Aerobic oxidative iodination of ketones catalysed by sodium nitrite "on water" or in a micelle-based aqueous system†

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Selective and efficient aerobic oxidative iodination of ketones in aqueous media was achieved by using molecular iodine as the source of iodine atoms, air as the terminal oxidant, sodium nitrite ($NaNO_2$) as the catalyst and H_2SO_4 as the activator of the overall catalytic process. The efficiency of the reaction, resulting in α-iodo ketones, was significantly improved in an aqueous solution of the anionic amphiphile sodium dodecyl sulfate (SDS), capable of self-assembly into micelle-based aggregates, thus forming a reactive micellar system. The regioselectivity of iodofunctionalization of aryl methyl ketones was regulated by the reaction medium used: in an aqueous micelle-based system the methyl group was iodinated, while in anhydrous MeCN aryl iodides were formed with high selectvity.

Introduction

Iodinated organic compounds and methods for selective iodination have received significant attention among the scientific community. Iodo-substituted organic compounds are important precursors and synthons in organic synthesis, above all in carbon-carbon, carbon-oxygen and carbon-nitrogen bond formation, for their useful properties reflected in medicine as contrast agents or radioactively labelled markers and further, many of them are biologically active.[1] Aryl iodides and α-iodo ketones are especially convenient tools for the mentioned purposes. The most logical choice of iodinating agent for introduction of iodine atoms into organic compounds is the use of molecular iodine (I_2) or the iodide anion (I^-), but since I_2 is very often poorly reactive, substantial efforts have been invested in development of efficient, mild and selective methods for direct introduction of an iodine atom into organic molecules. Synthetic strategies for electrophilic iodination of organic compounds using I_2 or I^- have been reviewed recently[2] and it is clear that oxidative iodination using these two sources of iodine atoms in combination with environmentally benign and atom efficient oxidants in non-volatile or non-toxic solvents seems to be the most promising methodology from the viewpoint of the green approach to organic synthesis.

The use of H_2O_2 or even O_2 as the most environmentally benign oxidants[3] and water as the reaction medium[4] represent promising options in the constant search for cheaper, cleaner and more efficient technologies for oxidative transformations of organic molecules. The potential inconvenience for performing organic reactions in water is very often connected with the incompatibility of organic molecules with water, although some organic reactions can be carried out simply by stirring the neat reactants in an aqueous suspension described under the term "on water" conditions.[5] The addition of amphiphiles in water ordinarily cause their self-association into micelles which is driven by the hydrophobic effect,[6] well described by solvation thermodynamics that play a role in the overlap of the hydratation shells of the hydrophobic parts of the molecules on self-assembly. Accommodation of insoluble organic compounds in such a media has been promoted and reviewed as a possible approach to performing organic reactions in water.[7] Reactions in micellar systems,[8] including the micellar catalysis approach of using acid-surfactant-combined catalysts,[9] have considerably extended organic chemistry in water.

Water-based aerobic catalytic systems received significant attention and made much progress in the past few years, but they were used mainly for aerobic oxidation of alcohols,[10] first promoted by Sheldon and co-workers[11] using a recyclable water-soluble palladium complex catalyst under 30-bar air pressure. Various transition-metal catalysts were used for these purposes,[12] while very recently a catalyst-free procedure of aerobic "on and in water" oxidation of aldehydes was reported.[13] A metal-free catalytic system for aerobic oxidation of alcohols was recently promoted using sodium nitrite ($NaNO_2$) in combination with an efficient co-catalyst in an organic solvent[14] or aqueous media,[15] performed in an air filled autoclave. Sodium nitrite is a simple, inexpensive inorganic compound with an unique redox property, which under acidic conditions releases nitric oxide (NO), known as a highly reactive unstable species oxidisable with molecular oxygen to nitrogen dioxide (NO_2), which is then involved in further oxidation processes, releasing NO and thus continuing the cycle.[14–16] This ability of $NaNO_2$ as a catalyst has been taken advantage of aerobic oxidative halogenation of organic compounds,[17] but organic solvents were always

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† Electronic supplementary information (ESI) available: 10 mmol scale synthesis procedures of compounds **4** and **10a** and isolation of products without using organic solvents; indentification data for known compounds **2**, **6**, **8**, **10b**, **12**, **20**, **10c**, and **21**; ^{1}H and ^{13}C NMR spectra of unknown compounds **10d**, **22**, **10e**, and **23**. See DOI: 10.1039/b902230a

used as the reaction medium. This leads us to the challenging question of if it is possible to perform selective and efficient catalytic aerobic oxidative halogenation of organic compounds successfully in water. In a view of our continuing efforts to develop new, environmentally benign, synthetic methods for selective halogenation of organic compounds,[17b–d,18] we now report the selective and efficient iodination of various types of ketones by an aerobic oxidative process catalyzed by the catalyst sodium nitrite in an aqueous micellar system.

Results and discussion

Oxidative iodination of organic compounds under an oxygen atmosphere was introduced by Radner who used lower nitrogen oxide species in order to catalyze the aerobic oxidative iodofunctionalisation of arenes and cyclohexene in organic solvents.[19] Later, only a few examples of aerobic oxidative iodination have been described and only arenes were efficiently iodinated with molecular iodine under an oxygen atmosphere using bismuth (III) salts[20] or polyoxometallate[21] catalysts in acetonitrile or nitrobenzene as reaction medium. We have recently demonstrated the efficient and selective aerobic oxidative iodination of arenes, carbonyls, alkenes and alkynes with molecular iodine or iodide using sodium nitrite as catalyst and air as the terminal oxidant performing the reactions under acidic conditions in organic solvents.[17b,c] To the best of our knowledge, there is no previous reports on an aerobic oxidative halogenation of organic compounds in water as reaction medium and this was a very compelling reason for further investigations of the $NaNO_2$-based catalytic system for aerobic oxidative iodination of organic molecules.

We started our investigation by studying the aqueous aerobic oxidative iodination of acetophenone **1** as a model substrate. Following the overall stoichiometric equations for aerobic oxidative iodination of organic compounds using I^- (1), the presence of at least one equivalent of protons is crucial for the reaction, while using I_2 (2) the presence of an acid would not be necessary. However, the presence of an acid is in both cases indispensable for the activation of the $NaNO_2$ catalytic oxidative cycle, thus tuning the overall process.

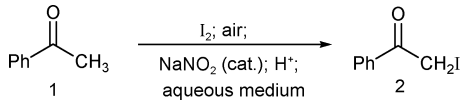
$$S\text{–}H + I^{\ominus} + 0.5\ O_2 + H^{\oplus} \rightarrow S\text{–}I + H_2O \quad (1)$$

$$2\ S\text{–}H + I_2 + 0.5\ O_2 \rightarrow 2\ S\text{–}I + H_2O \quad (2)$$

In a typical mmol-scale experiment, to a magnetically stirred dispersion of acetophenone **1** in water contained in a 50 mL vessel, I_2 or KI and acid was added, followed by addition of a catalytic amount of $NaNO_2$. The reaction vessel was closed with a balloon (1 L) filled with air and the reaction mixture magnetically stirred for 12 hours. The reaction parameters (iodine source, acid and its amount, amounts of $NaNO_2$ catalyst and reaction temperature) were varied and the conversion of acetophenone **1** to its iodinated derivative 2-iodo-1-phenylethanone **2** analyzed. As we have already reported, MeCN or EtOH could be appropriate reaction media for this transformation;[17b,c] though the efficiency of the reaction in pure water decreased considerably (entry 1, Table 1), it was improved by increasing the reaction temperature and the amounts of added acid and catalyst (entries 2,3). We found it possible to succeed in quantitative conversion of **1** to **2** by adding to the reaction system the anionic amphiphile sodium dodecyl sulfate (SDS), whose micellisation in aqueous media was well explored.[22] The addition of SDS in the amount required for critical micelle concentration (CMC; 8.1×10^{-3} M at 25 °C)[8,27] increased the conversion of starting material (entry 4) in comparison with the reaction in pure water medium, while the complete iodofunctionalisation to **2** was achieved in a 0.1 M SDS micellar aqueous solution at 60 °C in the presence of 0.5 mmol of H_2SO_4 and 12 mol% of $NaNO_2$ (entry 7) using molecular iodine as the reagent. The experiments also revealed that the presence of a strong acid like H_2SO_4 ($pK_a = -10$) is essential and beneficial for the efficiency of the reaction since the use of the same amount of the weaker acid $HClO_4$ ($pK_a = -7$) was found to be insufficient (entry 10) to successfully tune the reactivity of the aerobic system. The effect of the source of the iodine atom on aerobic oxidative iodination of target compound **1** was also studied and results showed clearly that iodination using I_2 was more efficient than using iodide anion (I^-) as the iodine source (entry 11). The iodinating system I_2/air/$NaNO_2$(cat.)/H_2SO_4 was thus found to be the right choice for efficient aerobic oxidative iodination of the model substrate acetophenone **1** in a SDS micelle-based aqueous system and this was then used in all further experiments.

It is known from the literature that in the case of reactions performed "on water" stirring of the reaction mixture has a crucial effect on the rate and efficiency of these reactions and that liquid substrates are usually more reactive than solid ones.[5c–g] Liquid substrates, or those solids with melting points lower than the reaction temperature, are disrupted by vigorous stirring into small droplets, forming a suspension having a much larger active surface thus enabling efficient interactions between reactants on the surface of water. In the case of solid substrates, vigorous stirring is even more important, but the

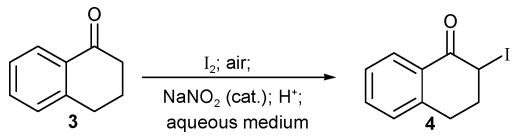
Table 1 Effect of reaction conditions on aqueous aerobic oxidative iodination of acetophenone **1** catalyzed by $NaNO_2$[a]



Entry	Aqueous medium	H_2SO_4 (mmol)	$NaNO_2$ (mol%)	T (°C)	Conv. of **1** to **2** (%)[b]
1	Pure H_2O	0.25	5	30	30
2	Pure H_2O	0.25	5	60	55
3	Pure H_2O	0.5	12	60	74
4	8.1×10^{-3} M SDS[c]	0.5	12	60	84
5	0.1 M SDS[d]	0.5	4	60	62
6	0.1 M SDS	0.5	10	60	79
7	0.1 M SDS	0.5	12	60	100[91]
8	0.1 M SDS	0.25	12	60	76
9	0.1 M SDS	0.5	12	30	53
10	0.1 M SDS	/[e]	12	60	82
11	0.1 M SDS[f]	1	12	60	74

[a] Reaction conditions: **1** (1 mmol); I_2 (0.5 mmol) or KI (1.05 mmol), 96% H_2SO_4 (0.25–1 mmol); $NaNO_2$ (4–12 mol%); solvent (5 mL); air balloon (1 L); stirring (500 rpm) for 12 h at T = 30–60 °C. [b] Determined from ^1H NMR spectra of crude reaction mixture, the value in bracket refers to isolated yield. [c] Critical micelle concentration (cmc) of SDS (0.04 mmol of SDS in 5 mL of H_2O, 8.1×10^{-3} M). [d] Above cmc of SDS (0.5 mmol of SDS in 5 mL of H_2O, 0.1 M). [e] 1 equiv. of $HClO_4$ ($pK_a = -7$) was used as acid. [f] KI was used as an iodine atom source.

Table 2 Effect of stirring on the efficiency of aerobic oxidative iodination of 3,4-dihydro-2*H*-naphthalen-1-one **3** catalyzed by $NaNO_2$[a]



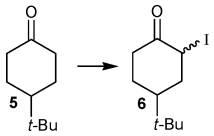
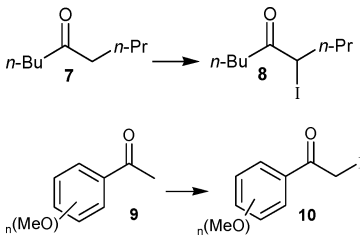
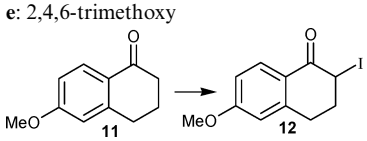
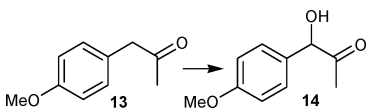
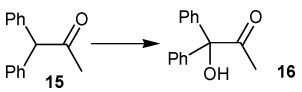
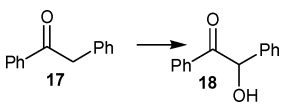
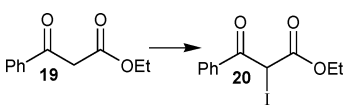
Entry	Aqueous medium	Time (h)	Stirring (rpm)	Conv. of **3** to **4** (%)[b]
1	Pure H_2O	0.5	0	24
2		24	0	41
3		0.5	700	71
4	0.1 M SDS	0.5	0	58
5		24	0	83
6		0.5	500	100[90]

[a] Reaction conditions: **3** (1 mmol); I_2 (0.5 mmol), 96% H_2SO_4 (0.5 mmol); $NaNO_2$ (12 mol%); pure water or 0.1 M aqueous SDS (5 mL); air balloon (1 L); magnetic stirring (0–700 rpm); T = 60 °C. [b] Determined from ^{1}H NMR spectra of crude reaction mixture, the value in bracket refers to isolated yield.

efficiency of interactions also depends on the size of the solid particles and their shape.[7d] The effect of stirring of the reaction mixture on the efficiency of aerobic oxidative iodination with the I_2/air/$NaNO_2$(cat)/H_2SO_4 system in micellar aqueous media or "on water" is presented in Table 2. Vigorous stirring was found to be crucial for iodotransformation of liquid model substrate 3,4-dihydro-2*H*-naphthalen-1-one **3** "on water" and a rate of 700 rpm gave the optimal result (entry 3). Reaction in 0.1 M SDS aqueous micellar medium magnetically stirred at 500 rpm (entry 6) resulted in the quantitative formation of 2-iodo-3,4-dihydro-2*H*-naphthalen-1-one **4**, while the effect of stirring was less exspressed (entries 4 and 5) than in the case of "on water" iodotransformations (entries 1 and 2). These two stirring intesities were thus applied in all further experiments.

Encouraged by these results and experimental insights for aerobic oxidative iodination of model substrates **1** and **3**, we applied the catalytic reaction system of I_2/air/$NaNO_2$(cat.)/H_2SO_4 to the iodination of a variety of substituted ketones in the micelle-based SDS aqueous medium, comparing the efficiency to that of transformations on water. The results are presented in Table 3. We started our evaluation with cycloalkyl ketone 4-*tert*-butyl-cyclohexanone **5** which was readily and quantitatively transformed to a mixture of 2-iodo substituted isomeric products **6** (*anti*/*syn* ratio 2:1) in the micelle-based SDS aqueous media, while the transformation was found to be less efficient on water (entry 1). Similar results were obtained in the case of the aerobic oxidative iodination of acyclic alkyl substituted ketone 5-nonanone **7** to 4-iodo-5-nonanone **8** (entry 2). Aerobic oxidative iodination with the catalytic iodinating system developed proved to be highly regiospecific in the case of substrates bearing an activated aromatic ring. 1-(4-Methoxy-phenyl)-ethanone **9a** was selectively transformed into its α-iodo functionalized derivative **10a** with excellent yield (entry 3). It seems that the SDS aqueous micelle as medium directs the regioselectivity of aerobic oxidative iodination of a series of methoxy substituted aryl methyl ketones **10b-e** and **11** (entries 4 to 8) to the α-carbonyl position, since in all these cases side chain iodofunctionalization was found

Table 3 Aerobic oxidative iodination of ketones catalysed by $NaNO_2$ on pure water (A) or in SDS micelle-based aqueous system (B)[a]

Entry	Iodotransformation	Time (h)	Yield[b] (%) A	B
1		2	69	100[85][c]
2		3	67	100[84]
3	**a**: 4-methoxy	3.5	70	100[90]
4	**b**: 2,4-dimethoxy	1	81	100[90]
5	**c**: 2,6-dimethoxy	4	80	100[73]
6	**d**: 3,5-dimethoxy	4	80	100[80]
7	**e**: 2,4,6-trimethoxy	4	80	100[85]
8		0.2	84	100[93]
9		4	73	100[80]
10		4	57	100[82]
11		12	71[d]	100[83]
12		8	48	90[81]

[a] Reaction conditions: Substrate (1 mmol), pure H_2O (5 mL; conditions A) or 0.1 M aqueous SDS (5 mL; conditions B), I_2 (127 mg, 0.5 mmol), 96% H_2SO_4 (47 mg, 0.5 mmol), $NaNO_2$ (8.4 mg, 0.12 mmol), air balloon (1 L), stirring at 700 rpm for A and 500 rpm for B conditions at 60 °C. [b] Conversion of starting material to iodinated product determined from ^{1}H NMR spectra of crude reaction mixture; values in square parentheses refer to isolated pure products obtained on a silica column. [c] Mixture of *anti* and *syn* products in the relative ratio 2:1. [d] Mixture of 2-iodo-1,2-diphenylethanone (51%) and **18** (20%).

to be exclusive and 1-(2,4-dimethoxy-phenyl)-2-iodo-ethanone **10b**, 1-(2,6-dimethoxy-phenyl)-2-iodo-ethanone **10c**, 1-(3,5-dimethoxy-phenyl)-2-iodo-ethanone **10d**, 1-(2,4,6-trimethoxy-phenyl)-2-iodo-ethanone **10e** or 2-iodo-6-methoxy-3,4-dihydro-2*H*-naphthalen-1-one **12** were quantitatively formed and isolated in excellent yields. In these cases the reactivity of the aerobic oxidative iodination process was also higher in the

micelle-based aqueous system than under "on water" reaction conditions. We further checked the selectivity of iodination on 1-(4-methoxyphenyl)propan-2-on **13** (entry 9) which possesses three potential positions for electrophilic derivatisation: the activated aromatic ring and two α-to carbonyl positions on the benzylic and methyl carbon atoms and established that exclusive functionalization of the benzylic position took place, giving the isolated product 1-hydroxy-1-(4-methoxyphenyl)propan-2-on **14**. The 1-iodo-1-phenyl-propan-2-ones are known as less stable compounds which could be stabilized with nucleophilic solvents like MeOH or H_2O to form 1-methoxy or 1-hydroxy-1-phenyl-propan-2-ones.[23] Regioselective α-hydroxylation of the benzylic position was also observed in the case of 1,1-diphenylpropan-2-one **15** (entry 10) and 1,3-diphenylpropan-2-one **17** (entry 11) where by using the I_2/air/$NaNO_2$(cat.)/H_2SO_4 system in the SDS aqueous micelle medium 1,1-diphenyl-1-hydroxypropan-2-one **16** or 1,3-diphenyl-1-hydroxypropan-2-one **18** were formed. The primary formation of iodinated product was proved in the case of the reaction of **17** on water, where a mixture of 1-iodo and 1-hydroxy derivatives was isolated. These findings could open an efficient method for selective hydroxylation of benzyl ketones. We finally tested the method on 3-oxo-3-phenyl-propionic acid ethyl ester **19** (entry 12) as a model 1,3-dicarbonyl compound and the formation of 2-iodo-3-oxo-3-phenyl-propionic acid ethyl ester **20** in high yield was observed in SDS aqueous micellar medium, while only a moderate yield of the transformation was found under "on water" reaction conditions. Isolation of products from the crude reaction mixtures obtained after the mmol scale reactions described in Table 3 was performed by extraction with *tert*-butyl methyl ether, while after larger scale experiments isolation without using organic solvents was applied.

The results in Table 3 illustrate that SDS aqueous micelle works as an excellent medium for side chain regiselective aerobic oxidative iodination of aryl methyl ketone. On the other hand, there still remains the question of regioselective ring functionalization of aryl methyl ketones with the I_2/air/$NaNO_2$(cat.)/H_2SO_4 reagent system, since the reaction conditions during iodination of ketones favour a higher degree of enolization of the ketone and consequently α-iodination, even in the case of aprotic solvent MeCN. In the case of F-TEDA-BF_4 mediated fluorination[24] or oxidative iodination,[25] this switches the regioselectivity towards aromatic ring functionalization. We thus had some doubts that solvent- directed regioselectivity of iodination could be achieved when the I_2/air/$NaNO_2$(cat.)/H_2SO_4 reagent system is used. When using freshly distilled and dried MeCN as the reaction medium, we finally succeeded in switching from side chain to aryl ring regioselectivity of the reaction. In dry MeCN at 30 °C 1-(3-iodo-2,6-dimethoxy-phenyl)-ethanone **21** was formed, with excellent regioselectivity (95%; 5% of **10c** was also formed) and eficiency (73% of pure product) of the process when **9c** was treated with iodinating system Similarly, 1-(3,5-dimethoxy-phenyl)-ethanone **10d** and 1-(2,4,6-trimethoxy-phenyl)-ethanone **10e** were transformed in anhydrous MeCN to 1-(2,6-diiodo-3,5-dimethoxy-phenyl)-ethanone **22** (75% of pure product) or 1-(3-iodo-2,4,6-trimethoxy-phenyl)-ethanone **23** (74% of pure product), also in these cases with high selectivity[26] and efficiency. Minimization of the presence of water was found to be very important in these cases, since the use of non-dried MeCN or adding a drop of water to the reaction system diminshed the ring/side chain regioselectivity considerably in favour of side chain iododerivatisation.

Conclusions

In conclusion, we successfully developed the efficient and selective oxidative iodination of ketones in aqueous media using molecular iodine, air as the terminal oxidant, $NaNO_2$ as catalyst, and H_2SO_4 as an activator of the overall catalytic process which enables maximum iodine atom economy. To the best of our knowledge, this is a first example of non-enzymatic aerobic oxidative halogenation of organic molecules in water and it was shown that the high efficiency of the catalytic aerobic process was significantly accelerated in the micelle-based aqueous system. The inexpensive anionic amphiphile sodium dodecyl sulfate (SDS) was found to be an excellent promoter of aerobic α-iodo-functionalization of a series of substituted ketones, while regioselective α-hydroxylation of benzyl-alkyl ketones was achieved. In the SDS micelle-based aqueous system, regiospecific side chain iodination of methoxy substituted aryl methyl ketones to iodomethyl-aryl ketones was established, while ring iodo-functionalization forming aryliodides was achieved in anhydrous MeCN. The use of water as a reaction medium and the methodology of "micellar catalysis"[27] for aerobic oxidative iodination of ketones with the I_2/air/$NaNO_2$(cat.)/H_2SO_4 reaction system made the investigated method attractive and interesting from both the economic and environmental points of view.

Experimental

Aerobic oxidative iodination of ketones in a micelle-based aqueous system. General procedure

Ketone (1 mmol) was placed in a two necked glass flask (50 mL, one neck closed with a rubber septum) equipped with a magnetic stirrer bar, 4 mL of water, SDS (144 mg, 0.5 mmol) and 96% sulfuric acid (47 mg, 0.5 mmol) were added and stirred for a few minutes. Afterwards fine powdered molecular iodine (127 mg, 0.5 mmol) was added to the reaction mixture, the open neck was then closed with a rubber balloon (1 L) filled with air and the stirred reaction flask heated to 60 °C. Sodium nitrite ($NaNO_2$) catalyst (8.28 mg, 0.12 mmol) dissolved in water (1 mL) was introduced through the septum into the reaction mixture in 3 portions (0.04 mmol, 2.76 mg of catalyst) at intervals of 1/4 reaction time and the reaction system stirred (500–700 rpm) at 60 °C until the reaction mixture lost the iodine colour (see Table 3). The reaction mixture was cooled to r.t., diluted with *tert*-butyl methyl ether (20 mL) and the ether phase without shaking separated from the water phase. Then the water phase was gently extracted with *tert*-butyl methyl ether (10 ml) and the combined ether phases were first discolored by adding a few drops of 40% aqueous solution of Na_2SO_3, neutralized with a few drops of saturated aqueous $NaHCO_3$ and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the crude products obtained were purified by column or TLC preparative chromatography (SiO_2, CH_2Cl_2:n-hexane 9:1) and identified by NMR and MS analysis. Spectroscopic data and

references for known compounds **2**, **4**, **6**, **8**, **10a-c**, **12**, and **20** are presented in the ESI.†

1-(3,5-Dimethoxyphenyl)-2-iodoethanone (10d). column chromatography (SiO_2, CH_2Cl_2/n-hexane 9.5:0.5); 245 mg (80%); white crystals (from n-hexane); mp(57–59 °C); ^{1}H NMR: δ = 3.84(s, 6H), 4.33(s, 2H), 6.67(t, J = 2.3 Hz, 1H), 7.11(d, J = 2.3 Hz, 2H); ^{13}C NMR: δ = 1.6(CH_2I), 55.6(CH_3), 106.0(CH), 106.7(CH), 135.2(C), 160.9(C), 192.5(CO); IR: ν(cm^{-1}) = 1675, 1611, 1593, 1468, 1431, 1355, 1304, 1211, 1164, 1020, 750, 673, 613; MS: m/z: 306(M^+, 100%), 165(100), 151(17), 137(8), 122(8), 77(10); HRMS: *m/z* calcd. for $C_{10}H_{11}O_3I$: 305.9761, found: 305.9752.

2-Iodo-1-(2,4,6-trimethoxyphenyl)-ethanone (10e). column chromatography (SiO_2, CH_2Cl_2/n-hexane 9.5:0.5); 285.5 mg (85%); white crystals (from n-hexane); mp(89–91 °C); ^{1}H NMR: δ = 3.81(s, 6H), 3.83(s, 3H), 4.29(s, 2H), 6.11(s, 2H); ^{13}C NMR: δ = 10.9(CH_2I), 55.5(CH_3), 56.0(CH_3), 90.5(CH), 109.3(C), 159.2(C), 163.3(C), 194.0(CO); IR: ν(cm^{-1}) = 1671, 1606, 1588, 1458, 1411, 1335, 1255, 1207, 1161, 1129, 999, 811; MS: m/z: 336(M^+, 11%), 321(7), 195(100); HRMS: *m/z* calcd. for $C_{11}H_{13}O_4I$: 335.9868, found: 335.9858.

1-Hydroxy-1-(4-methoxy-phenyl)-propan-2-one[23] (14). preparative TLC (SiO_2; CH_2Cl_2/EtOH = 9.5:0.5); 144 mg (80%); oily product; ^{1}H NMR: δ = 2.06(s, 3H), 3.81(s, 3H), 4.25(d, J = 4.7 Hz, 1H), 5.04(d, J = 4.7 Hz, 1H), 6.90(d, J = 8.7 Hz, 2H), 7.22(d, J = 8.7 Hz, 2H); ^{13}C NMR: δ = 25.1, 55.2, 79.5, 114.3, 128.5, 129.9, 159.8, 207.3; MS: m/z: 180(M^+, 2%), 163(15), 137(100), 109(18), 94(21), 77(24); HRMS: *m/z* calcd. for $C_{10}H_{12}O_3$: 180.0786, found: 180.0781.

1-Hydroxy-1,1-diphenyl-propan-2-one[28] (16). preparative TLC (SiO_2; CH_2Cl_2/EtOH = 9.5:0.5); 185 mg (82%); mp(63.0–65.0 °C); ^{1}H NMR: δ = 2.27(s, 3H), 4.85(broad s, 1H), 7.37(m, 10H); ^{13}C NMR: δ = 26.2, 85.7, 128.1, 128.2, 128.5, 141.3, 208.6; MS: m/z: 183(M^+-MeCO, 36%), 105(100), 77(11).

2-Hydroxy-1,2-diphenyl-ethanone[29] (18). preparative TLC (SiO_2; CH_2Cl_2/EtOH = 9.5:0.5); 176 mg (83%); mp(135.5–137.0 °C); ^{1}H NMR: δ = 4.57(d, J = 6 Hz, 1H), 5.95(d, J = 6 Hz, 1H), 7.25–7.50(m, 8H), 7.91(d, J = 9 Hz, 2H); ^{13}C NMR: δ = 76.2, 127.7, 128,5, 128.7, 129.1, 129.2, 133.9, 139.0, 198.9; MS: m/z: 212(M^+, 1%), 108(63), 105(100), 79(60), 77(92); HRMS: *m/z* calcd. for $C_{14}H_{12}O_2$: 212.0837, found: 212.0843.

Aerobic oxidative ring iodofunctionalization of aryl methyl ketones bearing an activated aromatic ring. General procedure

To a solution of a methyl aryl ketone (1 mmol; **9c**, **9d** or **9e**) in freshly distilled and dried MeCN (5 mL), 96% sulfuric acid (19 mg, 0.2 mmol) and molecular iodine (127 mg, 0.5 mmol for **9c** and **9e** or 254 mg, 1 mmol for **9d**) were added in a glass vessel (50 ml) and the reaction mixture stirred for a few minutes at 30 °C. $NaNO_2$ catalyst (4.15 mg, 0.06 mmol) was then added, the reaction system was immediately closed with a rubber balloon (1 L) filled with air and the reaction mixture magnetically stirred (500 rpm) for 8 hours at 30 °C. The solvent was then removed under reduced pressure, the residue dissolved in *tert*-butyl methyl ether (20 mL) and insoluble products filtered off. The solution was discolored with a few drops of 40% aqueous Na_2SO_3, neutralized with a few drops of saturated aqueous $NaHCO_3$ and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, the crude products obtained were identified from their spectroscopic data and purified using column chromatography (SiO_2, CH_2Cl_2:n-hexane 9.5:0.5). Spectroscopic data and the reference for known compound **21** are presented in the ESI.†

1-(2,6-Diiodo-3,5-dimethoxyphenyl)-ethanone (22). Preparative TLC chromatography (SiO_2, CH_2Cl_2/n-hexane 9.5:0.5; R_f = 0.65); 324 mg (75%); white crystals (from n-hexane); mp(148–151 °C); ^{1}H NMR: δ = 2.63(s, 3H), 3.92(s, 6H), 6.38(s, 1H); ^{13}C NMR: δ = 29.0(CH_3), 56.8(CH_3), 70.4(C), 94.9(CH), 152.2(C), 159.6(C), 204.3(CO); IR: ν(cm^{-1}) = 1705, 1562, 1464, 1413, 1358, 1322, 1219, 1042, 974, 822; MS: m/z: 432(M^+, 100%), 417(40), 374(10); HRMS: *m/z* calcd. for $C_{10}H_{10}O_3I_2$: 431.8728; found: 431.8719.

1-(3-Iodo-2,4,6-trimethoxyphenyl)-ethanone (23). column chromatography (SiO_2, CH_2Cl_2/n-hexane 9.5:0.5); 248.5 mg (74%); white crystals (from n-hexane); mp(94–95 °C); ^{1}H NMR: δ = 2.49(s, 3H), 3.79(s, 3H), 3.85(s, 3H), 3.91(s, 3H), 6.28(s, 1H); ^{13}C NMR: δ = 32.3(CH_3), 56.1(CH_3), 56.7(CH_3), 62.9(CH_3), 73.5(C), 91.9(CH), 119.6(C), 158.0(C), 158.6(C), 160.5(C), 201.0(CO); IR: ν(cm^{-1}) = 1687, 1585, 1382, 1324, 1242, 1210, 1105, 1011, 915, 810; MS: m/z: 336(M^+, 50%), 321(100), 306(20), 263(6); HRMS: *m/z* calcd. for $C_{11}H_{13}O_4I$: 335.9866, found: 335.9859.

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