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SHORT COMMUNICATION

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Preparation, X-ray Structure, and Reactivity of Triisopropylsilyl-Substituted Aryliodonium Salts

Mekhman S. Yusubov,*[a,b] Dmitrii Yu. Svitich,[a] Akira Yoshimura,[c] Brent J. Kastern,[c] Victor N. Nemykin,[c] and Viktor V. Zhdankin*[c]

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(4-Triisopropylsilylphenyl)phenyliodonium tosylate, an aryliodonium salt bearing an extremely bulky, electron-donating triisopropylsilyl (TIPS) substituent in the phenyl ring, was prepared by the reaction of (4-tributyltinphenyl)triisopropylsilane with [hydroxy(tosyloxy)iodo]benzene (Koser's reagent). The TIPS-substituted aryliodonium tosylate was further converted into (4-triisopropylsilylphenyl)phenyliodonium bromide, the structure of which was established by single-crystal X-ray diffraction. Reactions of the TIPS-substituted arylodonium tosylate with bromide, azide, and thiocyanate anions predominantly afforded products of nucleophilic substitution in the electron-rich aromatic ring bearing the TIPS substituent. This unusual result is explained by the steric effect of the extraordinary bulky *para*-TIPS substituent on the configuration of the reaction intermediate.

Introduction

In recent years, organohypervalent iodine compounds have attracted significant research activity as versatile and environmentally benign reagents for organic synthesis.[1] Aryliodonium salts, $Ar_2I^+X^-$, belong to an important class of organohypervalent iodine(III) derivatives with useful reactivity and broad practical applications in polymer chemistry,[1a] biological studies,[1a] and positron emission tomography.[2] From a practical viewpoint, particularly important are the applications of aryliodonium salts as cationic polymerization photoinitiators belonging to an important class of photoacid generators.[3] It has been demonstrated that alkyl-substituted diphenyliodonium cations bearing a bulky substituent in the *para* position, such as the bis(4-*tert*-butylphenyl)iodonium and 4-cumenyl-4′-tolyliodonium salts, have higher photoacid generation efficiency than the unsubstituted diphenyliodonium salts.[4] Alkyl-substituted aryliodonium salts as photoinitiators in general have the advantages of improved solubility, high photocuring ability, and low toxicity.[5]

Likewise, *para*-substituted alkyl- and alkoxyaryliodonium salts are also important reagents that are commonly used for the generation of radioactive [^{18}F]-radiotracers in positron emission tomography.[2] This application of alkyl- and alkoxyaryliodonium salts is possible because of the higher regioselectivity observed in the reactions of these substrates with nucleophilic fluoride. In the reaction of unsymmetrical diaryliodonium salts with nucleophiles, the identity of the reductively eliminated aryl iodide is typically dictated by electronic effects and steric factors; in particular, electron-rich aryl iodides and functionalized electron-poor aromatic compounds are the main products. The presence of an electron-donating substituent in the *para* position of an aryliodonium salt is critically important in these applications.

Considering the importance of aryliodonium salts bearing a bulky, electron-donating substituent in the phenyl ring, we decided to synthesize triisopropylsilyl (TIPS)-substituted iodonium salts and to investigate the effect of the TIPS group on the structure and reactivity of these compounds. It is well known that the electron-rich TIPS group has extraordinary bulk, which provides steric screening far beyond the atom to which TIPS is attached, and in addition, TIPS is a chemically stable group that can be readily introduced in the aromatic ring by the reaction of a lithiated aromatic precursor with triisopropylsilyl chloride or triflate.[6] In this paper, we describe the preparation of (4-triisopropylsilylphenyl)phenyliodonium salts and nucleophilic substitution reactions of the tosylate salt with bromide, azide, and thiocyanate anions.

Results and Discussion

We investigated several synthetic approaches to the target (4-triisopropylsilylphenyl)phenyliodonium salts. The first

[a] Tomsk Polytechnic University,
634050 Tomsk, Russia
E-mail: yusubov@mail.ru
[b] Siberian State Medical University,
634050 Tomsk, Russia
[c] Department of Chemistry and Biochemistry, University of Minnesota Duluth,
Duluth, MN 55812, USA
E-mail: vzhdanki@d.umn.edu
http://www.d.umn.edu/~vzhdanki/

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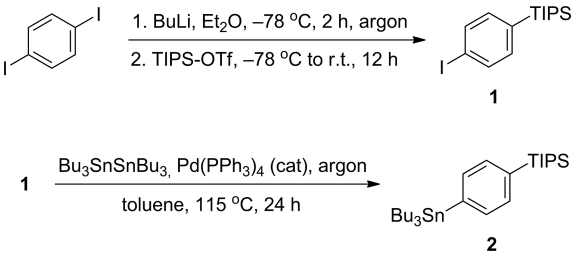
approach was based on the reaction of triisopropylsilylbenzene (PhTIPS) with electrophilic hypervalent iodine reagents such as hydroxy(tosyloxy)iodobenzene [PhI(OH)-OTs, Koser's reagent or HTIB], $PhIO{\cdot}Tf_2O$ (Zefirov's reagent), $PhIO{\cdot}BF_3$, $PhI(OAc)_2$/TMSOTf, and other highly electrophilic activated iodosylarene species.[7] Unfortunately, all these attempts were unsuccessful and resulted either in the isolation of unchanged PhTIPS or in the formation of a black tar. The low reactivity of PhTIPS in these reactions is probably related to the extraordinary bulk of the TIPS group, which blocks the phenyl ring from electrophilic attack.

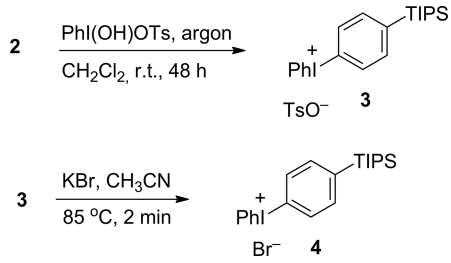
As the next step, we decided to investigate (4-iodophenyl)triisopropylsilane (**1**) as a key precursor to the target iodonium salts. Owing to the low reactivity of PhTIPS, compound **1** could not be prepared by direct oxidative iodination of the aromatic ring. However, we were able to synthesize iodide **1** starting from commercially available 1,4-diiodobenzene by iodine–lithium exchange followed by treatment with triisopropylsilyl triflate (TIPSOTf) (Scheme 1). Notably, this reaction is extremely sensitive to moist air and should be performed under an atmosphere of argon under absolutely dry conditions. In the presence of moist air, this reaction gives the respective silyloxy derivative, $4\text{-}IC_6H_4OTIPS$, as a major byproduct. (4-Iodophenyl)-triisopropylsilane (**1**) was further converted into (4-tributyltinphenyl)triisopropylsilane (**2**, Scheme 1), which is the immediate precursor to the target iodonium salt. Stannylation of iodoarene **1** was performed by a modified Stille coupling reaction by using hexabutylditin and tetrakis(triphenylphosphine)palladium(0) as the catalyst. This reaction was performed according to a previously reported procedure with little modification.[8] Arylstannane **2** was isolated in the form of a relatively stable clear oil and was identified by NMR spectroscopy and high-resolution mass spectrometry.



Scheme 1. Synthesis of precursors to (4-triisopropylsilylphenyl)-phenyliodonium salts.

The most common modern synthetic approach to substituted aryl(phenyl)iodonium salts utilizes a very mild reaction of arylstannanes with [hydroxy(tosyloxy)iodo]arenes.[9] In principle, the target (4-triisopropylsilylphenyl)phenyliodonium tosylate can be obtained by using two possible combinations of reactants: $PhSnBu_3$ + ArI(OH)OTs or $ArSnBu_3$ + PhI(OH)OTs. Our attempts to oxidize aryl iodide **1** to the respective hypervalent iodine reagents $4\text{-}TIPSC_6H_4I(OAc)_2$ and $4\text{-}TIPSC_6H_4I(OH)OTs$ were unsuccessful, and therefore, we concentrated our efforts on the second approach.

We found that the reaction of arylstannane **2** with [hydroxy(tosyloxy)iodo]arenes (Koser's reagent) slowly proceeded at room temperature under an atmosphere of argon to afford target iodonium tosylate **3** (Scheme 2). Iodonium salt **3** was isolated in 33% yield as a stable, white solid that possesses excellent solubility in dichloromethane. The low yield is in agreement with typical yields of other aryliodonium tosylates obtained by this method.[9] The structure of product **3** was confirmed by NMR spectroscopy and high-resolution ESI mass spectrometry.



Scheme 2. Preparation of (4-triisopropylsilylphenyl)phenyliodonium salts.

Iodonium tosylate **3** was further converted into (4-triisopropylsilylphenyl)phenyliodonium bromide (**4**, 34% yield) by treatment with KBr in boiling acetonitrile for 2 min (Scheme 2). Heating the mixture for a longer time should be avoided, because it leads to decomposition of the product. Iodonium bromide **4** was isolated in the form of a thermally stable, white, microcrystalline solid. The structure of product **4** was established by single-crystal X-ray crystallography (Figure 1).

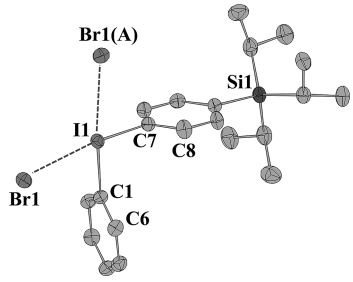


Figure 1. Perspective view of (4-triisopropylsilylphenyl)phenyliodonium bromide (**4**) with 50% ellipsoid probability. Selected distances [Å] and angles [°]: I1–C1 2.124(5), I1–C7 2.132(4), I1–Br1 3.238(5), I1–Br1(A) 3.196(5), C1–I1–C7 89.60(17), Br1–I1–Br1(A) 103.27(15), Br1–I1–C1–C6 76.19(12), Br1(A)–I1–C7–C8 87.19(15).

The hypervalent iodine ion in **4** was found in pseudo-square-planar coordination established by two covalent I–C bonds and two close contacts with bromide anions. Both I–C bonds are within the typical range for I^{III} compounds, whereas the C–I–C bond angle is close to an expected I^{III} T-shaped geometry (Figure 1). The I–Br contacts have distances smaller than the sum of the van der Waals radii of iodine and bromine. Each bromide anion forms two close contacts with two cations of **4**. Such $Br–I–(Br–I)_n$ contacts are oriented along the crystallographic *a* axis and are responsible for the observed polymeric structure of **4**. The Br–I–Br angle is slightly larger than the expected 90° angle

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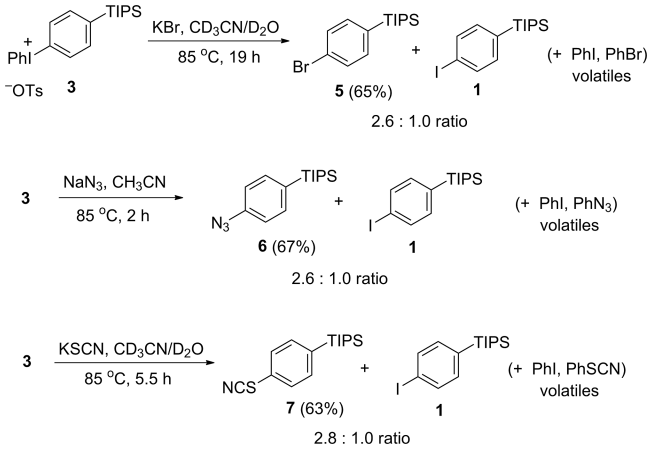
for pseudo-square-planar geometry around an iodine center. Both aromatic rings in structure of **4** are almost perpendicular to the 2C–I–2Br plane. The silicon atom in **4** has expected tetrahedral configuration and typical Si–C bond lengths.

Considering the practical importance of nucleophilic substitution reactions of aryliodonium salts in synthetic organic chemistry, we investigated reactions of tosylate salt **3** with several common nucleophiles. These reactions should proceed in agreement with the general regioselectivity pattern of reactions of nonsymmetrical iodonium salts with nucleophiles, in which substitution occurs predominantly in the more electron-deficient aromatic ring.[10]

The results of the reactions of tosylate salt **3** with bromide, azide, and thiocyanate anions are summarized in Scheme 3. The reactions were performed by heating iodonium salt **3** with the nucleophiles in acetonitrile or aqueous acetonitrile under reflux conditions. The reactions were monitored by NMR spectroscopy, and upon completion of the reactions, the organic products were separated from the inorganic salts and dried in vacuo for 10 h, which resulted in complete removal of the volatile monosubstituted benzenes from the mixtures to leave only nonvolatile TIPS-substituted products. The ratio of TIPS-substituted reaction products was determined by ^{1}H NMR spectroscopy.



Scheme 3. Reactions of (4-triisopropylsilylphenyl)phenyliodonium tosylate with nucleophiles.

To our surprise, reactions with each nucleophile predominantly afforded products **5**–**7** resulting from nucleophilic substitution in the electron-rich aromatic ring bearing the TIPS substituent (Scheme 3). This unexpected result can probably be explained by steric effects of the *para*-TIPS substituent, by analogy with the so-called "*ortho* effect".[11,12] It was previously observed that the *ortho*-methyl-substituted aromatic ring in a nonsymmetrical diaryliodonium salt shows enhanced reactivity toward nucleophiles, which is explained by the effect of steric factors on the configuration of the reaction intermediate. In a similar fashion, the presence of an extremely bulky TIPS group forces the Ar group to stay predominantly in the equatorial position of the trigonal bipyramidal intermediate and to participate in ligand coupling with the nucleophile, and this results in TIPS-substituted products **5**–**7**.[12]

Conclusions

In summary, we prepared (4-triisopropylsilylphenyl)-phenyliodonium tosylate, an aryliodonium salt bearing an extremely bulky, electron-donating triisopropylsilyl (TIPS) substituent in the phenyl ring. The TIPS-substituted aryliodonium tosylate was further converted into (4-triisopropylsilylphenyl)phenyliodonium bromide, the structure of which was established by single-crystal X-ray diffraction. Reactions of the TIPS-substituted arylodonium tosylate with bromide, azide, and thiocyanate anions predominantly afforded products of nucleophilic substitution in the electron-rich aromatic ring bearing the TIPS substituent. This unusual result can be explained by steric effects of the extraordinary bulky *para*-TIPS substituent on the configuration of the reaction intermediate.

Experimental Section

(4-Triisopropylsilylphenyl)phenyliodonium Tosylate (3): (4-Tributyltinphenyl)triisopropylsilane (**2**; 105 mg, 0.2 mmol), PhI(OTs)OH (78.4 mg, 0.2 mmol), and CH_2Cl_2 (3 mL) were placed in a flask, and the flask was purged with argon and then stirred for 48 h. The mixture was then evaporated to remove the solvent, which left a white solid. Diethyl ether (5 mL) was then added to the flask, and the resulting white suspension was stirred for 8 h. The precipitate was filtered to afford tosylate **3** as a white solid, yield 40 mg (33%); m.p. 169–170 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.98–7.96 (m, 2 H), 7.88–7.86 (m, 2 H), 7.67–7.66 (m, 2 H), 7.61 (t, J = 8.5 Hz, 1 H), 7.52–7.51 (m, 2 H), 7.45 (t, J = 7.5 Hz, 2 H), 7.10–7.09 (m, 2 H), 2.32 (s, 3 H), 1.37 (sept, J = 7.0 Hz, 3 H), 1.05–1.03 (m, 18 H) ppm. ^{13}C NMR (125 MHz, DMSO): δ = 140.3, 138.4, 138.0, 135.9, 134.4, 132.7, 132.3, 128.5, 126.0, 117.8, 116.4, 21.3, 18.7, 10.4 ppm. HRMS (ESI): calcd. for $C_{21}H_{30}ISi$ [M – OTs]$^+$ 437.1161; found 437.1159.

(4-Triisopropylsilylphenyl)phenyliodonium Bromide (4): A mixture of (4-triisopropylsilylphenyl)phenyliodonium tosylate (**3**; 14 mg, 0.023 mmol), CH_3CN (1.2 mL), H_2O (0.1 mL), and KBr (13 mg, 0.109 mmol) was heated at reflux (85 °C) for 2 min until a clear solution was formed. The resulting solution was cooled slowly to room temperature, which resulted in precipitation of colorless crystals. The mixture was then placed in a refrigerator overnight. The precipitate was filtered, washed with Et_2O, and dried to afford bromide **4** (4 mg, 34%); m.p. 152 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.98 (d, J = 8.5 Hz, 2 H), 7.90 (d, J = 8.5 Hz, 2 H), 7.55 (t, J = 7.5 Hz, 1 H), 7.48 (d, J = 8.5 Hz, 2 H), 7.40 (t, J = 7.5 Hz, 2 H), 1.36 (sept, J = 7.0 Hz, 3 H), 1.03 (d, J = 7.5 Hz, 18 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.3, 138.1, 134.8, 132.9, 131.7, 131.4, 120.8, 120.1, 18.5, 10.7 ppm. HRMS (ESI): calcd. for $C_{21}H_{30}ISi$ [M – Br]$^+$ 437.1161; found 437.1163.

X-ray crystallography: Single crystals of (4-triisopropylsilylphenyl)-phenyliodonium bromide (**4**) suitable for X-ray crystallographic analysis were obtained by slow crystallization from a dichloromethane/hexane solution. X-ray diffraction data of (4-triisopropylsilylphenyl)phenyliodonium bromide were collected with a Rigaku RAPID II Image Plate system by using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 123 K. The structure was

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solved by the Patterson method (SHELXS 86) and was refined by full-matrix least-squares refinement on F^2 by using the Crystals for Windows program. Crystal data for (4-triisopropylsilylphenyl) phenyliodonium bromide: $C_{21}H_{30}BrISi$, M = 517.36, a = 9.07770(10) Å, b = 14.3030(2) Å, c = 35.499(3) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 4609.1(3), R_f = 4.54.

CCDC-1061829 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Experimental procedures, characterization data of the products, crystallographic data, and copies of the ^{1}H NMR and ^{13}C NMR spectra.

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