Two new hypervalent iodine reagents containing furan and thiophene moieties in addition to a carbonyl group in the vicinity of the iodine atom were synthesised and characterised. The X-ray analysis of both compounds revealed a strong intramolecular contact between the carbonyl oxygen and the hypervalent iodine atom with tosylate as a counter ion. The two reagents showed a broad range of synthetic applications and proved to be versatile oxidizing agents.

The chemistry of hypervalent iodine compounds has expanded largely during the last two decades. Due to their readily availability, easy handling and diversity, organic hypervalent iodine reagents are widely used in modern synthetic organic chemistry. Their electrophilic nature, in addition to their superior leaving group ability (~10^6 times triflate) are the key features behind their unique reactivity.1,2 Hence, hypervalent iodine reagents found a wide range of synthetic applications, especially selective oxidative transformations including, but not limited to, oxidative C–C, C–heteroatom and heteroatom–heteroatom couplings,3–6 oxidative rearrangements,7–10 difunctionalisation of alkenes,11–13 and dearomatisation of phenols.14–18 Moreover, hypervalent iodine compounds are environmentally friendly alternatives to heavy metal oxidants as a result of their low toxicity and mild reaction conditions. As hypervalent iodine reagents are electrophilic in nature, heteroatoms in the vicinity of the electrophilic iodine centre affect the structural features, reactivity and selectivity of hypervalent iodine reagents.19–21 Various reagents incorporating nitrogen-containing heterocyclic units of various classes have been reported in literature (Figure 1).20–26

On the other hand, the pyrrole analogue 16 was prepared following a different synthetic route (Scheme 2).28,29 Iodoketone 16 was obtained in 85% overall yield starting from anthranilic acid over four steps. N-methylation of 16 afforded the iodoketone 17 in 88% yield. Having the iodoketones 10, 11 and 17 in hand, their oxidation to the corresponding hypervalent iodine reagents was investigated. Although the oxidation of simple iodoarenes usually proceeds smoothly, the oxidation of 10, 11 and 17 was cumbersome. A wide range of oxidants and oxidation protocols were investigated, but either there was no reaction at all, or the reaction mixture was very complex to isolate the oxidised products in a pure form, although the ^1H NMR of the crude reaction mixture showed an evidence of the formation of the corresponding iodine(III) species in many attempts.
Scheme 2. Synthesis of iodoketones bearing a pyrrole moiety.

Only the oxidation of iodoarenes 10 and 11 using m-chloroperbenzoic acid (mCPBA) in the presence of p-toluenesulfonic acid monohydrate was successful and the products 18 and 19 were isolated in a pure form in 86% and 85% yield, respectively (Scheme 3). The oxidation products of 10 and 11 were recrystallised from hexane-dichloromethane and characterised by single crystal X-ray crystallography. The solid-state structure of the products ruled out the initially expected Koser’s type structures with a close tosylate – iodine distance and confirmed the pseudocyclic forms 18 and 19 manifesting the Lewis-base assisted activation of the iodine centre.

Scheme 3. Oxidation of iodoketones 10 and 11.

Analysis of the X-ray data of tosylate 18 (Figure 2A) showed the presence of a strong intramolecular interaction of 2.342 Å between the carbonyl oxygen and the hypervalent iodine atom besides one short iodine-oxygen covalent bond [I(1)-O(1) = 1.945 Å] and the iodine-carbon covalent bond [I(1)-C(1) = 2.080 Å]. The observed angle [O(1)-I(1)-O(2)] of the iodonium ion fragment of 18 (167.7°) is in good agreement with the distorted T-shaped geometry characteristic to hypervalent iodine(III) compounds.

Although a single crystal of high quality of product 19 could not be obtained, a crystal structure showing only the cationic fragment of product 19 was obtained (Figure 2B). Similar to product 18, the analysis of the X-ray data of product 19 showed the presence of a strong intramolecular interaction of 2.326 Å between the carbonyl oxygen and the hypervalent iodine atom besides one short iodine-oxygen covalent bond [I(1)-O(1) = 1.943 Å] and iodine-carbon covalent bond [I(1)-C(1) = 2.155 Å] with an observed angle [O(1)-I(1)-O(2)] of 166.7° indicating a distorted T-shaped geometry characteristic to hypervalent iodine(III) compounds.

The iodonium ion of 19 showed a secondary interaction (2.830 Å) between the coordinated carbonyl oxygen (O(2)) and the sulfur atom (S(1)) of the thiophene ring which is not observed in the case of its furan analogue 18.

Figure 2. X-ray crystal structure of compound 18 (A) and the cationic fragment of compound 19 (B). Hydrogen atoms bound to carbon atoms were removed for clarity. Selected bond lengths and angles: 18: I(1)-O(1) 1.945 Å, I(1)-O(2) 2.342 Å, I(1)-C(1) 2.080 Å, O(1)-I(1)-O(2) 167.7°; 19: I(1)-O(1) 1.943 Å, I(1)-O(2) 2.326 Å, I(1)-C(1) 2.155 Å, O(1)-I(1)-O(2) 166.7°.

A broad range of potential synthetic applications of hypervalent iodine reagents 18 and 19 as versatile oxidizing reagents is demonstrated (Table 1). Generally, all the reactions with both reagents lead to the formation of the expected products in moderate to excellent yields. The furan-derived reagent 18 proved to be more reactive than its thiophene analogue 19 which might be attributed to the presence of additional secondary interaction in the case of compound 19 (vide supra) rendering it more stable and hence less reactive.

Sulfoxides 20 and 21 were obtained in excellent yields (90-92%) via the oxidation of the corresponding sulfides using 18 and 19. Oxidizing thiocianole under the same conditions with Koser’s reagent led to the isolation of 20 in 80% yield. Phenol deoxygenation of p-cresol and 2,4-dimethylphenol lead to the corresponding ketones 22 and 23 in 76 - 83% yield. When Koser’s reagent was used as the oxidant for the oxidative dearomatisation of p-cresol, the corresponding ketone 22 was obtained in 74% yield. Both compounds 18 and 19 affected the α-tosyloxylation of acetophenone and propiophenone in good yields. Performing the α-tosyloxylation of propiophenone in a catalytic manner using 10 mol% of 10, 11, and 17 as organocatalysts in the presence of mCPBA as the terminal oxidant led to the formation of product 25 albeit in low yields, 21%, 10%, and 13%, respectively. In addition, the oxidative rearrangement of benzalacetophenone mediated by 18 and 19 in methanol afforded the corresponding α-aryl ketone 26 in 56% and 53% yield, respectively. Moreover, Hofmann rearrangement of benzalacetophenone led to the corresponding carbamate 27 in good yield. Reagents 18 and 19 are efficient oxidants for oxidative heterocyclisations. 3,5-Diphenyl-1,2,4-thiadiazole (28) was obtained in 86% and 83% yield via oxidative dimerization of thiobenzamide using reagents 18 and 19, respectively. In the same context, the reaction of benzaldehyde oxime with 18 and 19 in acetonitrile and 2,2,2-trichloroacetanitride proceed smoothly to afford 1,2,4-oxadiazoles 29 and 30 in high yields.
Using 18 and 19, respectively; ϴϬ% using Koser’s reagent; ϰϰ% using Koser’s reagent.

Table 1. Synthetic applications of reagents 18 and 19.

In conclusion, the synthesis and structural elucidation of two new hypervalent iodine reagents 18 and 19 is reported. The X-ray analysis of 18 and 19 showed the presence of strong intramolecular interaction (2.342 and 2.326 Å) between the carbonyl oxygen and the hypervalent iodine atom of compounds 18 and 19. Reagents 18 and 19 are versatile reagents for a wide range of oxidative transformations such as oxidation of sulfides, phenol dearamatisation, oxidative rearrangements and heterocyclisations. In general, both reagents lead to the formation of the products in moderate to excellent yields. Moreover, the furan derived reagent 18 shows higher reactivity than its thiophene analogue 19 in most cases.

Table 1. Synthesis of reagents 18 and 19.

Conflicts of interest
The authors declare no conflicts of interests.

Notes and references


