Michael Additions and Iodanes

Synthesis, Characterization, and Reaction of Ethynyl(phenyl)-λ^3-Iodane Complex with [18]Crown-6

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Because of the powerful electron-withdrawing nature of the phenyl-λ^3-iodanyl group,[1] ethynyl(phenyl)-λ^3-iodane (**1**) [HCCI(Ph)X] (where X = heteroatom ligand) the parent member of the family of alkynyl(aryl)-λ^3-iodanes,[2] is highly electron deficient and hence serves as a good Michael acceptor towards a variety of nucleophiles. Commercially available ethynyl(phenyl)(tetrafluoroborato)-λ^3-iodane (**1a**: X = BF_4)[3] induces direct ethynylation of alkali-metal enolates derived from 1,3-dicarbonyl compounds and nitroalkanes under mild conditions.[4] Analogous ethynyl-λ^3-iodane **1b** (X = OTf; CF_3SO_3)[5] also affords ethynylation products by the reaction with sodium *p*-toluenesulfinate, sodium diethyl phosphate, and sulfonylamides.[6] These direct ethynylations of nucleophiles with λ^3-iodanes **1** probably involve tandem Michael addition/alkylidene–carbene rearrangement pathway.[2]

Synthetic use of ethynyl-λ^3-iodanes **1** with these prominent reactivity, however, is limited because of their relatively low thermal stability: for instance, the iodane **1a** gradually decomposes when left to stand at room temperature. The heteroatom ligand BF_4 is weakly nucleophilic and, therefore, its coordination (through a fluorine atom) to the iodine(III) center by hypervalent bonding is relatively loose,[7] which in turn increases the positive charge on the iodine atom of **1a**. These features tend to enhance the reactivity of **1a** toward nucleophiles as well as to decrease its stability. Introduction of more nucleophilic ligands, such as halogens, instead of BF_4 is expected to decrease the susceptibility of **1a** to decomposition, because of the decreased positive charge on the iodine(III) center; however, the attempted ligand exchange of ethynyl-λ^3-iodane **1a** with halide ions results in the Michael addition to the β carbon atom, instead of the formation of ethynyl(phenyl)(halo)-λ^3-iodanes.[8] To increase the stability of **1a,** development of a new type of heteroatom ligand that efficiently coordinates to the iodine(III) but not undergoes Michael additions is highly desirable.

Recently, we found that [18]crown-6 (18C6) forms a discrete complex with diphenyl(tetrafluoroborato)-λ^3-iodane, in which the iodine(III) center forms contacts with the three adjacent oxygen atoms of 18C6 through two hypervalent secondary bonding and a weak interaction.[9] Herein, we report synthesis and characterization of supramolecular complex **2** formed between ethynyl(phenyl)-λ^3-iodane **1a** and 18C6. The complexation with 18C6 not only stabilizes **1a** but also maintains its high reactivity toward nucleophiles. We also found that the presence of the ligand 18C6 in **2** makes it possible to synthesize the highly labile (*Z*)-(β-alkoxyvinyl)-phenyl-λ^3-iodanes as stable complexes with 18C6.

Slow evaporation of a dichloromethane/diethyl ether solution of a 1:1 mixture of **1a** and 18C6 at −20 °C afforded an 89% yield of single crystals of a 1:1 complex **2**. The complexation with 18C6 dramatically changed the solubility of **1a** in organic solvents: thus, **1a** is sparingly soluble in dichloromethane and chloroform, while the complex **2** is highly soluble in these solvents. More importantly, the stability of **1a** was much improved by the complexation and almost no decomposition of **2** was observed when it was left standing under ambient conditions over one month.

The X-ray crystal structure (Figure 1)[10] illustrates that, in the 1:1 complex **2**, the ethynyl(phenyl)-λ^3-iodanyl group protrudes above one face of 18C6. The iodine(III) center has contacts with three adjacent oxygen atoms (O2, O3, and O4) of 18C6 and the complex **2** adopts a distorted pentagonal-planar geometry about the iodine, with root-mean-square deviation of 0.355(9) Å for I1, C2, C3, O2, O3, and O4 from their least-squares plane and the sum of the iodine-centered bond angles $\Sigma°I = 363.0(4)°$.

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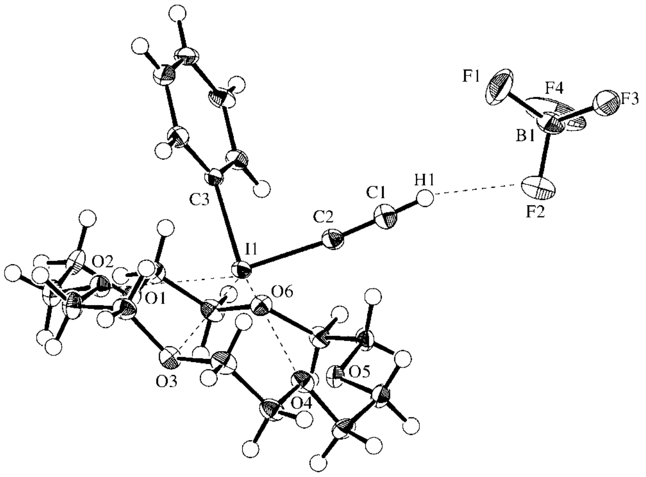


Figure 1. ORTEP drawing of **2**. Selected interatomic distances [Å] and angles [°]:I1-C2 2.009(4), I1-C3 2.116(4), I1···O2 2.918(3), I1···O3 3.120(3), I1···O4 2.923(3), H1···F2 2.34(5), C2-I1-C3 91.0(2), C2-I1···O2 164.0(5), C3-I1···O4 167.8(2), C1-H1···F2 160(5).

The I1···O2 and I1···O4 separations (2.918(3) and 2.923(3) Å) are considerably longer than the average covalent bond length (2.14 Å)[11] but shorter than the van der Waals distance (3.50 Å).[12] Both C2-I1···O2 and C3-I1···O4 are near-linear and therefore these close contacts are indicative of hypervalent secondary interactions, in which each oxygen atom donates an electron pair into an I–C σ^* orbital. The other I1···O3 contact is weak and considerably deviates from the linearity of three-center, four-electron (3c–4e) σ bonding.[13] The symmetry of the crown ether approximates to D_{3d}, the most frequently observed conformation in supramolecular complexes of 18C6.[14]

The heteroatom ligand BF_4 shows a close contact with the acetylenic hydrogen atom. The H1···F2 distance 2.34(5) Å is shorter than their combined contact radii (2.67 Å)[12] and the C1-H1···F2 bond shows a nearly linear conformation with an angle of 160(5)°. Hydrogen bonding reduces the thermal vibrations of the engaged residues. The ratio of isotropic displacement parameters (U(C1)/U(C2) = 1.23) is close to 1, which probably reflects H1···F2 hydrogen bonding.[15] Small isotropic displacement parameter of F2 (U = 0.0377(8)) compared to those of the other fluorine atoms (U(F1), 0.068(1); U(F3), 0.047(1); U(F4), 0.084(1)) also indicates reduction of the acceptor vibration through the hydrogen bonding.[16]

In general, C_{sp}–H groups act as good donors in hydrogen bonding, a directional interaction with a preference for linear geometry.[17] The highly acidic nature of H1 in **2** is responsible for the C–H···F hydrogen bonding.[18] The C_{sp}–H stretching frequency of **2** provides spectroscopic evidence for this interaction: it appears as a single sharp band at $\tilde{\nu} = 3208\,cm^{-1}$ (Nujol), whereas that of **1a** appears at higher frequency of $\tilde{\nu} = 3242\,cm^{-1}$.

In solution, ethynyl-λ^3-iodane **1a** forms 1:1 complex with 18C6. ^{1}H NMR spectroscopic analyses showed that a solution of 18C6 in $CDCl_3$ (0.01 M) dissolve 0.9 equivalents of solid λ^3-iodane **1a** at 23 °C, and the methylene singlet is shifted upfield by 0.06 ppm on complexation with **1a**, as observed in the $Ph_2IBF_4{\cdot}18C6$ complex.[9] Irradiation of the methylene protons of 18C6 gives rise to nuclear Overhauser effects (NOEs) for the *ortho* protons of **1a**, but not for the *meta* and *para* protons. The cold-spray ionization (CSI) MS spectrum for the complex **2** in dichloromethane showed the most prominent ion peak of 1:1 complex $[\mathbf{2}-BF_4]^+$ at *m/z* 493 (Figure 2).[19] The binding constant was measured by ^{1}H NMR spectroscopic titrations of $CDCl_3$ solutions of 18C6 with **1a** at 23 °C. The resulting binding curve gave an excellent fit with a 1:1 binding model and was analyzed by nonlinear least-squares method to give a binding constant (K_a) value of $1.92 \times 10^3\,M^{-1}$ (correlation coefficient 0.99).

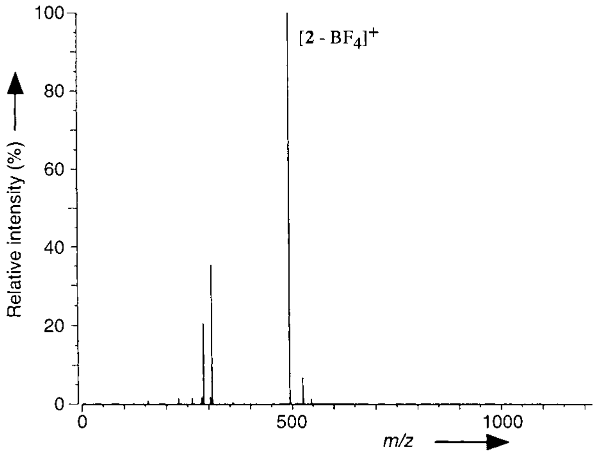
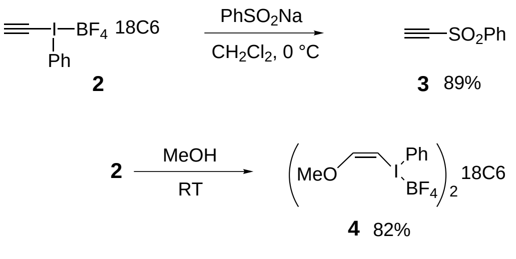


Figure 2. CSI-MS spectrum of **2** in CH_2Cl_2.

The 1:1 complex **2** has the desired high reactivity towards attack of nucleophiles and serves as a good Michael acceptor. Thus, on exposure to sodium benzenesulfinate in dichloromethane, **2** undergoes tandem Michael addition/alkylidene–carbene rearrangement to give the ethynyl sulfone **3** in a high yield under mild conditions (Scheme 1).[6a,20] Very interestingly, it is possible to synthesize the highly labile (Z)-(β-methoxyvinyl)-λ^3-iodane as a crown-ether complex **4**, directly from the complex **2** (Scheme 1):[21] thus, reaction of **2** with methanol at room temperature results in *anti* Michael addition yielding the 2:1 complex **4**, with a small vicinal coupling constant 3.7 Hz between vinylic protons, stereoselectively in 82 % yield. Ethanol and *tert*-butanol similarly undergo the Michael addition to give the analogous 2:1 complexes. In these reactions, 18C6 functions as a stabilizing ligand not only for the reactant ethynyl-λ^3-iodane **1a** but also



Scheme 1. Reaction of the 1:1 complex **2** with nucleophiles.

for the products (*Z*)-(β-alkoxyvinyl)-λ^3-iodanes, which have not been synthesized before. Without use of 18C6, the isolation and the purification of (*Z*)-(β-alkoxyvinyl)-λ^3-iodanes are very difficult, probably because of the facile *anti*-β-elimination[22] of the phenyl-λ^3-iodanyl group with remarkable nucleofugality.[23]

In conclusion, 18C6 was shown to be an excellent polydentate ligand of ethynyl- and (*Z*)-(β-alkoxyvinyl)-λ^3-iodanes. The X-ray crystal structure of the ethynyl(phenyl)-λ^3-iodane 18C6 complex **2** shows that the iodine(III) interacts with three adjacent oxygen atoms of 18C6 with a distorted pentagonal-planar geometry. Most importantly, the complexation with 18C6 increases the stability of these labile λ^3-iodanes.

Experimental Section

2: **1a** (103 mg, 0.33 mmol) and 18C6 (86 mg, 0.33 mmol) were dissolved in dichloromethane (1 mL) and the solution was stirred for 30 min at room temperature. After addition of diethyl ether (0.75 mL), a slow evaporation at −20 °C of the solvent by exposure to the atmosphere yielded **2** (169 mg, 0.29 mmol, 89 %) as colorless plates: m.p. 133–134 °C; ^{1}H NMR (300 MHz, CD_2Cl_2, 0.01 M, 24 °C, TMS): $\delta = 3.48$ (s, 1 H; CCH), 3.63 (s, 24 H; 18C6), 7.59 (dd, ^3J(H,H) = 8.2, 7.4 Hz, 2 H; *m*-H), 7.71 (t, ^3J(H,H) = 7.4 Hz, 1 H; *p*-H), 8.20 ppm (d, ^3J(H,H) = 8.2 Hz, 2 H; *o*-H); ^{13}C NMR (75 MHz, [D$_6$]acetone, 0.09 M, 24 °C, TMS): $\delta = 30.4$ (*C*CH), 70.7 (18C6), 98.1 (C*C*H), 116.6 (*ipso*-C), 133.2 (*m*-C), 134.1 (*p*-C), 137.0 ppm (*o*-C); IR (Nujol): $\tilde{\nu} = 746$ s, 835 s, 957 s, 1053 vs, 1108 vs, 2042 w, 3208 s cm^{-1}; CSI-MS (CH_2Cl_2): *m*/*z* 493 [$(M-BF_4)^+$]; elemental analysis calcd (%) for $C_{20}H_{30}BF_4IO_6$ (580.16): C 41.41, H 5.21; found: C 41.25, H 5.03.

4: **2** (25 mg, 0.042 mmol) was dissolved in methanol (1.2 mL) under argon and the solution was stirred for 18 h at room temperature. Evaporation of the solvent under reduced pressure, followed by repeated decantation at 0 °C with *n*-hexane and then with diethyl ether, gave **4** (16.7 mg, 0.017 mmol, 82 %) as colorless prisms after recrystallization from dichloromethane/*n*-hexane: m.p. 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 24 °C, TMS): $\delta = 3.68$ (s, 24 H; 18C6), 4.02 (s, 6 H; MeO), 6.02 (d, ^3J(H,H) = 3.7 Hz, 2 H; CHI), 6.96 (d, ^3J(H,H) = 3.7 Hz, 2 H; CHOMe), 7.49 (dd, ^3J(H,H) = 7.7, 8.4 Hz, 4 H; *m*-H), 7.65 (t, ^3J(H,H) = 7.7 Hz, 2 H; *p*-H), 7.94 ppm (d, ^3J(H,H) = 8.4 Hz, 4 H; *o*-H); IR (Nujol): $\tilde{\nu} = 742$ w, 1054 vs, 1104 s, 1257 w, 1614 s, 3110 w cm^{-1}; elemental analysis calcd (%) for $C_{30}H_{44}B_2F_8I_2O_8$ (960.08): C 37.53, H 4.62; found: C 37.41, H 4.50.

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