Preparation of bis(Heteroaryl)iodonium Salts *via* an Iodonium Transfer Reaction Between Di(cyano)iodonium Triflate and Organostannes

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Di(cyano)iodonium triflate **5** generated *in situ* from iodosyl triflate (O = I-OTf) and cyanotrimethylsilane is a preferred reagent for the preparation of various bis(heteroaryl)iodonium triflate salts **11-15** *via* an iodonium transfer reaction with the corresponding tributyltin substituted heterocycles **6-10**. Novel heteroaromatic iodonium salts **3, 11-15** were isolated in good yields as relatively stable microcrystalline solids and characterized by multinuclear nmr, ir and hrms data.

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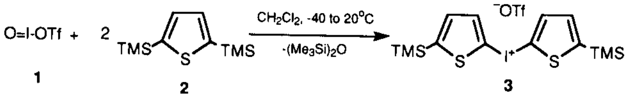
Diaryl and aryl(heteroaryl)iodonium salts are the most numerous and important class of iodine(III) compounds [1] due to their rich chemistry and practical application derived from their antimicrobial activity and photochemical properties [1d]. However, little is known about bis(heteroaryl)iodonium species [1]. The preparation of a few examples of bis-thienyl and furanyliodonium chlorides by the reaction of [(*trans*-chlorovinyl)dichloro]iodine with two equivalents of the corresponding lithium derivatives of thiophene or furan have been reported in modest yield [2]. Bis(heteroaryl)iodonium salts are useful reagents since they can serve as precursors for the preparation of a variety of substituted heterocycles *via* reaction with nucleophiles [2,3]. Hence, in this paper, we wish to report a general simple method for the preparation of a wide variety of bis(heteroaryl)iodonium salts.

Results and Discussion.

Recently we demonstrated that iodosyl triflate **1** [4] is a mild and efficient reagent for the preparation of bis(aryl)iodonium triflate salts from the trimethylsilyl substituted derivatives of aromatic compounds [5]. Consequently, it was of interest to apply this reaction to the synthesis of the hitherto unknown bis(heteroaryl)iodonium triflates. However, reactions of a variety of the trimethylsilyl substituted derivatives of heteroaromatic compounds, such as 2-trimethylsilylthiophene, 5-bromo-2-trimethylsilylthiophene, 2-trimethylsilylfuran, trimethylsilylpyrazol and others, resulted only in black tar formation. The only exception was the reaction of 2,5-bis(trimethylsilyl)thiophene **2** with reagent **1**, which afforded the desired iodonium salt **3** in a low yield (34%) along with a large amount of tar as by-products. The most reasonable explanation for the inability of this procedure to yield the desired iodonium salts is the instability of the starting heterocycles under the reaction conditions due to the strong oxidizing properties of the iodosyl triflate and the presence of trace amounts of triflic acid due to the hydrolysis of reagent **1**.



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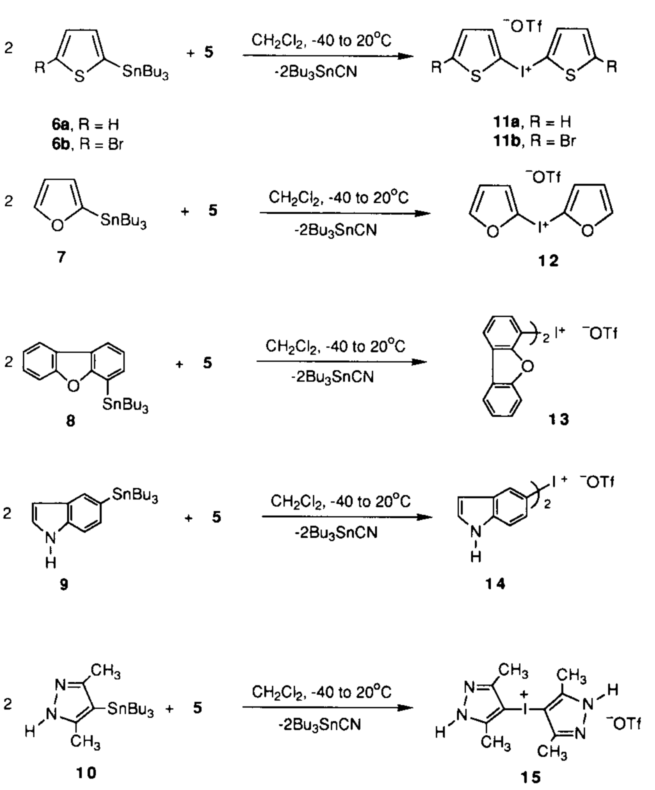
In an attempt to circumvent the undesirable properties encountered with the use of iodosyl triflate **1**, we developed a novel reagent, di(cyano)iodonium triflate **5** [6]. Analogous to other cyanated iodonium salts [7], triflate **5** can react with tributyltinacetylenes and -arenes forming iodonium triflates *via* an iodonium transfer process [6]. Reagent **5** is prepared by the reaction of iodosyl triflate **1** and cyanotrimethylsilane **4** in methylene chloride at −20° and, in crystalline form, is unstable at room temperature. It can, however, be efficiently used *in situ* at low temperature without isolation from the reaction mixture.

$$\underset{\mathbf{1}}{\mathrm{O{=}I{-}OTf}} + \underset{\mathbf{4}}{2\mathrm{NCSiMe_3}} \xrightarrow[\text{-(Me}_3\text{Si)}_2\text{O}]{\text{CH}_2\text{Cl}_2\text{, -78 to -20}^\circ\text{C}} \underset{\mathbf{5}}{(\mathrm{NC})_2\mathrm{I}^+\ {}^-\mathrm{OTf}}$$

We have studied the reactions of reagent **5** *in situ* with a variety of tin-substituted heterocycles **6-10**, which can be easily prepared by known procedures from the corresponding bromides, butyllithium and tri(butyl)tin chloride [8]. The reactions (Scheme I) proceed instantaneously at −40° upon mixing of the cold solution of reagent **5** with 2 molar equivalents of the appropriate tin-substituted heterocycle. The desired iodonium salts **11-15** are isolated from the reaction mixture by crystallization as relatively stable microcrystalline solids. Thienyl **11** and furyl **12,13** iodonium triflates are formed in good yields (48 to 78%), however, the isolated yields of the indolyl **14** and pyrazolyl **15** iodonium salts are much lower due to the instability of the products under the reaction conditions.

Bis(heteroaryl)iodonium triflates **3, 11-15** are fully characterized by multinuclear nmr, ir, high resolution mass spectra, and where stable, by microanalysis. Specifically, the expected molecular peaks $[M - TfO^-]^+$ of the monocationic part of salts **3, 11-15** are observed in the high resolution FAB mass spectra. The ir spectra show characteristic absorption for the respective heterocyclic moieties as well as for the triflate anion. The ir spectra of indolyl **14** and pyrazolyl **15** iodonium salts display characteristic N-H ab-

Scheme I



sorptions in the region 3380-3190 cm^{-1}. The ^{1}H nmr display the expected heteroaromatic resonances between δ 8.2 and 7 ppm as well as further characteristic patterns.

The ^{13}C nmr spectra are all consistent with the proposed structures, specifically, signals for the heteroaromatic carbons located at δ 150-110 ppm are in agreement with the heterocyclic structure. The presence of the triflate anion in **8-10** is confirmed by ^{19}F nmr.

It is worth emphasizing that the indolyl **14** and pyrazolyl **15** iodonium triflates represent the first examples of bis(aromatic)iodonium salts derived from nitrogen containing heterocycles. Our attempts to prepare iodonium salts from 2,3 and 4-(tributylstannyl)pyridines or tin-substituted pyrrols were unsuccessful and resulted mostly in black tar formation due to product decomposition, even at low temperature.

In conclusion, di(cyano)iodonium triflate **5** generated *in situ* from iodosyl triflate and cyanotrimethylsilane is a preferred reagent for the one-step preparation of various bis(heteroaryl)iodonium triflate salts **11-15** *via* an iodonium transfer reaction with the corresponding tributyltin substituted heterocycles **6-10**. Novel heteroaromatic iodonium triflate salts **3, 11-15** were isolated in good yield as relatively stable, microcrystalline solids and characterized by multinuclear nmr, ir and hrms data. We believe that these readily available, novel iodonium salts are highly useful compounds and will serve as precursors for a variety of transformations involving heterocycles.

EXPERIMENTAL

General Methods.

Melting points (uncorrected) were obtained with a Mel-Temp capillary melting point apparatus. Infrared spectra were recorded on a Mattson FT-ir spectrophotometer. NMR spectra were recorded on a Varian XL 300 spectrometer at 300 MHz (^{1}H nmr), 75 MHz (^{13}C nmr), 282 MHz (^{19}F nmr). Chemical shifts for ^{1}H and ^{13}C nmr are reported in parts per million (ppm) relative to internal tetramethylsilane or the proton resonance due to the residual protons in the deuteriated nmr solvent; the chemical shifts for ^{19}F nmr are relative to external fluorotrichloromethane. Mass spectra were obtained with a VG Micromass 7050E double focusing high resolution mass spectrometer with the VG data system 2000 under positive ion fast atom bombardment (FAB) conditions at 8 keV. 3-Nitrobenzyl alcohol was used as a matrix in dichloromethane or chloroform as solvent, polypropylene glycol was used as a reference for peak matching. Microanalysis were performed by Atlantic Micrblab Inc., Norcross, Georgia.

Materials.

All commercial reagents were ACS reagent grade and used without further purification. Iodosyl triflate **1** was prepared from iodine pentoxide, iodine and trifluoromethanesulfonic acid by a known procedure [4]. Bis-(2,5-trimethylsilyl)thiophene was prepared by a known method [9] from the corresponding dibromide, *n*-butyl lithium and chlorotrimethylsilane. Tributyltin heteroaromatic derivatives **6-10** were prepared by a known procedure [8] from the corresponding bromides, *n*-butyl lithium and tri-butyltin chloride. 2-Bromothiophene, 2,5-dibromothiophene, 2-bromofuran, 5-bromoindole, 4-bromo-3,5-dimethylpyrazol, tri-butyltin chloride, chlorotrimethylsilane, cyanotrimethylsilane and *n*-butyl lithium were purchased from Aldrich. All solvents used were dried by distillation over calcium hydride. The reaction flasks were flame-dried and flushed with nitrogen.

Bis[2-(5-trimethylsilyl)-thienyl]iodonium Triflate **3**.

Bis(2-trimethylsilyl)thiophene **2** (0.5 g, 2.2 mmoles) was added to a stirred suspension of iodosyl triflate (0.29 g, 1 mmole) in dichloromethane (15 ml) at −78° under nitrogen. The mixture was allowed to warm to room temperature and stirred for 10-15 minutes until the formation of a dark solution. The solution was evaporated, and the resulting dark oil crystallized by the addition of ether (20 ml). Filtration of the precipitate and washing it with dry ether (30 ml) afforded 0.2 g (34%) of **3** as a white microcrystalline solid, mp 119-121° dec; ir (carbon tetrachloride): 3098, 2960, 1558, 1253, 1165, 1028, 985 cm^{-1}; ^{1}H nmr (deuteriochloroform): 7.97 (d, J = 4.3 Hz, 2H), 7.30 (d, J = 3.7 Hz, 2H), 0.33 (s, 18H); ^{19}F nmr (deuteriochloroform): −78.44 (s, $CF_3SO_3^-$); ^{13}C nmr (deuteriochloroform): 143.2, 137.4, 121.54 (q, J = 320.5 Hz, $CF_3SO_3^-$), 102.5, −0.486; hrms: (FAB) m/z 436.973218 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_{14}H_{22}ISi_2S_2$: 436.974506.

General Procedure for Synthesis of Bis(heteroaryl)iodonium Triflates.

Cyanotrimethylsilane (0.54 ml, 4 mmoles) was added to a stirred suspension of iodosyl triflate (0.58 g, 2 mmoles) in dichloromethane (15 ml) at −78° under nitrogen. The mixture was allowed to warm to −20° and stirred at this temperature for 10-15 minutes until the formation of a clear solution of reagent **5**. The solution was cooled to −78° and transferred to a cold stirred solution of the appropriate tributyltin heteroaromatic derivative, **6-10**, (4-4.1 mmoles) in dichloromethane (15 ml). The mixture was allowed to warm to room temperature and crystallized by the addition of dry hexane (20-30 ml). The precipitate of the iodonium triflate was filtered under nitrogen, washed with dry ether (30 ml) and dried *in vacuo*. Analytically pure materials were obtained by recrystallization from a concentrated solution of the iodonium salt in acetonitrile by addition of dichloromethane and ether.

Bis(2-thienyl)iodonium Triflate **11a**.

Reaction of 2-tributylstannylthiophene (1.5 g, 4 mmoles) with a solution of reagent **5** obtained from iodosyl triflate (0.6 g, 2 mmoles) and cyanotrimethylsilane (0.54 ml, 4 mmoles) gave 0.66 g (75%) of **11a** as a white microcrystalline solid, mp 109-112° dec; ir (carbon tetrachloride): 3105, 3094, 1385, 1222, 1162, 1022 cm^{-1}; ^{1}H nmr (deuterioacetonitrile): 7.95 (d, J = 3.9 Hz, 2H), 7.82 (d, J = 5.4 Hz, 2H), 7.12 (dd, J = 5.5 Hz, J = 3.9 Hz, 2H); ^{19}F nmr (deuterioacetonitrile): −78.64 (s, $CF_3SO_3^-$); ^{13}C nmr (deuterioacetonitrile): 142.24, 139.16, 130.63, 121.61 (q, J = 320.4 Hz, $CF_3SO_3^-$), 99.58; hrms: (FAB) m/z 292.895447 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_8H_6IS_2$: 292.895157.

Bis[2-(5-bromo)thienyl]iodonium Triflate **11b**.

Reaction of 2-tributylstannyl-5-bromothiophene (1.8 g, 4 mmoles) with a solution of reagent **5** obtained from iodosyl triflate (0.6 g, 2 mmoles) and cyanotrimethylsilane (0.54 ml, 4 mmoles) gave 0.91 g (76%) of **11b** as a white microcrystalline solid, mp 141-143° dec; ir (carbon tetrachloride): 3097, 1385, 1232, 1181, 1022 cm^{-1}; ^{1}H nmr (deuterioacetonitrile): 7.76 (d, J = 4.3 Hz, 2H), 7.19 (d, J = 3.3 Hz, 2H); ^{19}F nmr (deuterioacetonitrile): −78.66 (s, $CF_3SO_3^-$); ^{13}C nmr (deuterioacetonitrile): 143.14, 133.87, 124.89, 121.54 (q, J = 320.5 Hz, $CF_3SO_3^-$), 99.42; hrms: (FAB) m/z 448.714360 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_8H_4Br_2IS_2$: 448.716493.

Anal. Calcd. for $C_9H_4Br_2F_3IO_3S_3$: C, 18.00; H, 0.67; S, 16.03. Found: C, 18.09; H, 0.65; S, 15.93.

Bis(2-furyl)iodonium Triflate **12**.

Reaction of 2-tributylstannylfuran **7** (1.4 g, 4.0 mmoles) with a solution of reagent **5** obtained from iodosyl triflate (0.6 g, 2 mmoles) and cyanotrimethylsilane (0.54 ml, 4 mmoles) gave 0.54 g (66%) of **12** as a white microcrystalline solid, mp 114° dec; ir (carbon tetrachloride): 3151, 3132, 1444, 1233, 1157, 1023 cm^{-1}; ^{1}H nmr (deuterioacetonitrile): 7.82 (d, J = 1.1 Hz, 2H), 7.43 (d, J = 3.4 Hz, 2H), 6.63 (dd, J = 3.4 Hz, J = 1.9 Hz, 2H); ^{19}F nmr (deuterioacetonitrile): −78.79 (s, $CF_3SO_3^-$); ^{13}C nmr (deuterioacetonitrile): 153.37, 127.56, 115.08, 121.69 (q, J = 320.2 Hz, $CF_3SO_3^-$), 111.69; hrms: (FAB) m/z 260.941284 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_8H_6IO_2$: 260.941131.

Bis(4-dibenzofuryl)iodonium Triflate **13**.

Reaction of 4-tributylstannyldibenzofuran **8** (1.96 g, 4.3 mmoles) with a solution of reagent **5** obtained from iodosyl triflate (0.6 g, 2 mmoles) and cyanotrimethylsilane (0.54 ml, 4 mmoles) gave 0.60 g (48%) of **13** as a white microcrystalline solid, mp 221-223° dec; ir (carbon tetrachloride): 3070, 1285, 1230, 1163, 1030 cm^{-1}; ^{1}H nmr (deuteriodimethyl sulfoxide/deuteriochloroform): 8.15 (d, J = 7.9 Hz, 2H), 8.03 (d, J = 7.5 Hz, 2H), 7.83 (d, J = 7.3 Hz, 2H), 7.55 (d, J = 8.31 Hz, 2H), 7.44 (m, 2H), 7.28 (m, 4H); ^{19}F nmr (deuteriodimethyl sulfoxide/deuteriochloroform): −78.16 (s, $CF_3SO_3^-$); ^{13}C nmr (deuteriodimethyl sulfoxide/deuteriochloroform): 154.84, 153.12, 132.67, 128.23, 125.47, 124.85, 124.71, 123.50, 122.78, 120.97, 120.00 (q, J = 321.6 Hz, $CF_3SO_3^-$), 111.24, 95.69; hrms: (FAB) m/z 461.001710 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_{24}H_{14}IO_2$: 461.003732.

Anal. Calcd. for $C_{25}H_{14}F_3IO_5S_3$: H, 2.30; S, 5.26. Found: H, 2.51; S, 5.16.

Bis(5-indolyl)iodonium Triflate **14**.

Reaction of 5-tributylstannylindole **9** (1.66 g, 4.1 mmoles) with a solution of reagent **5** obtained from iodosyl triflate (0.6 g, 2 mmoles) and cyanotrimethylsilane (0.54 ml, 4 mmoles) gave 0.10 g (10%) of **14** as a white microcrystalline solid which decomposed to a dark oil upon isolation; ir (carbon tetrachloride): 3378, 3116, 1464, 1256, 1157, 1028 cm^{-1}; ^{1}H nmr (deuterioacetonitrile): 9.91 (s, 1H), 8.35 (d, J = 1.9 Hz, 2H), 7.70 (dd, J$_1$ = 1.9 Hz, J$_2$ = 8.8 Hz, 2H), 7.55 (d, J = 8.8 Hz, 2H), 7.41 (dd, J = 2.8 Hz, 2H), 6.59 (m, 2H); ^{19}F nmr (deuterioacetonitrile): −78.64 (s, $CF_3SO_3^-$); ^{13}C nmr (deuterioacetonitrile): 138.11, 131.48, 129.64, 129.28, 127.60, 122.08 (q, J = 320.7 Hz, $CF_3SO_3^-$), 116.33, 103.78, 103.36; hrms: (FAB) m/z 359.005914 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_{16}H_{12}N_2I$: 359.004400.

Bis[4-(3,5-dimethyl)pyrazolyl]iodonium Triflate **15**.

Reaction of 3,5-dimethyl-4-tributylstannylpyrazole (1.63 g, 4.3 mmoles) with a solution of reagent **5** obtained from iodosyl triflate (0.6 g, 2 mmoles) and cyanotrimethylsilane (0.54 ml, 4 mmoles) gave 0.37 g (41%) of **15** as a white microcrystalline solid, mp 193-195° dec; ir (carbon tetrachloride): 3190, 3106, 3041, 2968, 1404, 1305, 1231, 1163, 1022 cm^{-1}; ^{1}H nmr (deuteriodimethyl sulfoxide/deuterioacetonitrile): 2.38 (s, 6H); ^{19}F nmr (deuteriodimethyl sulfoxide/deuterioacetonitrile): −78.53 (s, $CF_3SO_3^-$); ^{13}C nmr (deuteriodimethyl sulfoxide/deuterioacetonitrile): 148.3, 121.9 (q, J = 320.7 Hz, $CF_3SO_3^-$), 84.2, 12.6; hrms: (FAB) m/z 317.025914 [M - $CF_3SO_3^-$]$^+$; Calcd. for $C_{10}H_{14}N_4I$: 317.026198.

Anal. for $C_{11}H_{14}F_3IN_4O_3S$: C, 28.32; H, 3.03; N, 12.02. Found: C, 28.57; H, 3.06; N, 12.08.

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