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1-AMIDO-3-(1*H*)-1,2-BENZIODOXOLES: STABLE AMIDOIODANES AND REAGENTS FOR DIRECT AMIDATION OF ORGANIC SUBSTRATES

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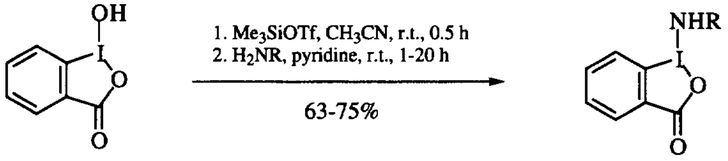
Abstract: Amidobenziodoxoles **2** can be prepared from benziodoxole **1**, trimethylsilyltriflate and the appropriate amides in the form of stable, microcrystalline compounds. Amidobenziodoxoles **2** react with adamantane **3** or *N,N*-dimethylarylamines **5** to afford the corresponding products of amidation, **4** and **6**.

Hypervalent iodine derivatives with I-N bonds are generally less common than those with I-O bonds.[1] Most of these compounds lack stability and are sensitive to moisture. The known compounds of this type are represented by iminoiodanes, PhI=NR, and azidoiodanes, $ArI(N_3)X$.[1] In particular, iminoiodanes have found some synthetic application as efficient reagents for direct aziridination of unsaturated organic substrates,[1] while azidoiodanes are useful azidating reagents.[1,2] Only few examples of the very unstable amidoiodanes, PhI[NHC(O)R]X (R = alkyl or aryl; X = OTs, OAc) are known.[3] In this communication we wish to report the preparation and chemical reactivity of stable amidoiodanes, derivatives of benziodoxole.

Amidobenziodoxoles **2** can be conveniently prepared in one step from the commercial 2-iodosylbenzoic acid **1**, trimethylsilyltriflate and the appropriate amide, RNH_2 (R = acyl or tosyl). All five adducts **2a-e** were isolated as thermally stable, white, non-hygroscopic, microcrystalline solids and identified by spectral data and elemental analyses.[4]

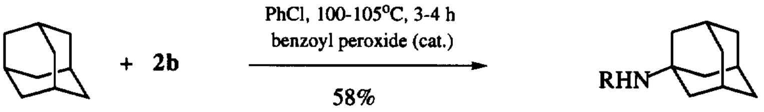


1

2a, R = $C(O)CH_3$
2b, R = $C(O)C_6H_4Cl$-*p*
2c, R = $C(O)C_2H_5$
2d, R = $C(O)NH_2$
2e, R = Ts

Proton NMR spectra of these compounds show signals and splitting patterns typical of *o*-substituted benzene rings, as well as the expected signals of the substituent R in the amido group. We propose the cyclic, benziodoxole structure **2** for all adducts, based on available X-ray data for other known 1-substituted benziodoxoles, such as hydroxy,[1] methoxy,[1] azido,[2] and cyanobenziodoxoles.[5] The cyclic structure of products **2a-e** is further confirmed by IR spectra, in which the carbonyl peak is observed at 1615-1620 cm^{-1}. In contrast, the carbonyl group in the non-cyclic 2-iodosyl benzoate derivatives, such as 3-alkyl-2-iodosylbenzoic acids, has a noticeably higher wavenumber at 1710 cm^{-1}.[6]

Preliminary studies of chemical reactions of amidobenziodoxoles **2** indicate that their reactivity is generally similar to that of the previously reported azidobenziodoxoles.[2] In particular, amidobenziodoxoles **2** can be used as amidating reagents toward polycyclic alkanes under radical conditions. For example, reagent **2b** reacts with adamantane **3** in chlorobenzene at 100-105°C in the presence of a catalytic amount of benzoyl peroxide to afford 1-amidoadamantane **4** in a moderate yield.[7] It should be mentioned that, compared to azidobenziodoxoles, amides **2** are less reactive toward hydrocarbons, and yields of products are generally lower.

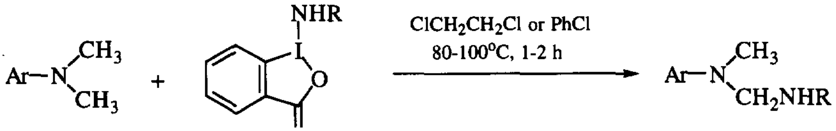


3

4
R = $C(O)C_6H_4Cl$-*p*

Analogous to azidobenziodoxoles, compounds **2** can serve as efficient amido transfer reagents toward *N,N*-dialkylarylamines. In a typical experiment, reagent **2** reacts with *N,N*-dimethylanilines **5** in dichloroethane at reflux to afford the corresponding *N*-amidomethyl-*N*-methylanilines **6** as major products.

Products **6** were identified by ^{1}H NMR and GC-MS of the reaction mixture.[8]



5 **2**

6a, R = $C(O)CH_3$, Ar = Ph
6b, R = $C(O)C_6H_4Cl$-*p*, Ar = *p*-BrC_6H_4

In conclusion, we have prepared and isolated as individual, stable compounds amidobenziodoxoles **2a-e**. Compounds **2** are potentially useful reagents for direct amidation of adamantane and *N,N*-dialkylarylamines.

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† Participants of the UMD Department of Chemistry Summer 1996 Undergraduate Research Program.

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4. *General Procedure for the Preparation of 1-Amido-3-(1H)-1,2-benziodoxoles (2)*: To a stirred suspension of 2-iodosylbenzoic acid **1** (0.528 mg, 2 mmol) in dry CH_3CN (5 ml), trimethylsilyltriflate (0.425 ml, 2.2 mmol) was added under nitrogen at room temperature. The reaction mixture was stirred 30 min and then pyridine (0.158 ml, 2 mmol) and the appropriate amide (4 mmol) were added. The resulting mixture was additionally stirred for 1 to 20 h until the formation of a white precipitate. The precipitate was filtered, washed with anhydrous acetone (5 ml) and dried in vacuo to afford analytically pure products **2**.

   For **2a**: yield 0.43 g (70%), mp 180-181°C; IR (CCl_4): 3220 (s, br, NH), 3090 (m, Ar), 2921 (m, CH_3), 1675 and 1615 (s, C=O) cm^{-1}; ^{1}H NMR ($CDCl_3/CF_3CO_2H$, 20:1): δ 8.27 (d, 1H, J = 8 Hz), 7.90 (m, 2H), 7.68 (t, 1H, J = 8 Hz), 2.23 (s, 3H, Me). Anal: Calc. for $C_9H_8INO_3$: C, 35.43; H, 2.64; N, 4.59. Found: C, 35.53; H, 2.64; N, 4.48.

   For **2b**: yield 0.60 g (75%), mp 173-174°C; IR (KBr): 3181 (s, br, NH), 3090 and 3083 (m, Ar), 1656

and 1615 (s, C=O) cm^{-1}; ^{1}H NMR ($CDCl_3/CF_3CO_2H$, 20:1): δ 8.30 (d, 1H, J = 8 Hz), 8.10 (t, 1H, J = 8 Hz), 7.95 (d, 1H, J = 8 Hz), 7.80 (t, 1H, J = 8 Hz), 7.75 (d, 2H, J = 8 Hz, p-C_6H_4Cl), 7.50 (d, 2H, J = 8 Hz, p-C_6H_4Cl). Anal: Calc. for $C_{14}H_9ClINO_3 \cdot 0.5H_2O$: C, 40.95; H, 2.45; N, 3.41. Found: C, 40.50; H, 2.24; N, 3.41.

For **2c**: yield 0.47 g (73%), mp 173-175°C; IR (KBr): 3241 (s, br, NH), 3090 (m, Ar), 2975, 2934 (m, C_2H_5), 1669 and 1615 (s, C=O) cm^{-1}; ^{1}H NMR ($CDCl_3/CF_3CO_2H$, 20:1): δ 8.30 (d, 1H, J = 8 Hz), 8.10 (t, 1H, J = 8 Hz), 7.96 (d, 1H, J = 8 Hz), 7.78 (t, 1H, J = 8 Hz), 2.50 (q, 2H, CH_2), 1.26 (t, 3H, CH_3). Anal: Calc. for $C_{10}H_{10}INO_3$: C, 37.64; H, 3.16; N, 4.39. Found: C, 37,40; H, 3.14; N, 4.28.

For **2d**: yield 0.38 g (63%), mp 201-203°C; IR (KBr): 3300-3100 (s, br, NH and NH_2), 3090 (m, Ar), 1690 and 1620 (s, C=O) cm^{-1}; ^{1}H NMR ($CDCl_3/CF_3CO_2H$, 20:1): δ 8.30 (d, 1H, J = 8 Hz), 8.10 (t, 1H, J = 8 Hz), 7.95 (d, 1H, J = 8 Hz), 7.80 (t, 1H, J = 8 Hz). Anal: Calc. for $C_8H_7IN_2O_3$: C, 31.40; H, 2.31; N, 9.15. Found: C, 31.32; H, 2.27; N, 9.14.

For **2e**: yield 0.50 g (67%), mp 207-209°C; IR (KBr): 3181 (s, br, NH), 3090 and 3083 (m, Ar), 2921 (m, CH_3), 1656 (s, C=O), 1325 (s, SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3/CF_3CO_2H$, 20:1): δ 8.33 (d, 1H, J = 8 Hz), 8.12 (t, 1H, J = 8 Hz), 7.95 (d, 1H, J = 8 Hz), 7.85 (t, 1H, J = 8 Hz), 7.75 (d, 2H, J = 8 Hz, p-C_6H_4Me), 7.35 (d, 2H, J = 8 Hz, p-C_6H_4Me), 2.50 (s, 3H, Me). Anal: Calc. for $C_{14}H_{12}INO_4S$: C, 40.30; H, 2.90; N, 3.36. Found: C, 40.34; H, 2.92; N, 3.38.

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6. Panetta, C.A.; Garlick, S.M.; Durst, H.D.; Longo, F.R.; Ward, J.R. *J. Org. Chem.* **1990**, *55*, 5202.
7. *Amidation of Adamantane by Amidobenziodoxole **2b***: To a stirred mixture of amidobenziodoxole **2b** (0.2 g, 0.5 mmol) and adamantane **3** (0.07g, 0.47 mmol) in dry chlorobenzene (20 ml), a catalytic amount of benzoyl peroxide (5 mg) was added under nitrogen at room temperature. The reaction mixture was heated to 100-105 °C for 3-4 hrs, and then evaporated in vacuum to give a residual oil which was separated by column chromatography on silica gel to give amidoadamantane **4** as a waxy solid; R_f (dichloromethane) = 0.5, yield 0.08 g (58%), ^{1}H NMR ($CDCl_3$): δ 7.75 (d, 2H, J = 8 Hz, p-C_6H_4Cl), 7.50 (d, 2H, J = 8 Hz, p-C_6H_4Cl), 6.5 (br. m, 1H, NH), 2.2-1.1 (m, 15H). Hydrolysis of amide **4** affords the known 1-aminoadamantane.
8. *Reaction of N,N-Dimethylaniline with 1-Amido-3-(1H)-1,2-benziodoxole **2a***: To a stirred mixture of amidobenziodoxole **2a** (0.225 g, 0.824 mmol) in dry 1,2-dichloroethane (20 ml) *N,N*-dimethylaniline (0.099 g, 0.824 mmol) was added under nitrogen at room temperature. The reaction mixture was then refluxed for 1 hr and evaporated in vacuum to give a darkening, semisolid residue. A relatively unstable product **6a** was identified by ^{1}H NMR and GC-MS of the reaction mixture: ^{1}H NMR ($CDCl_3$): δ 6.6-7.2 (m, 6H, Ph and NH), 5.5 (s, 2H, CH_2); 2.95 (s, 3H, CH_3); 2.10 (s, 3H, Ac); MS (EI, 70 eV): m/z (%) 178 (10), M^+.

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