Preparation of Nitrogen-Containing Bis(heteroaryl)iodonium Salts

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Dedicated to Professor Manfred Regitz on the occasion of his 60th birthday

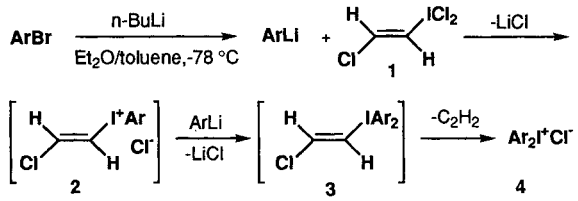
Hitherto unknown nitrogen-containing bis(heteroaryl)iodonium chlorides are prepared by the reaction of the appropriate aryllithium with β-chlorovinyliodonium dichloride. The bis(heteroaryl)iodonium chlorides may be readily converted to the corresponding triflate salts via reaction with trimethylsilyl triflate.

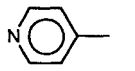
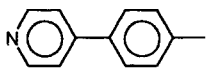
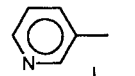
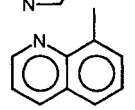
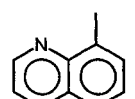
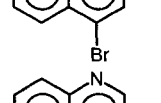
Polyvalent organoiodine compounds have been known for over one hundred years. The most prevalent class of these compounds are the diaryliodonium salts. Despite the widespread use of diaryliodonium salts, for example, in lithography and as cationic polymer initiators, as well as arylation reagents, little is known about nitrogen-containing heteroaryliodonium species.[1] Moreover, a number of iodonium salts and in particular various heterocyclic diaryliodonium compounds have potent biocidal and antimicrobial properties.[1,2] Hence, in this paper we wish to report the preparation of a variety of nitrogen-containing bis(heteroaryl)iodonium chlorides.

Interestingly, more modern, current[3,4] methods of preparing iodonium salts employing PhICNOTf or PhIOIPh · 2OTf as reagents did not work[5] for the preparation of the desired nitrogen-containing aryliodonium salts, although they work well for sulfur and other heteroaryl systems.[6] This fact likely also accounts for the lack of examples of these species. In contrast, the more classical method of using aryllithium and *trans*-chlorovinyliodonium dichloride (**1**),[7] as outlined in the Scheme, works well, albeit in only low to moderate overall yields.

Halogen–metal exchange of the appropriate bromopyridine or bromoquinoline with butyllithium in diethyl ether at low temperatures gives the needed aryllithium, which when reacted with 0.5 equivalent of **1** and after the loss of lithium chloride and acetylene, followed by appropriate workup, results in the desired bis(heteroaryl)iodonium chlorides **4**. Interestingly, when 5,8-dibromoquinoline is employed, halogen–metal exchange proceeds exclusively in the eight position of the quinoline ring, presumably because of the close proximity of this halogen to the nitrogen, where initial coordination of the lithium species can occur. Most of the bis(aryliodonium) chlorides **4** are stable, microcrystalline solids with high decomposition points. They can be readily characterized by a number of physical and spectral means, specifically ^1H and ^{13}C NMR, as summarized in the experimental.

The bis(aryliodonium) chlorides **4** may be readily converted to the corresponding triflate ($CF_3SO_3^-$) salts via reaction with trimethylsilyl triflate (TMSOTf). However, in some cases the triflate salts are less stable, presumably due to the formation of oligomers and polymers, than the original chlorides **4**. The triflate salts may be employed in the modular self-assembly[8] of hybrid, iodonium-transition metal cationic tetranuclear macrocyclic squares, whereas the chlorides are being evaluated for biological activity.



4	Ar	Yield(%)
a		27
b		32
c		71
d		29
e		36
f		23

Scheme

All reactions were conducted under a dry N_2 atmosphere using Schlenk techniques. IR spectra were recorded on a Mattson Polaris FT-IR spectrophotometer. NMR spectra were recorded on a Varian XL-300 or Unity-300 spectrometer. ^1H NMR spectra were recorded at 300 MHz, and all chemical shifts (δ) are reported in ppm relative to TMS as an internal standard or the proton resonance resulting from incomplete deuteration of the NMR solvent: CD_3OD (3.31 ppm) or $(CD_3)_2CO$ (2.05 ppm). ^{13}C NMR spectra were recorded at 75 MHz, and all chemical shifts (δ) are reported in ppm relative to the carbon-resonance of the deuterated methanol (49.0 ppm). Microanalyses were performed by Atlantic Microlab Inc., Norcross, Georgia. Melting points were obtained with a Mel-Temp capillary melting point apparatus and are uncorrected.

Solvents were purified as follows: toluene was purified by literature procedure[9] and was distilled over CaH_2; Et_2O and THF were purified by literature procedures[9] and were distilled over Na/benzophenone. All solvents were freeze-thaw-pump degassed three times before use. All commercial reagents were ACS reagent grade and were obtained as follows: 3-bromoquinoline (Aldrich), 4-bromopyridine hydrochloride (Aldrich), ICl_3 (Aldrich or Fluka), quinoline

Table. Bis(heteroaryl)iodonium Compounds **4a–f** Prepared

Compound[a]	mp(°C) (dec.)	IR (Neat) ν (cm^{-1})	^1H NMR (solvent/TMS) δ, J(Hz)	^{13}C NMR (Methanol-d_4/TMS) δ
4a[b]	82–84	1639, 1546, 1406, 1211, 829	(acetone-d_6) 8.17 (d, J = 6.0, 4H, H_β-Py), 8.64 (d, J = 6.0, 4H, H_α-Py)	–
4b	187–189	1603, 1472, 1401, 1120, 994, 807	(methanol-d_4) 7.72 (d, J = 6.3, 4H, H_β-Py), 7.91 (d, J = 8.8, 4H, H_β-PhI), 8.37 (d, J = 8.8, 4H, H_α-PhI), 8.63 (d, J = 6.3, 4H, H_α-Py)	117.8 (s, C_i-I), 123.5 (s, C_β-Py), 131.8 (s, C_β-PhI), 137.4 (s, C_α-PhI), 143.2 (s, C_γ-PhI), 148.4 (s, C_γ-Py), 151.0 (s, C_α-Py)
4c	183–185	1630, 1573, 1467, 1417, 1010, 810	(methanol-d_4), 7.57 (dd, J = 8.0, 4.4, 2H, H_5), 8.68 (dd, J = 8.0, 2.0, 2H, H_4), 8.83 (dd, J = 4.4, 2.0, 2H, H_6), 9.26 (d, J = 2.0, 2H, H_2)	116.8 (s, C_i-I), 128.4 (s, C_5), 144.1 (s, C_4), 153.8 (s, C_6), 154.8 (s, C_2)
4d	168–171[c]	1593, 1487, 1451, 1370, 1307, 946	(acetone-d_6) 7.72 (t, J = 7.4, 2H, H_6), 7.82 (dd, J = 8.3, 4.2, 2H, H_3), 8.21 (dd, J = 7.4, 1.0, 2H, H_5), 8.38 (dd, J = 7.4, 1.0, 2H, H_7), 8.61 (dd, J = 8.3, 1.5, 2H, H_4), 9.07 (dd, J = 4.2, 1.5, 2H, H_2)	118.8 (s, C_8), 125.3 (s, C_6), 130.2 (s, C_5), 131.2 (s, C_{10}), 134.4 (s, C_3), 138.1 (s, C_7), 138.9 (s, C_4), 145.5 (s, C_9), 154.1 (s, C_2)
4e	172–175[c]	1594, 1541, 1470, 1376, 958	(methanol-d_4) 7.89 (dd, J = 8.3, 4.2, 2H, H_3), 8.03 (d, J = 7.8, 2H, H_6), 8.14 (d, J = 7.8, 2H, H_7), 8.77 (dd, J = 8.3, 1.3, 2H, H_4), 9.09 (dd, J = 4.2, 1.3, 2H, H_2)	118.7 (s, C_8), 126.5 (s, C_6), 129.0 (s, C_5), 130.4 (s, C_{10}), 133.8 (s, C_3), 138.1 (s, C_7), 138.3 (s, C_4), 145.8 (s, C_9), 154.9 (s, C_2)
4f	184–187	1317, 1250, 1161, 1028, 749	(methanol-d_4) 7.79 (t, J = 5.5, 2H, H_6), 7.96 (t, J = 6.9, 2H, H_7), 8.06 (d, J = 8.0, 2H, H_5), 8.13 (d, J = 8.1, 2H, H_8), 9.43 (d, J = 2.0, 2H, H_4), 9.49 (d, J = 2.0, 2H, H_2)	111.4 (s, C_3), 129.9 (s, C_6), 130.1 (s, C_7), 130.2 (s, C_5), 130.7 (s, C_{10}), 134.4 (s, C_8), 145.9 (s, C_4), 149.3 (s, C_9), 152.8 (s, C_2)

[a] Satisfactory elemental analyses were obtained: C ± 0.40, H ± 0.25, N ± 0.12, total halogen content ± 0.2 (except for compound **4a**).
[b] **4a** has both too low solubility and stability to be unambiguously characterized by ^{13}C NMR.
[c] The compound gradually decomposed at a temperature above 161 °C, when placed in a melting point apparatus.

(Aldrich), 3-bromopyridine (Aldrich), BuLi (Aldrich) and were used as received. *trans*-Chlorovinyliodonium dichloride[7] and 4,4′-bromophenylpyridine[8] were prepared by a modified literature procedure, 8-bromoquinoline[10] and 5,8-dibromoquinoline[11] were prepared from quinoline by modified literature procedures. 4-Bromopyridine was obtained from its hydrochloride via deprotonation with triethylamine.

Bis(heteroaryl)iodonium Salts 4a–f; General Procedure:
A 100 mL Schlenk flask was charged with toluene (25 mL), Et_2O (25 mL) and the desired bromoheterocycle (9.6 mmol). The mixture was cooled to − 78 °C using a dry ice-acetone bath. A 2.5 M solution of BuLi in hexanes (4.2 mL, 10.5 mmol) was added with a syringe and the mixture was stirred at − 78 °C for 15 min. *trans*-Chlorovinyliodonium dichloride (**1**; 1.29 g, 4.97 mmol) was then added all at once and the mixture was stirred at − 78 °C for an additional 1–1.5 h, then the temperature was allowed to warm gradually to r.t. during 3 h. After stirring at r.t. for an additional 1 h, the heterogeneous mixture was filtered using an aspirator pump under a N_2 stream. For the preparation of **4a** and **4b**, the mixture after addition of BuLi was warmed up to − 50 and − 30 °C, respectively, and maintained at these temperatures for 5 min, before cooling back to − 78 °C and addition of *trans*-chlorovinyliodonium dichloride. The crude mixtures of bis(heteroaryl)iodonium chlorides were suspended in THF (25 mL) and stirred for 30 min to remove the LiCl. After filtration under N_2, the products were dried in vacuo for 6–18 h. The compounds were recrystallized from MeCN (**4c, 4e**), Et_2O/MeOH (**4b**), or by the slow diffusion of an $Et_2O/CHCl_3$ mixture (1:1) into a solution of the product in MeOH (**4d, 4f**). Product **4a** is too unstable to be recrystallized. The physical and spectroscopic data of bis(heteroaryl)iodonium chlorides are reported in the Table.

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