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Synthesis of phosphate stabilised iodanes and their application in intramolecular aryl migrations†

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A diverse set of hydroxy-benzo[e]iodadioxaphosphinine oxides and derived diaryl iodonium salts are prepared and two examples are characterized by X-ray crystallography, featuring an out-of-plane geometry of the hypervalent bond for both compound classes. Treatment of the phosphate-stabilized diaryliodonium salts with $\text{Ca}(\text{OH})_2$ results in an efficient base-induced intramolecular aryl migration under aqueous conditions, yielding iodo-substituted diaryl ethers with yields up to 94%. Our findings highlight the synthetic potential of this previously underexplored compound class in organic transformations.

Hypervalent iodine compounds are versatile reagents for oxidative transformations in organic synthesis.¹ Substrates like phenyliodine (iii)diacetate (PIDA), 2-iodoxybenzoic acid (IBX) and Dess–Martin–Periodinan (1, DMP) can be used in alcohol oxidations,² alkene functionalization³ or heterocycle syntheses.⁴ Most *O*-stabilized iodanes like IBX or DMP are characterized by a cyclic benziodoxolone structure, leading to higher thermal stability and more controlled reactivity.⁵ Such beneficial cyclic structures can also be accomplished with alcohol functionalities⁶ (2) or through pseudo-cyclic interactions with tethered *N*-heterocycles⁷ (3) or sulfonyl-groups⁸ (4, Fig. 1A). So far, only a limited amount of phosphorus oxoacid substituted iodanes were described. Examples include [hydroxy(phosphoryloxy)iodo]arenes 5 and its cyclic derivative 6. While most phosphorus-containing iodanes like 5 and 6 are based on P–O ligands at the I(III) center,⁹ only a few examples of intramolecular P–O-stabilization are known. Balthazor *et al.* reported the synthesis of the five-membered iodane 7 (Fig. 1B), whereas Protasiewicz *et al.* published the synthesis

of a phosphorus-containing iodane with a pseudo cyclic structure.¹⁰ The first intramolecular phosphate stabilized iodane (8a) was synthesized by J. E. Leffler and H. Jaffe in 1973 by treating the corresponding phosphoric acid with peracetic acid.¹¹ However, these initial investigations are focused on the structure of these compounds without investigating their further reactivity. Herein, we want to present the synthesis of various phosphate-substituted iodanes, their transformation into the stabilized-diaryl derivatives 9 and their reactivity in a base induced aryl migration (10, Fig. 1C).

Starting with the oxidation of various *o*-iodo phenyl phosphates (11), the corresponding cyclic iodosophenylphosphoric acids 8a–f and 8h–i were obtained by using *m*CPBA as the oxidant (Scheme 1). The established oxidation reagents like Oxone[®] and Selectfluor[®] were incompatible due to the formation of various side products like multiple fluorinations. Electron-rich and poor substituted iodanes (8a–f, 8h–i) in *ortho*-, *meta*- and *para*-position regarding the iodine

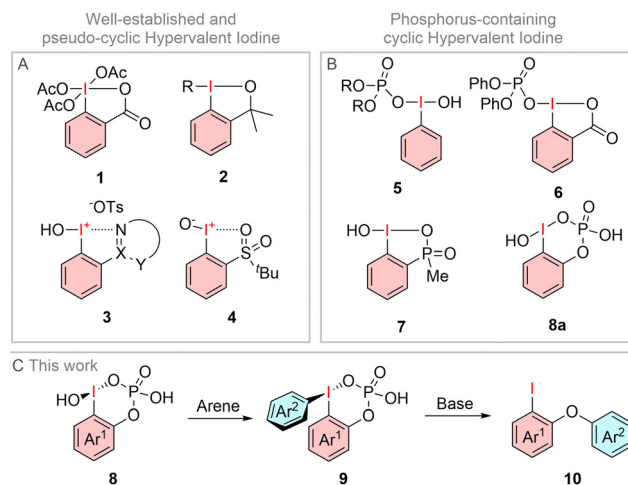


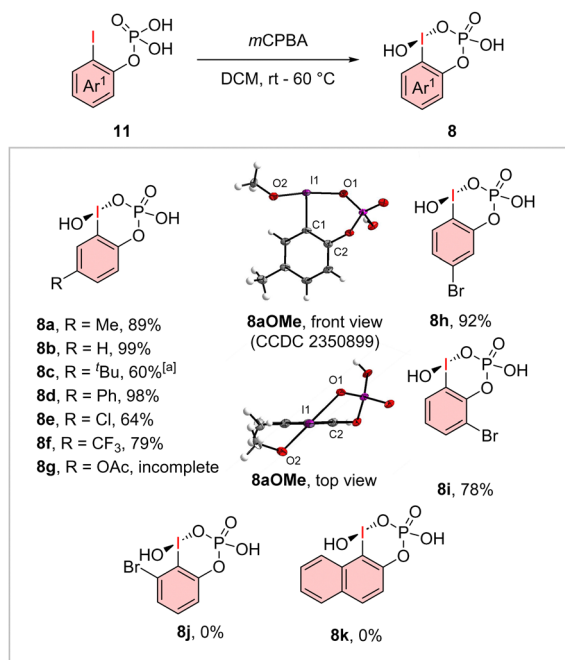
Fig. 1 (A) Common intramolecular stabilized iodanes 1–4, (B) P–O-stabilized iodanes 5–8, (C) aim of this work.

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† Electronic supplementary information (ESI) available: Experimental procedures, analytical data (¹H-, ¹³C- and ¹⁹F-NMR-chemical shifts, IR-bands, melting points) including the corresponding NMR-spectra and X-ray data can be found in the supporting information. CCDC 2350898 and 2350899. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d4cc04934a>





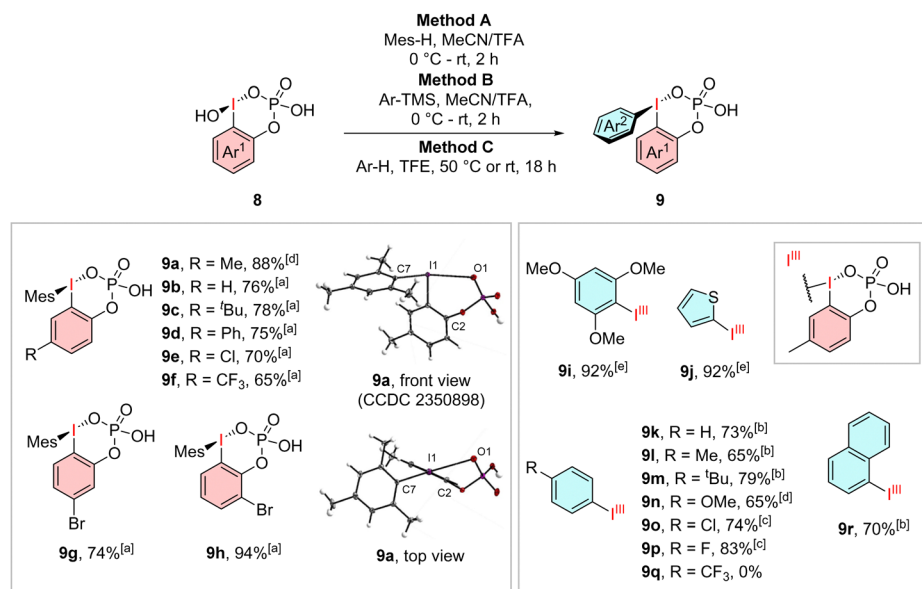
Scheme 1 Oxidation of *o*-iodo phenyl phosphates into iodosophenyl-phosphoric acids **8a–k** and X-ray structure of **8aOMe**. General reaction conditions: **11** (1.00 eq.), *m*CPBA (2.00 eq.), DCM (0.2 M), stirring 5 min at rt and 2 h at 60 °C. ^a reaction at rt with 1.20 eq. *m*CPBA.

center was obtained in high yields of up to 99%. The acetylated derivative **8g** was not accessible due to incomplete oxidation. The 4- and 5-methoxy derivatives could be synthesized, but they were obtained as impure materials and proved to be too unstable for further transformations. Substrates with a second *ortho*-substituent next to the iodine (**8j–k**) could also not be

isolated due to the *ortho*-effect in stabilised-iodanes.¹² Also, instead of the desired oxidation instant diiodination was observed. We obtained the X-ray structure of the methoxy ligand-exchanged derivate **8aOMe** and gained further insights into the solid-state structure. Therein, the cyclic structure was confirmed with an I1–O1 distance of 2.27 Å and an O1–I1–C1–C2 angle of 43.8° which generates an out-of-plane geometry.

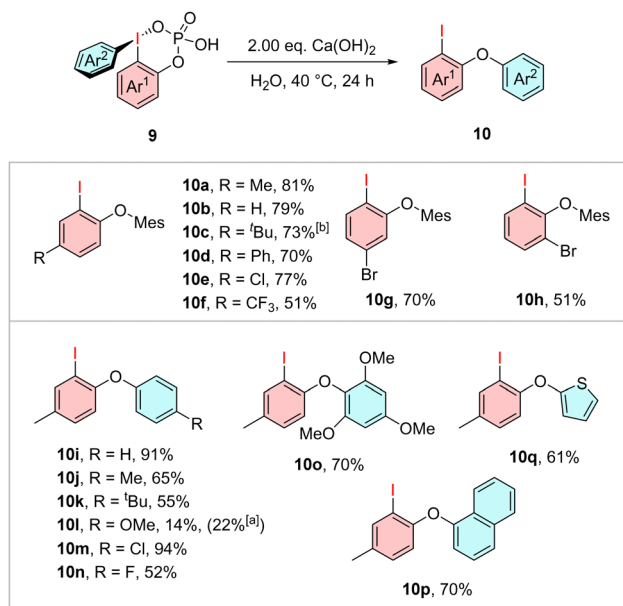
We then further examined their reactivity and tried to synthesize their diarylated analogues (Scheme 2). By using an excess of mesitylene, as suitable electron-rich arene for the coupling, in an MeCN/TFA mixture, we were able to generate the *ortho*-phosphate stabilized species **9a–h** in high yields of up to 94%. The synthesis of other strong electron-rich derivatives **9i–j** and **9n** can be carried out in high yields of up to 92% but reaches its limits already for *tert*-butylbenzene. The regioselective coupling of arenes with more than one reactive side was achieved using an excess of their trimethylsilyl substituted derivatives in MeCN/TFA. Using this method, we were able to obtain the less electron rich compounds **9k–m**, **9o–p** and **9r** in yields from 65–83%. Utilization of one equivalent of the fluorinated and chlorinated trimethylsilyl arenes suppressed the formation of an undesired diaryliodonium species. Arenes with stronger electron-withdrawing trifluoromethyl groups could not be converted into the desired product **9q**. Again, we were able to obtain a crystal structure for the phosphate-stabilized iodane **9a**, which shows the same cyclic geometry, but with an elongated I1–O1 bond length of 2.99 Å whereas the O1–I1–C1–C2 angle of 40.3° creates a similar out-of-plane geometry as observed in **8a**.

To demonstrate the reactivity of these phosphate-stabilized diaryliodonium salts the aryl migration into diaryl ethers was investigated. A reaction which was previously described for *ortho*-triflate-substituted iodonium salts by Han *et al.*¹³ Starting



Scheme 2 Arylation of iodosophenylphosphoric acids into **9a–r** and X-ray structure of **9a**. General reaction conditions: ^a method (A) **8** (1.00 eq.), mesitylene (2.00 eq.), MeCN/TFA (1:1, 0.1 M), stirring 5 min at 0 °C and 2 h at rt. ^b Method B: **8** (1.00 eq.), TMS-arene (1.50 eq.), MeCN/TFA (1:1, 0.1 M), stirring 5 min at 0 °C and 2 h at rt. ^c Method B with 1.00 eq. of TMS-arene. ^d Method C: **8** (1.00 eq.) arene (2.00 eq.), TFE (0.1 M), stirring at 50 °C for 18 h. ^e Method C with stirring at rt.





Scheme 3 Substrate scope of diaryl ethers **10a–q** synthesized from **9**. General reaction conditions: **9** (100 μmol), Ca(OH)₂ (2.00 eq.), H₂O (2 mL), 40 °C, 24 h. ^aAt room temperature, ^b48 h reaction time.

with the literature conditions of Cs₂CO₃ in MeCN the diaryl ether **10a** was obtained in a high yield of 98%, whereas the reaction was carried out at 80 °C instead of room temperature. Due to their potential physiological relevance, we investigated this reaction under aqueous conditions (see ESI,[†] Table S1) and obtained the diaryl ether **10a** in a yield of 81% with the use of Ca(OH)₂ as base at 40 °C. Under these optimized conditions, all the previously synthesized arylated iodanes **9** were examined (Scheme 3). Different substitutions in *meta*- and *para*-position to the iodine center caused a minor variance in the reactivity, which yielded the ethers **10b–e** and **10g** in up to 79%. The CF₃-substituted derivative **10f** was isolated in 51% yield. Another substitution in the second *meta*-position to the iodine also resulted in diminished yields of 51% as observed in product **10h**. The phenyl-substituted derivative **10i** yielded the diaryl ether in 91%, whereas the toluyl-substituted compound **10j** was obtained in a lower yield of 65%. Even more electron-rich arenes, like *tert*-butyl- and methoxy-substituted derivatives **10k** and **10l**, resulted in moderate yields of 55% and a low yield of 14%, respectively. For the latter the yield could be increased to 22% by conducting the reaction at room temperature.

In contrast to the high yield of 94% for the chlorinated derivative **10m**, the fluorinated ether **10n** was obtained just in a moderate yield of 52%, while the main side product was generally the iodinated arene as mentioned in the optimization (see ESI,[†] Table S1). Furthermore, the TMP-, naphthalene- and thiophene compounds **10o**, **10p**, and **10q** were obtained in good yields of up to 70%.

In summary, we synthesized a variety of different iodosophenylphosphoric acids, which could be subsequently converted towards their phosphate-stabilized diarylated species through ligand exchange with different arenes. The X-ray data

of both compounds confirmed a cyclic structure that leads to an out-of-plane distortion of the hypervalent bond. These novel arylated iodanes could successfully applied in base-induced intramolecular aryl migration in an aqueous medium to obtain various iodo-substituted diaryl ethers in yields up to 94%. Since this interesting reactivity was observed in aqueous solution under ambient conditions a potential physiological relevance might be operational and is part of further investigations in our laboratory.

Data availability

The data supporting this study, including detailed experimental procedures, spectroscopic data, and additional information, are available in the ESI.[†] Crystallographic data for the structures reported in this article have been deposited at the Cambridge Crystallographic Data Centre (CCDC) under deposition numbers: 2350899 and 2350898.

Conflicts of interest

There are no conflicts to declare.

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