Bis(pyridine)iodonium Tetrafluoroborate (IPy_2BF_4): A Versatile Oxidizing Reagent

José Barluenga,* Francisco González-Bobes, Marcelo C. Murguía, Sreenivasa R. Ananthoju, and José M. González[a]

Abstract: The use of bis(pyridine)iodonium tetrafluoroborate (IPy_2BF_4) as an oxidizing agent towards different types of alcohols is reported. The observed reactivity involves different reaction pathways, as a function both of the structures of the starting materials and of the experimental conditions. Interestingly, the title iodine-containing compound is capable of a tuneable reaction with simple cycloalkanols, providing straight and selective access either to ω-iodocarbonyl compounds or to ketones, a previously unreported and chemoselective range of oxidation potential. Furthermore, appropriate conditions for the preparation of aldehydes and esters from primary alcohols by easily performed experimental procedures were also established. The β-scission reactions of cycloalkanols and the α-oxidation processes of primary, secondary and benzylic alcohols are discussed.

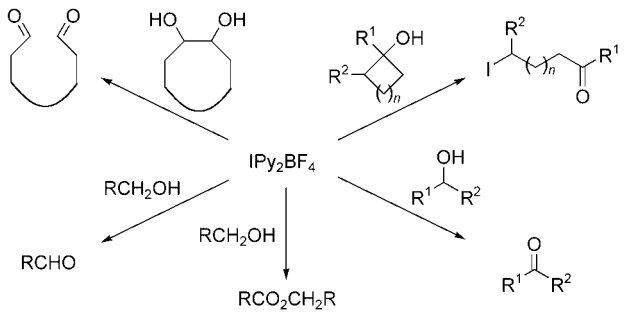
Keywords: aldehydes · cleavage reactions · esters · ketones · oxidation

Introduction

The development of new approaches to oxidation reactions of alcohols has become a central area of research in chemistry. In this field, the use of iodine(v) derivatives such as Dess–Martin reagent (DMP)[1] or *o*-iodoxybenzoic acid (IBX)[2] is a testament to this valuable transformation. However, the atmospheric instability of some of these iodine(v) compounds[3] and the potential explosiveness of others,[4] have driven the search for new competitive alternatives. Polymer-bonded reagents,[5] water-soluble derivatives,[6] and the use of iodine(III)[7] and iodine(I)[8] compounds are amongst the agents that have focused interest in this field in stoichiometric approaches.[9]

Recently, the synthetic dominance of reagents such as DMP and IBX has been further highlighted by their capability to effect new chemoselective synthetic chemical transformations.[10]

We report here on the use of bis(pyridine)iodonium tetrafluoroborate (IPy_2BF_4)[11] as a reagent for the execution of interesting oxidation chemistry of alcohols under photochemical or thermal conditions, leading to β-scission reactions of cycloalkanols,[12] and oxidation processes of alcohols and diols (Scheme 1).



Scheme 1. IPy_2BF_4 as an oxidizing reagent.

Results and Discussion

Our initial studies on the interaction of IPy_2BF_4 with alcohols resulted in general and previously unreported β-scission processes of secondary and tertiary cycloalkanols, which gave rise to ω-iodofunctionalized systems.[12,13] The main features of this novel procedure are briefly summarized in Table 1.

The reactions were conducted at room temperature and took place under photochemical conditions (irradiation with a 100 W lamp). The corresponding ω-iodinated derivative was obtained as the major or even as the single reaction

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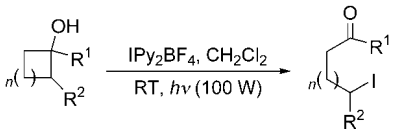
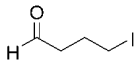
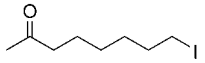
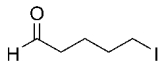
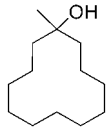
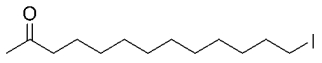
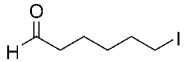
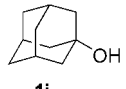
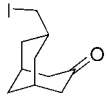
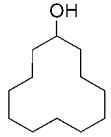
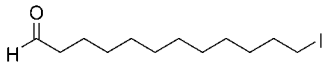
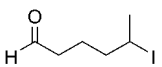
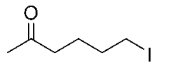
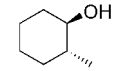
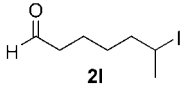
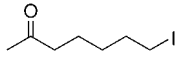
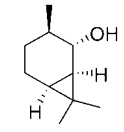
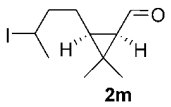
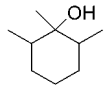
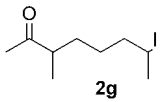
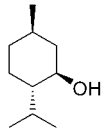
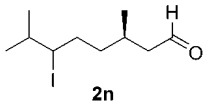
Table 1. Synthesis of ω-iodocarbonyl compounds **2** from cycloalkanols **1**.[a]



Entry	Substrate **1**	Cs_2CO_3 [equiv]	Product **2**	Time [h]	Yield [%][b]	Entry	Substrate **1**	Cs_2CO_3 [equiv]	Product **2**	Time [h]	Yield [%][b]
1	 **1a**	–	 **2a**	12	92	8	 **1h**	5	 **2h**	24	55[d]
2	 **1b**	–	 **2b**	12	91	9	 **1i**	5	 **2i**	24	91
3	 **1c**	10	 **2c**	20	85[c]	10	 **1j**	10	 **2j**	24	32[e]
4	 **1d**	10	 **2d**	20	76[c]	11	 **1k-(±)**	–	 **2k**	12	92
5	 **1e**	5	 **2e**	8	93	12	 **1l-(±)**	5	 **2l**	14	89
6	 **1f**	5	 **2f**	8	88	13	 **1m-(-)**	5	 **2m**	7	94[f]
7	 **1g**	5	 **2g**	6	70	14	 **1n-(-)**	10	 **2n**	24	37[e,f]

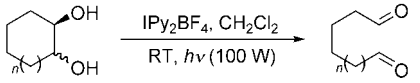
[a] All reactions were performed with employment of 1.25 equiv of IPy_2BF_4 and a 0.1 M concentration of The relevant alcohol unless otherwise specified. [b] Yield of isolated **2** based on starting cycloalkanol **1**. [c] 2.5 equiv of IPy_2BF_4 and a 0.02 M concentration of alkanol were used. [d] A 0.04 M concentration of the alcohol was employed. [e] For a 35% conversion of the starting alkanol. [f] Obtained as a 1:1 (NMR analysis) mixture of epimers around the new stereocenter formed.

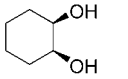
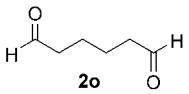
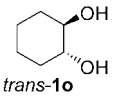
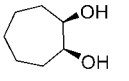
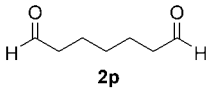
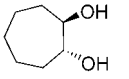
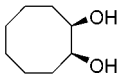
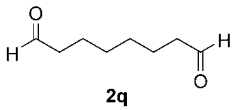
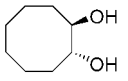
product from the transformation of the starting alcohol **1**.[14] The reaction takes place with secondary and tertiary cycloalkanols of different sizes (Table 1). The tools employed to control the outcome of the reported transformation are the reaction time, the concentration of the reagents and the use of a heterogeneous base (Cs_2CO_3).[15] This β-scission process is regioselective: as a rule, the more highly substituted carbon–carbon bond adjacent to the alcohol functionality undergoes this oxidative cleavage process (see Table 1).

The reactivity of 1,2-diols under those experimental conditions was also tested. In this case, α,ω-dialdehydes are generated as the sole reaction product (Table 2).[16]

As can be observed, the outcome of the reaction does not depend on the stereochemistry of the starting substrate, and the process can be executed in a satisfactory manner with diols of different sizes, providing the corresponding aldehydes in high purity after a simple extraction (Table 2).

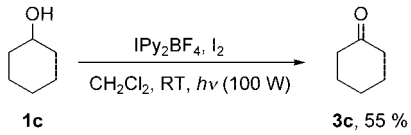
Table 2. Synthesis of α,ω-dialdehydes **2** from cyclic diols **1**.[a]



Entry	Substrate **1**	Time [h]	Product **2**	Yield [%][b]
1	 *cis*-**1o**	24	 **2o**	63
2	 *trans*-**1o**	24		66
3	 *cis*-**1p**	18	 **2p**	77
4	 *trans*-**1p**	18		79
5	 *cis*-**1q**	12	 **2q**	91
6	 *trans*-**2q**	12		92

[a] Two equivalents of IPy_2BF_4 and a 0.04 M concentration of the corresponding diol were employed. [b] Isolated yield based on starting diols. The reported yields have not been optimized.

When the β-scission reaction of cyclohexanol (**1c**) was studied, the formation of small amounts of cyclohexanone (**3c**) as a function of the experimental conditions was noted. This initial observation prompted us to explore the oxidizing capability of IPy_2BF_4 further, in search of a suitable reaction medium that would allow selective preparation of the carbonyl product resulting from an alternative α-oxidation process.[17] Interestingly, the addition even of sub-stoichiometric amounts of iodine has been found to be appropriate to achieving this goal (Scheme 2).



Scheme 2. Initial observation of α-oxidation of alcohols promoted by IPy_2BF_4-I_2. Reaction conditions: IPy_2BF_4 (2.5 equiv), I_2 (0.4 equiv), 12 h.

Exploratory studies to improve this reaction sequence were conducted with the use of 2-octanol (**1r**) as model compound. Thermal rather than photochemical conditions were found more efficient to accomplish this alternative oxidation mode. Furthermore, careful optimization of the stoichiometry, the selection of an appropriate solvent and the presence of a base were required to carry out the desired oxidation reaction (Table 3).

The combination of IPy_2BF_4 and I_2 under thermal conditions affords the corresponding ketones in rather good isolated yields and in reasonable reaction times (Table 3).

Benzyl alcohol derivatives also reacted well with this combination of reagents. In this case, addition of potassium carbonate (K_2CO_3) gave better experimental results than the corresponding cesium salt, so it was routinely employed (Table 4).

The described conditions allow for the satisfactory oxidation of several benzylic alcohols bearing different substituents (entries 4–8, Table 4). The corresponding carbonyl compounds were obtained as single reaction products. Even benzyl alcohol (**4b**) was cleanly oxidized to afford benzaldehyde (**5b**) without any noticeable evidence of over-oxidation[2a] taking place (entry 2, Table 4).

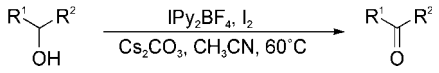
Primary alkanols react under these conditions to afford either aldehydes or esters. Interestingly, a simple modification of the experimental conditions can be nicely used to drive the formation of the observed products selectively (Table 5).

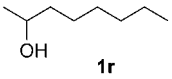
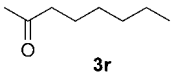
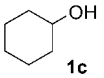
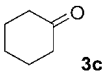
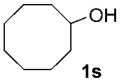
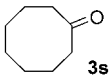
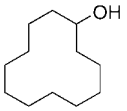
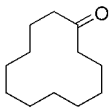
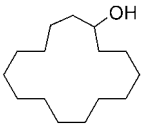
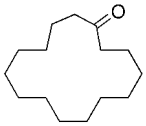
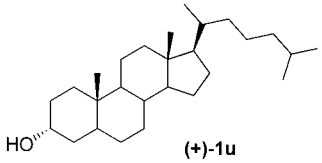
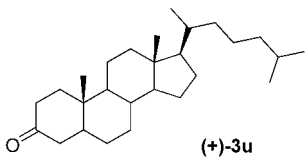
As shown, the concentration of the reagents, the reaction temperature, the addition of an inorganic base[18] and the presence of different additives[19,20] were optimized to direct this unconventional reaction range,[21] to produce both families of oxidation products exclusively (Table 5).

In terms of reaction mechanism, the different oxidation processes could be interpreted as involving the generation of several intermediate species in a sequential manner (Scheme 3).

A reasonable proposal could invoke the initial formation of the oxonium ion (**A**), resulting from interaction between the alkanol and IPy_2BF_4.[22] Subsequent deprotonation in the presence of the base affords the iodane (**B**).[23] Different pathways might be operative as a function of the experimental conditions, accounting for the different observed reaction products. Thus, homolytic decomposition of **B** under photochemical conditions would form the alkoxyl radical (**C**),[24] which could undergo the well established β-scission process,[13] affording the carbon-centered radical (**D**). The reac-

Table 3. Oxidation of secondary alcohols **1** to ketones **3** with IPy_2BF_4-I_2.[a]



Entry	Substrate **1**	Time [h]	Product **2**	Yield [%][b]
1	 **1r**	2	 **3r**	92
2	 **1c**	6	 **3c**	87
3	 **1s**	3	 **3s**	91
4	 **1d**	4	 **3d**	98
5	 **1t**	7	 **3t**	92
6	 **(+)-1u**	7	 **(+)-3u**	92

[a] Reactions were performed with the following stoichiometry: IPy_2BF_4 (3 equiv), I_2 (0.5 equiv) and Cs_2CO_3 (5 equiv). A 0.06 M concentration of The relevant alcohol (1 equiv) was employed. [b] Yield of isolated product relative to the starting alkanol **1**.

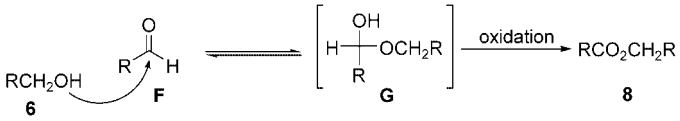
tion of **D** and the previously formed bis(pyridine)iodanyl radical would lead to the bifunctional derivative (Scheme 3).[12]

Conversely, an oxidative ligand-exchange reaction with molecular iodine might drive the conversion of **B** into the bis(iodo)alkoxy-λ^3-iodane **E**.[25] Lastly, a hydrogen elimination reaction, common in the chemistry of these species,[26] would furnish the resulting ketones and regenerate iodine in the reaction medium (Scheme 3).[27]

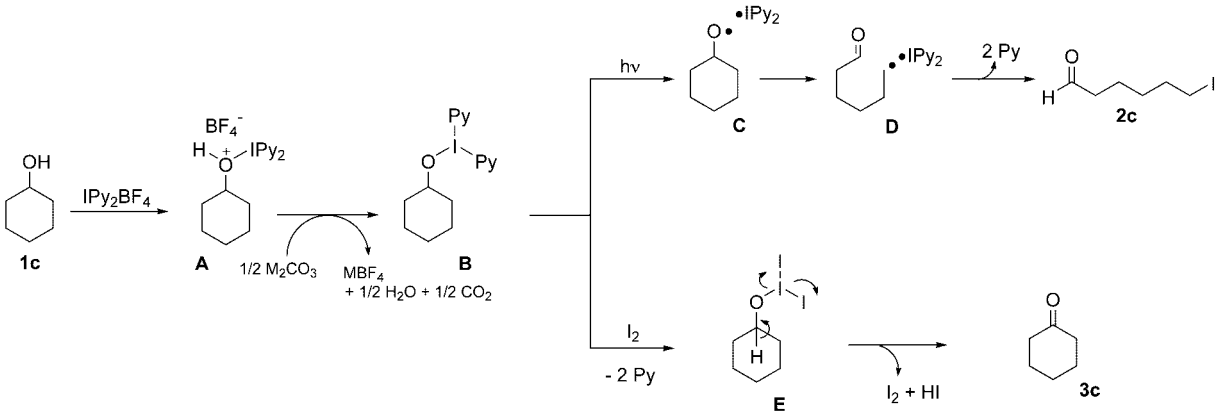
The observed formation of esters with the oxidation of primary alcohols could be explained by assuming a prior generation of an aldehyde (**F**), in agreement with the sequence discussed above. The evolution of **F** through the hemiketal-like intermediate (**G**) and its eventual oxidation would furnish esters (Scheme 4).[28]

Conclusion

It has been demonstrated that IPy_2BF_4 is able to promote different oxidation processes of alcohols in a clean and satisfactory manner, just by appropriate choice of reaction conditions. All materials employed in these transformations are commercially available and easy to handle and store. In addition, simple variations in the experimental procedure allow for the selective preparation of different families of carbonyl deriva-

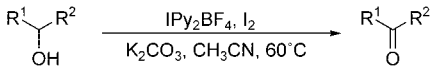


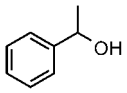
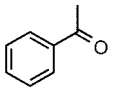
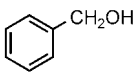
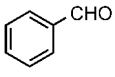
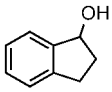
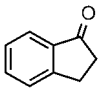
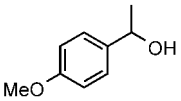
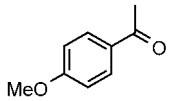
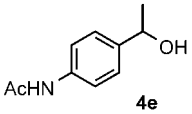
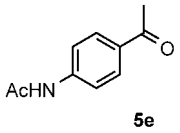
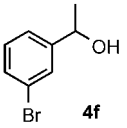
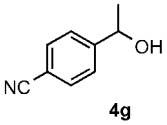
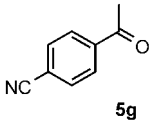
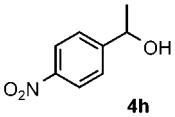
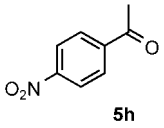
Scheme 4. Mechanistic proposal for the formation of esters from primary alkanols.



Scheme 3. Proposed reaction pathways.

Table 4. Oxidation of benzylic alcohols **4** with IPy_2BF_4-I_2.[a]



Entry	Substrate **4**	Time [h]	Product **5**	Yield [%][b]
1	 **4a**	14	 **5a**	86
2	 **4b**	14	 **5b**	88
3	 **4c**	14	 **5c**	80
4	 **4d**	3	 **5d**	94
5	 **4e**	3	 **5e**	91
6	 **4f**	36	 **5f**	73
7	 **4g**	21	 **5g**	85
8	 **4h**	24	 **5h**	64

[a] Reactions were performed with the following stoichiometry: IPy_2BF_4 (3 equiv), I_2 (0.5 equiv) and K_2CO_3 (2.5 equiv). A 0.06 M concentration of The relevant alcohol (1 equiv) was employed. [b] Yield of isolated product relative to the starting alkanol **4**.

tives in a straightforward manner. Overall, the given transformations constitute a new example of the versatility of this reagent and expand its application profile.

Experimental Section

General: All reactions were carried out under positive nitrogen atmosphere. CH_2Cl_2 and CH_3CN were distilled from CaH_2 and stored under nitrogen. Analytical thin-layer chromatography plates were Merck UV-active silica gel 60 F_{254} on aluminium. Flash column chromatography was carried out on silica gel 60, 230–240 mesh, with appropriate mixtures of hexane and ethyl acetate or methylene chloride as eluent. ^{1}H NMR (200, 300, 400 MHz) and ^{13}C NMR (50, 75, 100 MHz) spectra were measured at room temperature on Bruker AC 200, AC 300 and AMX 400 instruments with tetramethylsilane (^{1}H NMR) or $CDCl_3$ (^{13}C NMR) as internal standards. Carbon multiplicities were assigned by DEPT techniques. High-resolution mass spectra (HRMS) were determined on a Finnigan MATT 95 spectrometer. Elemental analyses were carried out on a Perkin–Elmer 2400 microanalyzer. Melting points were determined on a Büchi–Tottoli machine and have not been corrected. Optical rotation was measured on a Perkin–Elmer 241 polarimeter.

General procedure for the preparation of 2a, 2b, and 2k (Table 1): The relevant alcohol (2 mmol, 1 equiv) was added to a solution of IPy_2BF_4 (2.5 mmol, 1.25 equiv, 0.93 g) in CH_2Cl_2 (20 mL), and the mixture was irradiated for 12 hours. $Na_2S_2O_3$ (5% solution in water, 40 mL) was added, and the mixture was extracted with CH_2Cl_2 (4×20 mL). The organic layer was washed with H_2SO_4 (1 M, 2×50 mL) and water (2×50 mL) and dried (Na_2SO_4). Evaporation of the solvents afforded the ω-iodoaldehydes essentially pure.

4-Iodobutanal (2a): yellow oil. R_f = 0.55 (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.81 (t, J = 1.2 Hz, 1H), 3.23 (t, J = 6.5 Hz, 2H), 2.60 (td, J = 6.9, 1.2 Hz, 2H), 2.15 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.5 (CH), 44.1 (CH_2), 25.3 (CH_2), 5.6 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1722 cm^{-1}; elemental analysis calcd (%) for C_4H_7IO: C 24.26, H 3.56; found: C 24.42, H 3.57.

5-Iodopentanal (2b): yellow oil. R_f = 0.58 (hexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.67 (t, J = 1.4 Hz, 1H), 3.11 (t, J = 6.5 Hz, 2H), 2.60 (td, J = 7.1, 1.4 Hz, 2H), 1.75–1.60 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.5 (CH), 42.2 (CH_2), 32.2 (CH_2), 22.5 (CH_2), 6.1 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1724 cm^{-1}; elemental analysis calcd (%) for C_5H_9IO: C 28.32, H 4.27; found: C 28.18, H 4.13.

5-Iodohexanal (2k): yellow oil. R_f = 0.40 (hexane/ethyl acetate 4:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.71 (t, J = 1.5 Hz, 1H), 4.13 (m, 1H), 2.46 (dt, J = 6.6, 1.5 Hz, 2H), 1.87 (d, J = 6.9 Hz, 3H), 1.76 (m, 2H), 1.65 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.6 (CH), 42.5 (CH_2), 41.6 (CH_2), 29.2 (CH), 28.5 (CH_3), 22.0 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1723 cm^{-1}; HRMS: calcd for $C_6H_{11}O$ $[M-I]^+$: 99.0809; found 99.0804.

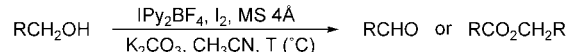
General procedure for the preparation of 2c, 2d, and 2n (Table 1): Cs_2CO_3 (10 mmol, 10 equiv, 3.25 g) was added to a solution containing IPy_2BF_4 (2.5 mmol, 2.5 equiv, 0.93 g) and the alkanol (1 mmol, 1 equiv) in CH_2Cl_2 (50 mL). The resulting heterogeneous mixture was vigorously stirred and irradiated (100 W) for the time indicated in Table 1. The reaction mixture was cooled in an ice-water bath, hydrolysed with H_2SO_4 (1 M, 50 mL) and allowed to warm to room temperature. The mixture was extracted with CH_2Cl_2 (4×20 mL), and the combined organic layers were washed with $Na_2S_2O_3$ (5% solution in water, 2×50 mL) and water (2×50 mL) and dried (Na_2SO_4). Evaporation of the solvent and column chromatography (hexane/ethyl acetate) gives pure samples of the bifunctional compounds.

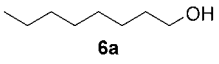
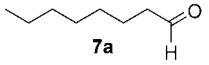
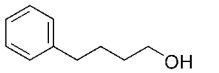
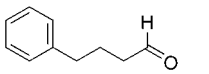
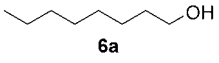
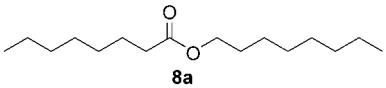
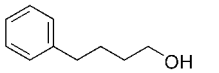
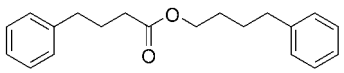
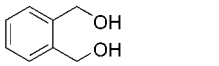
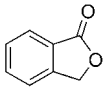
6-Iodohexanal (2c): yellow oil. R_f = 0.63 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 15:1; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.73 (t, J = 1.4 Hz, 1H), 3.12 (t, J = 6.8 Hz, 2H), 2.43 (td, J = 7.3, 1.4 Hz, 2H), 1.81 (m, 2H), 1.62 (m, 2H), 1.42 (2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.0 (CH), 43.3 (CH_2), 32.9 (CH_2), 29.7 (CH_2), 20.7 (CH_2), 6.4 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1724 cm^{-1}; HRMS: calcd for $C_6H_{11}O$ $[M-I]^+$: 99.0809; found 99.0806.

12-Iododecanal (2d): yellow oil. R_f = 0.85 (CH_2Cl_2); chromatography: hexane/CH_2Cl_2 1:1; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.76 (t, J = 1.7 Hz, 1H), 3.18 (t, J = 7.1 Hz, 2H), 2.60 (td, J = 7.4, 1.7 Hz, 2H), 1.81 (c, J = 6.8 Hz, 2H), 1.63 (m, 2H), 1.27 (14H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.8 (CH), 43.8 (CH_2), 33.4 (CH_2), 30.4 (CH_2), 29.3 (CH_2×3), 29.2 (CH_2), 29.0 (CH_2), 28.4 (CH_2), 21.9 (CH_2), 7.2 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1725 cm^{-1}; HRMS: calcd for $C_{12}H_{23}O$ $[M-I]^+$: 183.1748; found 183.1749.

(3*R*)-3,7-Dimethyl-6-iodooctanal (2n): yellow oil. R_f = 0.22 (hexane/CH_2Cl_2 3:1); chromatography: hexane/CH_2Cl_2, 3:1; ^{1}H NMR (300 MHz, $CDCl_3$) for the mixture of epimers: δ = 9.75 (s, 2H), 4.1–4.06 (m, 2H), 2.44–2.12 (m, 4H), 2.10–1.83 (m, 4H), 1.74–0.98 (m, 8H), 0.97–0.89 (m, 18H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) for the mixture of epimers: δ = 202.3 (CH), 51.7 (CH), 51.6 (CH), 51.0 (CH_2), 50.5 (CH_2), 36.8 (CH_2×2), 35.9 (CH_2), 35.7 (CH_2), 34.8 (CH), 34.5 (CH), 27.5 (CH), 27.2 (CH), 23.0 (CH_3), 20.0 (CH_3), 19.8 (CH_3), 19.7 (CH_3), 19.5 (CH_3) ppm; IR (neat): $\tilde{\nu}$ = 1724 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_{19}IO$: C 42.57, H 6.79; found: C 42.71, H 6.75.

Table 5. Oxidation of primary alcohols **6** with IPy_2BF_4-I_2.



Entry	Substrate **6**	Conc. [M][a]	T [°C][b]	t [h]	Product **7** or **8**	Yield [%][c]
1[d]	 **6a**	0.02	60	14	 **7a**	83
2[d]	 **6b**	0.02	60	14	 **7b**	85
3[e]	 **6a**	0.4	40	24	 **8a**	90
4[e]	 **6b**	0.4	40	24	 **8b**	75
5[e]	 **6c**	0.4	40	20	 **8c**	70

[a] Concentration of the alcohol **6**. [b] Oil bath temperature. [c] Yield of isolated product relative to the starting alkanol **6**. [d] Experiments conducted with the following stoichiometry: IPy_2BF_4 (3 equiv), I_2 (4 equiv), K_2CO_3 (5 equiv). [e] Experiments conducted with the following stoichiometry: IPy_2BF_4 (3 equiv), I_2 (0.5 equiv), K_2CO_3 (2 equiv), *t*BuOH (2.5 equiv).

General procedure for the preparation of 2e–2i, 2l, and 2m (Table 1): Cs_2CO_3 (10 mmol, 5 equiv, 3.25 g) was added to a solution containing IPy_2BF_4 (2.5 mmol, 1.25 equiv, 0.93 g) and the alkanol (2 mmol, 1 equiv) in CH_2Cl_2 (20 mL). In all cases the workup was equivalent to that reported above.

6-Iodohexan-2-one (2e): yellow oil. R_f = 0.42 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 10:1; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.07 (t, J = 6.8 Hz, 2H), 2.36 (t, J = 7.2 Hz, 2H), 2.03 (s, 3H), 1.70 (m, 2H), 1.55 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.7 (C), 41.9 (CH_2), 32.3 (CH_2), 29.6 (CH_3), 24.3 (CH_2), 5.6 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1712 cm^{-1}; HRMS: found 99.0803 $[M-I]^+$; $C_6H_{11}O$ calcd 99.0809.

7-Iodoheptan-2-one (2f): yellow oil. R_f = 0.57 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 10:1; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.12 (t, J = 6.9 Hz, 2H), 2.39 (t, J = 7.2 Hz, 2H), 2.07 (s, 3H), 1.76 (q, J = 6.9 Hz, 2H), 1.50–1.10 (m, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.3 (C), 43.1 (CH_2), 32.9 (CH_2), 29.7 (CH_3), 29.7 (CH_2), 22.3 (CH_2), 6.5 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1714 cm^{-1}; elemental analysis calcd (%) for $C_7H_{13}IO$: C 35.02, H 5.45; found: C 35.17, H 5.31.

7-Iodo-3-methyloctan-2-one (2g): yellow oil. R_f = 0.32 (hexane/ethyl acetate 20:1); chromatography: hexane/ethyl acetate 20:1; ^{1}H NMR (300 MHz, $CDCl_3$) for the mixture of diastereoisomers: δ = 4.2–4.07 (m, 2H), 2.49–2.44 (m, 2H), 2.10 (s, 3H), 2.09 (s, 3H), 1.87 (d, J = 6.9 Hz, 3H), 1.85 (d, J = 6.9 Hz, 3H), 1.79–1.25 (m, 12H), 1.05 (d, J = 7.0 Hz, 3H), 1.04 (d, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) for the mixture of diastereoisomers: δ = 212.1 (C), 46.6 (CH×2), 42.5 (CH_2), 42.4 (CH_2), 31.5 (CH_2), 31.3 (CH_2), 29.8 (CH), 28.7 (CH_3), 27.9 (CH_3), 27.2 (CH_3), 27.2 (CH_2), 27.0 (CH_2), 16.1 (CH_3), 16.0 (CH_3) ppm; IR (neat): $\tilde{\nu}$ = 1710 cm^{-1}; elemental analysis calcd (%) for $C_9H_{17}IO$: C 40.31, H 6.39; found: C 40.12, H 6.65.

8-Iodooctan-2-one (2h): yellow oil. R_f = 0.37 (hexane/ethyl acetate 5:1); chromatography: hexane/ethyl acetate 10:1; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.18 (t, J = 6.9 Hz, 2H), 2.43 (t, J = 7.4 Hz, 2H), 2.14 (s, 3H), 1.81 (q, J = 6.9 Hz, 2H), 1.57 (q, J = 7.4 Hz, 2H), 1.45–1.24 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.5 (C), 43.2 (CH_2), 32.9 (CH_2), 29.9 (CH_2), 29.6 (CH_3), 27.6 (CH_2), 23.1 (CH_2), 6.9 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1714 cm^{-1}; elemental analysis calcd (%) for $C_8H_{15}IO$: C 37.81, H 5.95; found: C 37.97, H 5.99.

13-Iodotridecan-2-one (2i): yellow oil. R_f = 0.53 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 10:1; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.16 (t, J = 7.0 Hz, 2H), 2.39 (t, J = 7.4 Hz, 2H), 2.1 (s, 3H), 1.81–1.74 (m, 2H), 1.63–1.24 (16H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 209 (C), 43.6 (CH_2), 33.2 (CH_2), 30.3 (CH_2), 29.7 (CH_3), 29.3 (CH_2), 29.2 (CH_2×3), 28.9 (CH_2), 28.3 (CH_2), 23.6 (CH_2), 7.1 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1704 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{25}IO$: C 48.15, H 7.77; found: C 48.22, H 7.50.

6-Iodoheptanal (2l): yellow oil. R_f = 0.57 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 10:1; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.75 (t, J = 1.5 Hz, 1H), 4.12 (m, 1H), 2.42 (td, J = 7.2, 1.5 Hz, 2H), 1.87 (d, J = 6.9 Hz, 3H), 1.82–1.29 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.1 (CH), 43.5 (CH_2), 42.3 (CH_2), 29.7 (CH_3), 29.1 (CH_2), 28.7 (CH), 20.9 (CH_2) ppm; IR (neat): $\tilde{\nu}$ = 1723 cm^{-1}; elemental analysis calcd (%) for $C_7H_{13}IO$: C 35.02, H 5.45; found: C 35.11, H 5.38.

***cis*-(*1R,3S*)-3-(3′-Iodobutyl)-2,2-dimethylcyclopropanecarbaldehyde (2m)**: yellow oil. R_f = 0.65 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 10:1; ^{1}H NMR (400 MHz, $CDCl_3$) for the mixture of epimers: δ = 9.53 (d, J = 5.6 Hz, 1H), 9.50 (d, J = 5.9 Hz, 1H), 4.15 (m, 2H), 2.04–1.50 (m, 10H), 1.90 (d, J = 6.8 Hz, 6H), 1.44–1.23 (m, 2H), 1.33 (d, J = 2.5 Hz, 6H), 1.55 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) for the mixture of epimers: δ = 201.7 (CH), 42.9 (CH_2), 42.6 (CH_2), 38.4 (CH), 38.3 (CH), 36.6 (CH), 36.4 (CH), 29.9 (C), 29.8 (C), 29.2 (CH), 29.1 (CH), 28.9 (C), 28.8 (C), 24.7 (CH_2), 24.4 (CH_2), 15.0 (CH_3), 14.9 (CH_3) ppm; IR (neat): $\tilde{\nu}$ = 1693 cm^{-1}; HRMS: found: 280.0326 $[M]^+$; $C_{10}H_{17}IO$ calcd 280.0324.

Preparation of 2j (Table 1): An equivalent procedure to that above was followed, but with use of 10 equiv of Cs_2CO_3.

7-Iodomethylbicyclo[3.3.1]nonan-3-one (2j): yellow oil. R_f = 0.35 (hexane/ethyl acetate 3:1); chromatography: hexane/ethyl acetate 10:1; m.p. = 71–73 °C (decomp); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.95 (d, J = 6.8 Hz, 2H), 2.60–2.34 (m, 4H), 2.29–2.09 (m, 2H), 1.91–1.56 (m, 3H), 0.87 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 212.0 (C), 50.1 (CH_2), 34.3 (CH_2), 32.0 (CH_2), 28.4 (CH), 28.2 (CH_2), 14 (CH_2) ppm; IR (KBr): $\tilde{\nu}$ = 1708 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_{15}IO$: C 43.18, H 5.48; found: C 42.91, H 5.51.

General procedure for the preparation of 2o–2q (Table 2): The appropriate diol (2 mmol, 1 equiv) was added to a magnetically stirred solution of IPy_2BF_4 (2.5 mmol, 1.25 equiv, 0.93 g) in CH_2Cl_2 (50 mL), and the resulting mixture was irradiated for the time indicated in Table 2. $Na_2S_2O_3$ (5% solution in water, 40 mL) was added, and the mixture was extracted with CH_2Cl_2 (4×20 mL). The organic layer was washed with H_2SO_4 (1 M, 2×50 mL) and water (2×50 mL) and dried (Na_2SO_4). Evaporation of the solvents afforded the α,ω-dialdehydes in high purity. Analytical samples were prepared by column chromatography (hexane/ethyl acetate).

General procedure for the preparation of compounds 3 (Table 3): The relevant alcohol (2 mmol, 1 equiv), I_2 (1 mmol, 0.5 equiv, 0.25 g) and Cs_2CO_3 (10 mmol, 5 equiv, 3.25 g) were sequentially added to a stirred solution of IPy_2BF_4 (6 mmol, 3 equiv, 2.23 g) in CH_3CN (30 mL). The heterogeneous mixture was heated (60 °C) for the time specified in Table 3. The crude reaction mixture was then allowed to cool, filtered through Celite and washed with CH_2Cl_2 (25 mL). The filtrate was concentrated under vacuum, redissolved in CH_2Cl_2 (25 mL) and stirred with HCl (1 N, 25 mL) for 15 min. The reaction mixture was then transferred to a separation funnel, and the aqueous layer was further extracted with CH_2Cl_2

(5×15 mL). The combined organic phases were sequentially washed with $Na_2S_2O_3$ (5% solution in water, 2×50 mL) and H_2O (2×50 mL) and dried (Na_2SO_4). Pure ketones were isolated after concentration of the solvent and column chromatography, and displayed data identical with those of commercial samples.

General procedure for the preparation of 5a–5h (Table 4): The procedure was totally equivalent to that described above, except for the use of K_2CO_3 (5 mmol, 2.5 equiv, 0.7 g) instead of Cs_2CO_3.

General procedure for the preparation of 7a–7b (Table 5): The relevant alcohol (1 mmol, 1 equiv), I_2 (4 mmol, 4 equiv, 1 g), MS (4 Å, 4 g), and K_2CO_3 (10 mmol, 5 equiv, 0.7 g) were sequentially added to a stirred solution of IPy_2BF_4 (3 mmol, 3 equiv, 1.1 g) in CH_3CN (50 mL). The heterogeneous mixture was heated (60 °C) for 16 h. The crude reaction mixture was then allowed to cool, filtered through Celite and washed with CH_2Cl_2 (12 mL). The filtrate was concentrated under vacuum, redissolved in CH_2Cl_2 (12 mL) and stirred with HCl (1 N, 12 mL) for 15 min. The reaction mixture was then transferred to a separating funnel, and the aqueous layer was further extracted with CH_2Cl_2 (5×15 mL). The combined organic phases were sequentially washed with $Na_2S_2O_3$ (5% solution in water, 2×50 mL) and H_2O (2×50 mL) and dried (Na_2SO_4). Removal of the solvent under vacuum and column chromatography (hexane/ethyl acetate) gave pure aldehydes.

General procedure for the preparation of 8a–8c (Table 5): IPy_2BF_4 (6 mmol, 3 equiv, 2.23 g) was dissolved in CH_3CN (5 mL) at 40 °C. The alcohol (2 mmol, 1 equiv), *t*BuOH (5 mmol, 2.5 equiv, 0.5 mL), I_2 (1 mmol, 0.5 equiv, 0.25 g), MS (4 Å, 1 g), and K_2CO_3 (4 mmol, 2 equiv, 0.56 g) were added sequentially. The mixture was heated at 40 °C for the time indicated in Table 5. Workup was equivalent to that described for the preparation of **7a** and **7b**. The esters were isolated by column chromatography (hexane/ethyl acetate).

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