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One-Pot Regioselective Synthesis of Chromanyl(phenyl)-λ^3-iodanes: Tandem Oxidative Cyclization and λ^3-Iodanation of 3-Phenylpropanols

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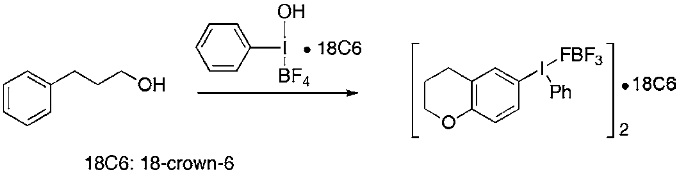
ABSTRACT



Reaction of 3-phenylpropanol with an activated iodosylbenzene–18-crown-6 complex [PhI(OH)BF$_4$–18C6] in dichloromethane in the presence of BF$_3$–Et$_2$O afforded directly the 6-chromanyl(phenyl)-λ^3-iodane–18C6 complex through tandem oxidative intramolecular cyclization yielding chroman and its regioselective phenyl-λ^3-iodanation.

Diaryl-λ^3-iodanes are versatile arylation agents in organic synthesis.[1] Because of their highly electron-deficient nature and the hyperleaving group ability of aryl-λ^3-iodanyl groups,[2] they serve as highly activated species of aryl halides in nucleophilic aromatic substitution reactions and undergo transfer of the aryl group to a variety of organic substrates including carbon, nitrogen, phosphorus, and group 16 element-centered nucleophiles under mild conditions. They are also viable alternatives to aryl halides for copper- and palladium-catalyzed cross-coupling reactions with amines, alkenes, terminal alkynes, organoboranes, silanes, and stannanes.[3] 2-(Trimethylsilyl)-phenyl-λ^3-iodanes serve as useful progenitors for the quantitative generation of benzynes.[4] Chromium(II)-mediated reactivity umpolung of diaryl-λ^3-iodanes was recently developed.[5] Furthermore, some diaryliodanes are effective catalysts for the cationic and/or the free radical polymerizations and have found many practical applications as photoinitiators for polymerizations.[6]

Diaryl-λ^3-iodanes are prepared by the reaction of arenes with iodosyl-, (diacyloxyiodo)arenes, or their derivatives in the presence of an acid catalyst.[1] Use of the activated arene with a silyl, stannyl, or boryl group makes it possible to

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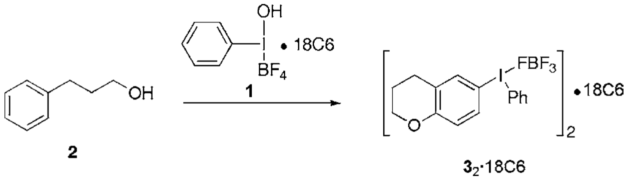
synthesize diaryliodanes in an exclusively regioselective manner under mild conditions.[7] Double ligand exchange on iodine(III) of inorganic λ^3-iodanes such as $(OI)_2SO_4$, OIOTf, $(RCO_2)_3I$, and $(NC)_2IOTf$ with arylsilanes and stannanes directly affords diaryliodanes.[8] β-Chlorovinyl- and β-(triflyloxy)vinyl-λ^3-iodanes also undergo ligand exchange on iodine(III) by the reaction with aryllithiums, yielding diaryliodanes.[9] We report herein a direct synthesis of 6-chromanyl(phenyl)-λ^3-iodanes from 3-phenylpropanols by the reaction with aryl-λ^3-iodanes, which involves the oxidative intramolecular cyclization yielding chromans, followed by their regioselective phenyl-λ^3-iodanation. Interestingly, an intermediate spirocyclohexadiene **5** favors the 1,2-shift of a carbon−carbon bond over that of a carbon−oxygen bond.

Recently, we reported a synthesis of a protonated iodosylbenzene monomer−18-crown-6 complex **1** as crystals, in which intermolecular hypervalent I(III)···O interactions play an essential role in the complexation[10] and dramatically increase the stability of the highly labile hydroxy(phenyl)-λ^3-iodane $PhI(OH)BF_4$.[11] The complex **1** serves as an efficient oxidant for a broad range of functional groups such as olefins, alkynes, enones, silyl enol ethers, sulfides, and phenols under mild conditions, especially in water as a solvent. Very interestingly, exposure of 3-phenyl-1-propanol (**2**) to the hydroxy-λ^3-iodane complex **1** (1.2 equiv) in dichloromethane at room temperature resulted in the oxidative intramolecular cyclization yielding chroman, followed by the phenyl-λ^3-iodanation of the aromatic ring, with formation of 6-[phenyl(tetrafluoroborato)-λ^3-iodanyl]chroman (**3**) as a 2:1 complex with 18-crown-6 (18C6) albeit in a low yield (13%) (Scheme 1).[12,13] Aryl-λ^3-iodanes undergo oxidation of alcohols to carbonyl compounds;[1] however, in this reaction, formation of 3-phenylpropanal was found to be a minor process with less than 2% yield.

Scheme 1



Use of 3 equiv of λ^3-iodane complex **1** in refluxing dichloromethane afforded the 2:1 complex $\mathbf{3}_2$−18C6 in 37% yield (Table 1, entry 2). A good yield of the product was obtained by using a Lewis acid additive, BF_3−Et_2O, which probably increases the reactivity of λ^3-iodane complex **1** via the coordination to the oxygen atom of the hydroxy group (entry 4). In this reaction, simple λ^3-iodanation of the aromatic ring in **2** competes with the oxidative cyclization and afforded the byproduct diaryl-λ^3-iodane **4** in 20% yield. Instead of the crown ether complex **1**, use of iodosylbenzene in the presence of BF_3−Et_2O (3 equiv) increased the yield of **3** to 61% (entry 7).

Table 1. Direct Synthesis of 6-Chromanyl(phenyl)-λ^3-iodane **3** from Alcohol **2**[a]

entry	iodane	additive (equiv)	temp (°C)	time (h)	yield (%)[b]
1	**1**		25	24	23[c]
2	**1**		40	23	37[c]
3	**1**		81	5	41[c]
4	**1**	BF_3−Et_2O (3)	40	7	51 (63)[c,e]
5	PhIO	Tf_2NH (3)	40	7	38
6	PhIO	HBF_4−Me_2O (3)	25	5	(41)
7	PhIO	BF_3−Et_2O (3)	40	3	61

[a] Unless otherwise noted, reactions were carried out using 3−3.1 equiv of λ^3-iodanes in dichloromethane under Ar. [b] Isolated yields. Parentheses are ^{1}H NMR yields. [c] Yields of the 2:1 complex $\mathbf{3}_2$−18C6. [d] In MeCN. [e] Diaryl-λ^3-iodane **4** (20%) was obtained.

Figure 1 illustrates solid-state structures of the 2:1 complex $\mathbf{3}_2$−18C6, in which two independent molecular complexes A and B exist.[14] In each complex A or B, chromanyl(phenyl)-λ^3-iodanyl groups protrude face of the 18C6, providing a perching type of host−guest relationship. The 2:1 complex A adopts a distorted trigonal bipyramidal geometry about the iodines with a phenyl group and an oxygen O5 occupying apical positions and with a chromanyl group and two oxygens

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(12) For radical cyclizations of 3-phenylpropanols to 6-iodochromans by the reaction with (diacetoxyiodo)benzene and molecular iodine under irradiation with a tungsten lamp, see: (a) Muraki, T.; Togo, H.; Yokoyama, M. *Tetrahedron Lett.* **1996**, *37*, 2441. (b) Togo, H.; Muraki, T.; Hoshina, Y.; Yamaguchi, K.; Yokoyama, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 787.

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(14) Crystallographic data for the 2:1 complex $\mathbf{3}_2$−18C6: $C_{42}H_{52}B_2F_8I_2O_8$, $M = 1112.28$, $T = 123$ K, orthorhombic, space group Fdd2 (No. 43), $a = 18.7743(3)$ Å, $b = 29.9639(6)$ Å, $c = 31.9847(8)$ Å, $V = 17993.0(6)$ Å^3, $Z = 16$, $D_c = 1.642$ g cm^{-3}, μ(Mo Kα) = 14.819 cm^{-1}. 10 291 reflections were collected; 10 291 were unique. R1 = 0.0270 [$I > 2\sigma(I)$], wR2 = 0.0580 [$I > 3\sigma(I)$]. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-635734. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

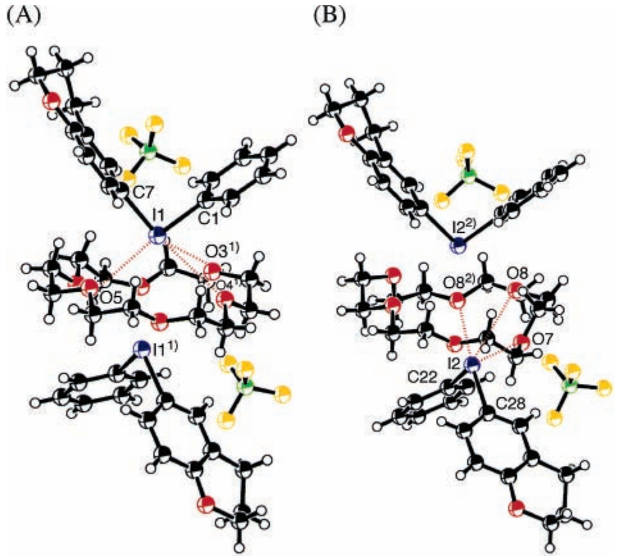
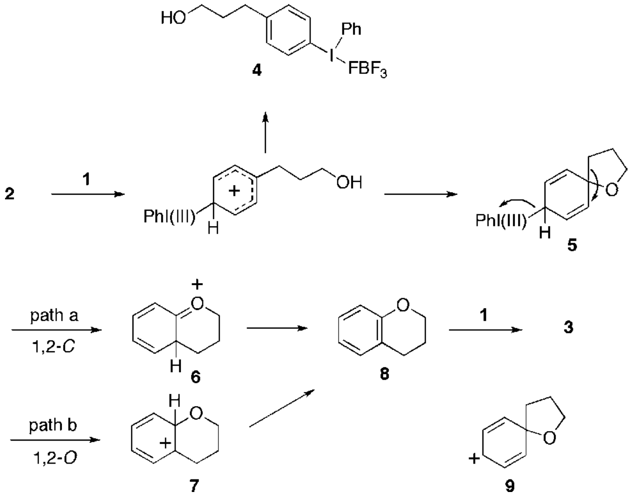


Figure 1. ORTEP structures of the 2:1 complex $\mathbf{3}_2$−18C6 (thermal ellipsoids drawn at the 50% probability level). Left, the complex A; right, the complex B. Selected interatomic distances (Å) and angles (°): I1−C1 2.110(2); I1−C7 2.095(2); I2−C22 2.109(2); I2−C28 2.087(2); C1−I1−C7 95.04(10); C22−I2−C28 95.85(10). Symmetry operations: $^{1)}$ $-X + 1/2, -Y + 1/2 - 1, Z$; $^{2)}$ $-X + 1/2, -Y + 1/2, Z$.

O3$^{1)}$ and O4$^{1)}$ in equatorial sites. On the other hand, the complex B shows a distorted pentagonal planar coordination around the iodines, in which each iodine atom contacts with the three adjacent oxygen atoms of 18C6, O7, O8, and O8$^{2)}$, for I2. The I1⋯O5, I2⋯O7, and I2⋯O8$^{2)}$ distances (3.242(4), 2.9669(19), and 2.9227(18) Å) are shorter than the van der Waals distance (3.50 Å),[15] and all of the C1−I1⋯O5, C22−I2⋯O7, and C28−I2⋯O8$^{2)}$ triads are near-linear (164.51(8), 165.70(8), and 171.31(9)°). Therefore, these close contacts are indicative of the hypervalent secondary interactions, in which each oxygen atom donates an electron pair into the I−C σ^* orbital.[10]

Scheme 2 illustrates a reaction pathway leading to the formation of 6-chromanyl-λ^3-iodane **3**. Nucleophilic attack of 3-phenyl-1-propanol (**2**) at the para position to the positively charged iodine(III) of λ^3-iodane **1**, followed by internal cyclization via nucleophilic attack of the intramolecular hydroxy group, will produce the spiro-1,4-cyclohexadiene **5**. On the other hand, instead of the intramolecular cyclization, simple aromatization through deprotonation gives the diaryl-λ^3-iodane **4** regioselectively. A 1,2-shift of a carbon−carbon bond in **5** (path a) with reductive elimination of iodobenzene, evoked by the excellent nucleofugality of the phenyl-λ^3-iodanyl group which shows a leaving group ability about 10^6 times greater than triflate,[2] produces chroman (**8**). An alternative 1,2-shift of a carbon−oxygen bond in **5** (path b) will also afford chroman (**8**). In addition to these concerted ring-expanding rearrangements of **5**, intervention of a spirocyclohexadienyl cation **9** produced by a stepwise initial elimination of the phenyl-λ^3-iodanyl group with hyperleaving group ability should be considered. Finally, phenyl-λ^3-iodanation of chroman (**8**) with the hydroxy-λ^3-iodane **1** would take place regioselectively at C6 yielding 6-chromanyl(phenyl)-λ^3-iodane **3**. Use of BF_3−Et_2O (3 equiv) as an additive (entry 4) probably decreases the rate of intramolecular cyclization of a hydroxy group yielding spirocyclohexa-1,4-diene **5**, because of the decreased nucleophilicity of the hydroxy group by the coordination of the Lewis acid to the oxygen atom. Therefore, in the presence of the external BF_3−Et_2O, the direct aromatization yielding the diaryl-λ^3-iodane **4** will compete with the tandem oxidative cyclization and λ^3-iodanation of 3-phenyl-1-propanol (**2**) to a significant extent.

Scheme 2



1,2-Migration of spiro-1,4-diene **5** with ring expansion was evaluated by the reaction of deuterated 3-phenylpropanol **11** with 88 and 58% deuterium contents at the ortho and benzylic positions, being prepared from dichlorocinnamic acid **10** (Scheme 3). Deuterium contents in the cyclization product **3-d** obtained were determined by ^{1}H NMR to be 12% at C5 and 78% at C8. These results clearly indicate a preference for the 1,2-shift of a carbon−carbon bond in spirocyclohexadiene **5-d** yielding chroman **8-da** over that of a carbon−oxygen bond affording **8-db** in a ratio of 87:13. Stability differences between carbocations **6** and **7** will be reflected in the transition states for these 1,2-migrations of **5**.

In fact, 1-oxaspiro[4,5]deca-6,9-dien-8-one (**12**) exclusively undergoes the acid-catalyzed dienone−phenol rearrangement through a carbon−carbon bond migration and affords 6-methoxychroman (**13**) after methylation with MeI/NaOH (Scheme 4).[16]

Recent molecular orbital calculations of transition-state energies for the ring expansion of the spirocyclohexadienyl

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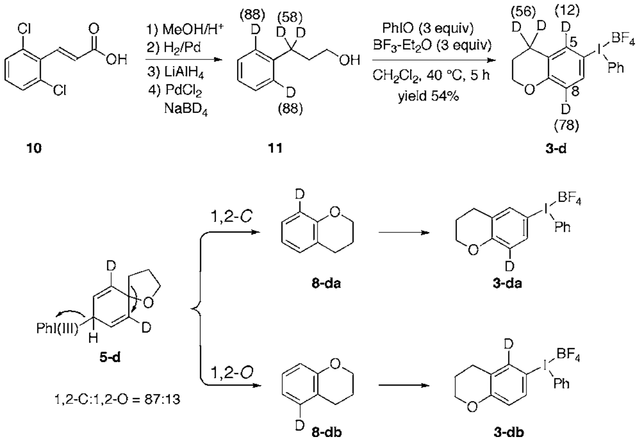
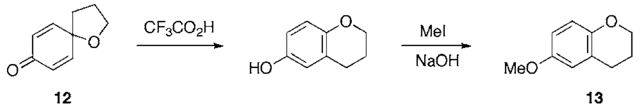
Scheme 3[a]



[a] Parentheses are % deuterium contents. Some benzylic deuteriums were omitted for clarity.

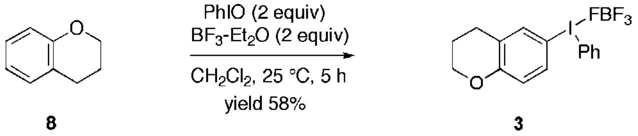
cation **9** at ab initio (MP2/6-31G*) and density functional (B3LYP/6-31G*) levels show that migration of the carbon−carbon bond is favored by 24 kJ mol^{-1} over that of the carbon−oxygen bond,[17] which is in good agreement with our experimental results.[18]

Scheme 4



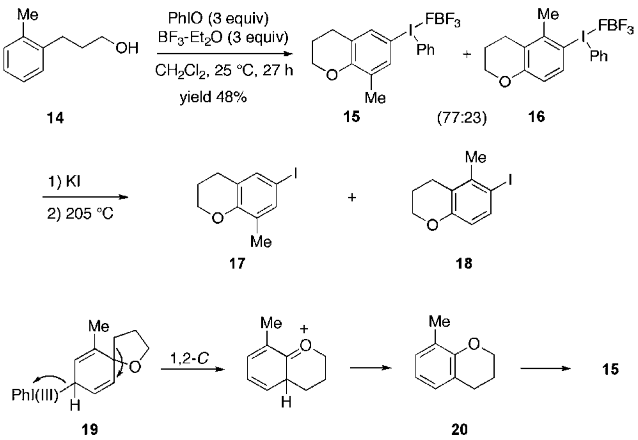
The last step of the tandem oxidative cyclization and λ^3-iodanation of phenylpropanol **2**, i.e., introduction of the hypervalent phenyl-λ^3-iodanyl group to chroman (**8**) at C6, was found to occur regioselectively as shown in Scheme 5. Both nitration of chroman (**8**) with 60% nitric acid[19] and radical iodination with acetyl hypoiodite[12] have been shown to take place similarly at C6 and afford 6-nitro- and 6-iodochromans regioselectively.

Scheme 5



(2-Methylphenyl)propanol **14** undergoes the tandem cyclization and λ^3-iodanation by the reaction with iodosylbenzene and BF_3−Et_2O and afforded a 77:23 mixture of 8-methyl- **15** and 5-methyl-6-chromanyl-λ^3-iodane **16** in a moderate yield (Scheme 6). The structure of these λ^3-iodanes was determined by the conversion to the corresponding iodides **17** and **18**, through ligand exchange on iodine(III) with KI and the subsequent thermal nucleophilic aromatic substitution.[20] Predominant formation of the 8-methyl-6-chromanyl-λ^3-iodane **15** is compatible with a facile 1,2-shift of a carbon−carbon bond in spirocyclohexadiene **19** yielding 8-methylchroman (**20**).

Scheme 6



In conclusion, both hydroxy-λ^3-iodane−18-crown-6 complex **1** [$PhI(OH)BF_4$−18C6] and iodosylbenzene in the presence of BF_3−Et_2O serve as useful agents for tandem oxidative cyclization and λ^3-iodanation of 3-phenylpropanols, which directly produces 6-chromanyl(phenyl)-λ^3-iodanes with high regioselectivity.

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Supporting Information Available: Typical experimental procedures, spectral data for new compounds, and crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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