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Facile Synthetic Entry into the 1,3-Dihydro-3-methyl-3-phenyl-1,2-benziodoxole Family of λ^3-Iodanes

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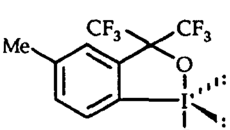
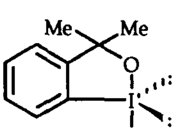
***Abstract*:** The synthesis of a series of 1,3-dihydro-3-methyl-3-phenyl-1,2-benziodoxoles, **7**, containing chloro, tosyloxy, acetoxy, trifluoroacetoxy and azido ligands and the optical resolution of 2-iodo-α-methylbenzhydrol, the starting material for the synthesis of **7**, are reported. Copyright © 1996 Elsevier Science Ltd

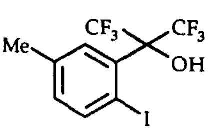
Cyclic iodanes possessing internal alkoxy ligands, namely the 1,3-dihydro-1,2-benziodoxoles **1a-d** and **2a-d**, were first described by Amey and Martin in the late 1970s.[1] Synthesis of the 1-halo-1,2-benziodoxoles **1a-c** and **2a** was achieved by oxidation of the 2-iodocumyl alcohols **3** and **4** with appropriate hypohalites or molecular halogens; i.e., CF_3OF, *t*-BuOCl or Cl_2, KH followed by Br_2. The fluorobenziodoxole was also made from **1b** with HgO and 48% aqueous HF in CH_2Cl_2. Basic hydrolysis of chloroiodane **2a** gave the hydroxybenziodoxole **2b**, while exposure of **2b** to anhydrous HBr in the presence of P_2O_5 gave the bromobenziodoxole **2c**. The bis(alkoxy)iodanes **1d** and **2d** were prepared from the chlorobenziodoxoles with potassium hexafluorocumylate in CH_2Cl_2 or CCl_4. Zhdankin and his coworkers have recently added the 1-azido[2] and 1-cyano[3] analogs **5a** and **2e** to the list of stable 1,3-dihydro-1,2-benziodoxoles. These compounds were made by treatment of the hydroxybenziodoxoles **5b** and **2b** with Me_3SiN_3 and Me_3SiCN, respectively. Finally, the tricyclic bis(alkoxy)iodanes **6a**[4] and **6b**[5] are also known.



1a, L = F
1b, L = Cl
1c, L = Br
1d, L = $PhC(CF_3)_2O$



2a, L = Cl
2b, L = OH
2c, L = Br
2d, L = $PhC(CF_3)_2O$
2e, L = CN



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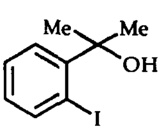

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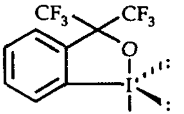
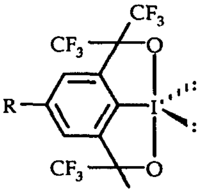


5a, L = N_3
5b, L = OH

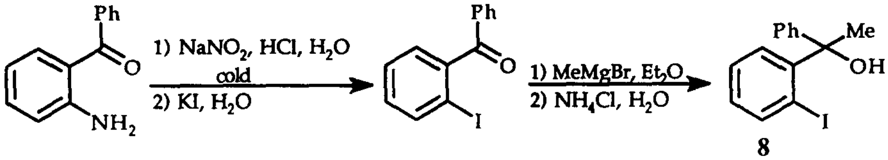


6a, R = Me
6b, R = *t*-Bu

A remarkable feature of the 3,3-disubstituted-1,3-dihydro-1,2-benziodoxole nucleus is its capacity to stabilize iodine(III)-Br and iodine(III)-N_3 hypercovalent bonds and the bis(alkoxy)iodane structures. Compounds **1c** and **2c** are the only reported examples of stable organo(bromo)iodanes, while the azidoiodane generated *in situ* from PhI=O and Me_3SiN_3 in CH_2Cl_2 collapses to iodobenzene, molecular nitrogen and hexamethyldisiloxane at 0° C.[6,7] (Dimethoxyiodo)benzene [$PhI(OMe)_2$] can be isolated as a crystalline solid and stored at -30° C,[8] but it is prone to thermal decomposition at room temperature.[9] Amey and Martin did note,[1] however, that "The trifluoromethyl-substituted species are markedly more stable than their simple methyl analogs." This was attributed to the higher electronegativity of the fluorine containing apical ligands and attending stabilization of the [3c-4e] bonds of λ^3-iodanes.

We now report the synthesis of a series of 1,3-dihydro-3-methyl-3-phenyl-1,2-benziodoxoles, **7**. These compounds possess an asymmetric carbon atom and contain chloro, carboxy, tosyloxy and azido ligands. Because the alkoxy ligand in **7** lacks fluorine atoms, we were surprised at the stability of these λ^3-iodanes and the ligand combinations that they support. Among acyclic iodanes, ArI(OR)X[10] and $ArI(OR)O_3SR'$ [11,12] are rare, while ArI(OR)OCOR' is unknown.

2-Iodo-α-methylbenzhydrol (**8**), the starting material for the synthesis of **7**, is a known compound[13] and was made from 2-aminobenzophenone by the standard sequence of operations shown in equation 1. The benziodoxoles **7** were prepared either by direct oxidations of **8** (eq. 2) or by displacement reactions of chlorobenziodoxole **7a** with appropriate nucleophiles (eq. 3). Conditions and yields for the synthesis of **7a-7e** are summarized in Table 1. All of the benziodoxoles were characterized by NMR (600 MHz ^{1}H, ^{13}C) and elemental (C,H) analysis, and their structures have been confirmed by single crystal X-ray studies.[14] The X-ray structures of **7a-e** will be reported elsewhere.



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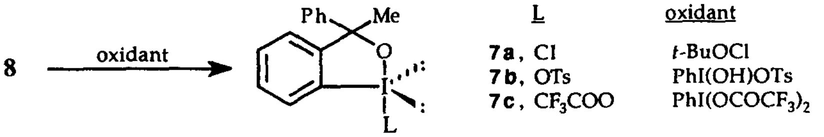

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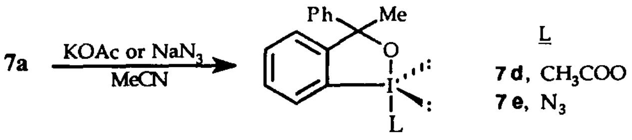

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Table 1. Conditions and Yields for the Synthesis of 7a-7e.[a]

Reactants (mmol)	Solvent (mL)	Time (h)	Product,[b] Yield
8, (11.3), *t*-BuOCl (12.1)	CCl_4 (6)	0.58	**7a**, 82%
8 (3.18), PhI(OH)OTs (3.19)	CH_2Cl_2 (17)	9.83	**7b**, 83%
8 (4.78), $PhI(OCOCF_3)_2$ (4.77)	CH_2Cl_2 (25)	4.5	**7c**, 50%
7a (8.36), KOAc (16.3)	MeCN (60)	1	**7d**, 85%
7a (2.79), NaN_3 (3.2)	MeCN (40)	2	**7e**, 83%

[a] All reactions were conducted at room temperature [b] CH analyses within ± 0.3% of calculated values [c] Mp (° C, uncorrected): **7a** (108-110), **7b** (142-145), **7c** (130-132), **7d** (133-135), **7e** (80-83).

Following Amey and Martin, the chlorine ligand was introduced by the treatment of **8** with *t*-BuOCl in CCl_4.[1] The chloroiodane **7a** separated from the solvent and was collected by filtration and washed with hexanes. The tosylate and trifluoroacetate analogs were prepared by ligand transfer oxidations[15] with appropriate iodine(III) reagents. Admixture of **8** and [hydroxy(tosyloxy)iodo]benzene [HTIB, PhI(OH)OTs][16] in dichloromethane resulted in gradual disappearance of the crystalline HTIB phase. Concentration of the solution gave an oil containing **7b** and iodobenzene. Treatment of this material with pentane to remove PhI delivered solid **7b**. Similar oxidation of **8** with [bis(trifluoroacetoxy)iodo] benzene [$PhI(OCOCF_3)_2$, soluble in CH_2Cl_2], concentration of the solution and treatment of the residual oil with hexanes gave solid **7c**.

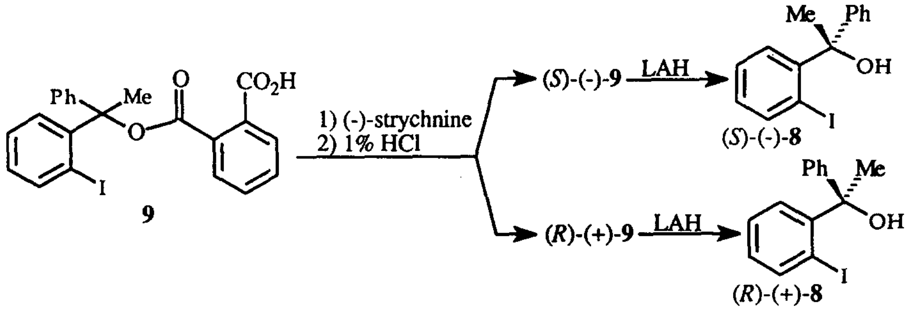
The acetoxy- and azidobenziodoxoles **7d** and **7e** were prepared by stirring solutions of the chlorobenziodoxole **7a** in acetonitrile with KOAc or NaN_3. After 1 or 2 hours, the mixtures were filtered to remove insoluble salts, and the filtrates were concentrated. The acetoxyiodane, thus obtained, was a solid. The azidoiodane, initially an oil, solidified on standing and was treated with hexanes prior to final isolation.

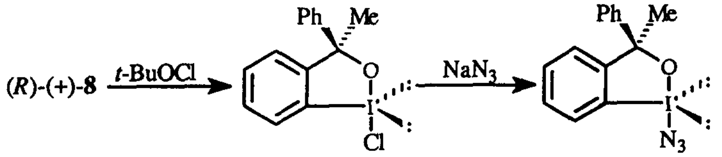
Samples of the chloro- and trifluoroacetoxybenziodoxoles, isolated as described above, gave satisfactory elemental analyses without further purification. The remaining members of the series were also quite clean (^1H NMR analysis), although all samples submitted for elemental analysis were recrystallized materials; **7b** (CH_2Cl_2-hexanes), **7d** (CH_2Cl_2-hexanes), **7e** (hot hexanes).

Optical resolution of (±)-2-iodo-α-methylbenzhydrol (**8**) was achieved *via* its conversion (*t*-BuOK, phthalic anhydride, toluene) to the racemic half-phthalate ester, **9**. Fractional recrystallization of (±)-**9** from CH_2Cl_2-hexanes with (-)-strychnine and treatment of the diastereomeric strychnine salts with 1% HCl(aq) gave (*R*)-(+)-**9** and (*S*)-(-)-**9**. Reduction of the homochiral esters with $LiAlH_4$ delivered the enantiomeric benzyhydrols, (*R*)-(+)-**8** [$[\alpha]_D^{29}$ = +36.6° (CH_2Cl_2)] and (*S*)-(-)-**8** [$[\alpha]_D^{29}$ = -34.4° (CH_2Cl_2)]. The absolute configurations assigned to the enantiomeric alcohols are based on a single crystal X-ray study[14] of the (-)-**9** • strychnine salt from which the levorotatory benzhydrol was ultimately obtained.

The availability of the enantiomeric benzhydrols provides ready access to optically active members of the benziodoxole family, **7**. For example, treatment of (*R*)-(+)-**8** with *t*-BuOCl gave chlorobenziodoxole (+)-**7a** [$[\alpha]_D^{29}$ = +221° (CH_2Cl_2)]. When this compound was mixed wi th NaN_3, (+)-**7e** [$[\alpha]_D^{29}$ = +115° (CH_2Cl_2)] was obtained. The dextrorotatory chloro- and azidobenziodoxoles are presumably of the *R* configuration at C-3.

Efforts by us and by French and his coworkers[17] to employ homochiral benziodoxoles for asymmetric functionalization reactions will be reported later.





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REFERENCES AND NOTES

1. Amey, R.L.; Martin, J.C. *J. Org. Chem.* **1979**, *44*, 1779.
2. Zhdankin, V.V.; Kuehl, C.J.; Krasutsky, A.P.; Formaneck, M.S.; Bolz, J.T. *Tetrahedron Lett.* **1994**, *35*, 9677.
3. Zhdankin, V.V.; Kuehl, C.J.; Krasutsky, A.P.; Bolz, J.T.; Mismash, B.; Woodward, J.K.; Simonsen, A.J. *Tetrahedron Lett.*, **1995**, *36*, 7975.
4. Nguyen, T.T.; Amey, R.L.; Martin, J.C. *J. Org. Chem.* **1982**, *47*, 1024.
5. Nguyen, T.T.; Wilson, S.R.; Martin, J.C. *J. Am. Chem. Soc.* **1986**, *108*, 3803.
6. Magnus, P.; Lacour, J. *J. Am. Chem. Soc.* **1992**, *114*, 767.
7. Zefirov, N.S.; Safronov, S.O.; Kaznacheev, A.A.; Zhdankin, V.V. *J. Org. Chem. USSR (Engl. Transl.)* **1989**, *25*, 1633 (Plenum, 1990).
8. Schardt, B.C.; Hill, C.L. *Inorg. Chem.* **1983**, *22*, 1563.
9. Observations in our laboratory.
10. Tanner, D.D.; Gidley, G.C. *Can. J. Chem.* **1968**, *46*, 3537.
11. Koser, G.F.; Wettach, R.H. *J. Org. Chem.* **1980**, *45*, 4988.
12. Ray III, D.G.; Koser, G.F. *J. Am. Chem. Soc.* **1990**, *112*, 5672.
13. Yamataka, H.; Yamaguchi, K.; Takatsuka, T.; Hanafusa, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1157.
14. The X-ray studies were conducted by David B. McConville.
15. Koser, G.F.; Wettach, R.H. *J. Org. Chem.* **1980**, *45*, 1542.
16. Moriarty, R.M.; Vaid, R.K.; Koser, G.F. *Synlett* **1990**, 365.
17. Dr. Andrew N. French (Radford University) has initiated research on the synthesis of chiral benziodoxoles with aryl and perfluoroalkyl substituents at C-3 and the use of such compounds for the asymmetric functionalization of alkenes; personal communication from A.N. French to G.F. Koser.

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