49.37 (49.13)	5.18 (5.20)	4.80 (4.74)
3b	81	124-126/1.0 (42-44)	1565 (C=N) 790-750 ($SnMe_3$)	0.35(9H,s) 7.2-8.1(5H,m) 8.82(1H,d;J=2 Hz)	293(M^++1) 292(M^+)	49.37 (49.36)	5.18 (5.11)	4.80 (4.80)
3c	74	128-130/1.0	1560 (C=N) 760($SnMe_3$)	0.43(9H,s) 7.2-8.1(5H,m) 8.68(1H,d;J=4 Hz)	293(M^++1) 292(M^+)	49.37 (49.32)	5.18 (5.14)	4.80 (4.64)
3d	88	81-83/10.0*	1570 (C=N) 770 ($SnMe_3$)	0.30(9H,s) 6.8-7.6(3H,m) 8.5-8.6(1H,m)	243(M^++1) 242(M^+)	39.72 (39.51)	5.42 (5.32)	5.79 (5.57)
3e	87	116-118/16.0	1560 (C=N) 770 ($SnMe_3$)	0.33(9H,s) 6.8-7.2(1H,m) 7.5-7.7(1H,m) 8.2-8.5(2H,m)	243(M^++1) 242(M^+)	39.72 (39.44)	5.42 (5.38)	5.79 (5.75)
3f	61	104-106/10.0	1575 (C=N) 770 ($SnMe_3$)	0.30(9H,s) 2.43(3H,s) 6.9-7.2(2H,m) 8.26(1H,d;J=4 Hz)	257(M^++1) 256(M^+)	42.24 (42.39)	5.91 (5.85)	5.77 (5.49)

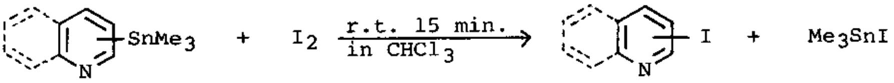
* lit. bp 75°/4.0.[1)]

SYNTHESIS OF IODO-PYRIDINES AND -QUINOLINES:

The cleavage reaction of Sn–C bond with halogen, i.e. halodemetallation of organotin compounds, has been well investigated theoretically and practically.[3)] Application of iododemetallation for the stannyl-pyridines and -quinolines would provide an efficient route to synthesis of iodo derivatives of pyridine and quinoline. With this view, the reaction of 3 with iodine was carried out. For example, to a stirred solution of 3a (2.92 g, 10 mmol) in chloroform (15 ml) was added a suspension of iodine (2.54 g, 10 mmol) in chloroform (50 ml) at room temperature. The reaction mixture allowed to stand for 15 min, and then washed twice with saturated potassium fluoride solution to remove iodotrimethylstannane produced. The organic layer was dried and concentrated. Distillation of the resulting liquid afforded 2-iodoquinoline (4a) in quantitative yield. The product 4a was identical with a sample prepared by treatment of 2-chloroquinoline (2a) with sodium iodide and hydrogen iodide according to the literature procedure.[4)]

In a similar manner, iodo-pyridines (4d-f) and -quinolines (4b,c) were prepared in satisfactory yields. The results are summarized in Table 2.

Extension of this stannylation-iodination reaction is under way.



3a-f

4a-f

3a : 2-TMSn-Q.
b : 3-TMSn-Q.
c : 4-TMSn-Q.
d : 2-TMSn-Py.
e : 3-TMSn-Py.
f : 2-Me-4-TMSn-Py.

4a : 2-I-Q.
b : 3-I-Q.
c : 4-I-Q.
d : 2-I-Py.
e : 3-I-Py.
f : 4-I-2-Me-Py.

Scheme 2

Table 2. Preparation of Iodo-pyridines and -quinolines.

Product	Bp(°C)/torr (lit. bp)	Mp (°C) (lit. mp)	Yield (%)
4a	98-100/0.35	53-55 (54-55)4)	97
4b	105-107/0.25	60-62 (61-62)6)	96
4c	108-111/0.27	98-100 (97-99)7)	91
4d	100-102/25.0 (93/13)5)		75
4e	90-92/14.0	48-50 (50)8)	78
4f	102-103/25.0	42-44 (42)9)	79.5

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Received, 31st March, 1981