EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Metal-Free Iodine-mediated Deoxygenation of Alcohols in ☐ alpha-Position to Electron-withdrawing Group

Authors: Maëva M. Pichon, Fabien Stauffert, Luis G. Addante-Moya, Anne Bodlenner, and Philippe Compain

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201800051

Link to VoR: http://dx.doi.org/10.1002/ejoc.201800051

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201800051

WILEY-VCH

Metal-Free Iodine-mediated Deoxygenation of Alcohols in α-Position to Electron-withdrawing Groups

Maëva M. Pichon, Fabien Stauffert, Luis G. Addante-Moya, Anne Bodlenner, Philippe Compain*

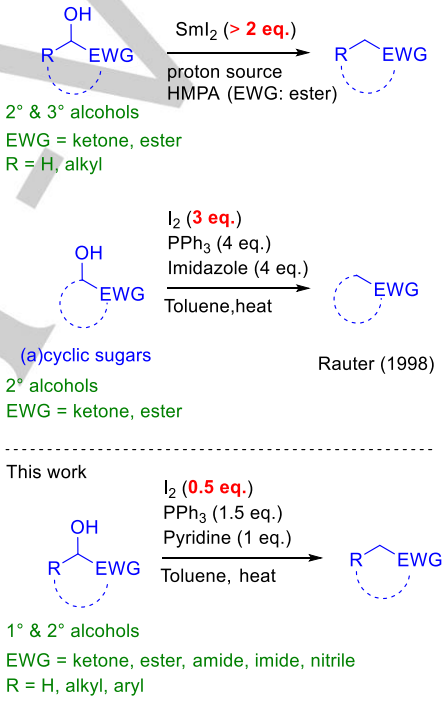
Abstract: The use of sub-stoichiometric amount of molecular iodine in the presence of PPh_3 and pyridine effects a direct deoxygenation of primary and secondary alcohols in α-position to a variety of activating electron-withdrawing groups including ketones, esters, amides, imides and nitrile groups.

Introduction

Selective deoxygenation of alcohols is undoubtedly a useful reaction in the multistep synthesis of relevant molecules. For example, deoxysugars constitute an important class of carbohydrates being constituents of, inter alia, antibiotics, anticancer agents and nucleic acids.[1,2] Deoxygenation of densely functionalized sugars is a primary goal to access enantiopure starting materials for the synthesis of non-carbohydrate compounds.[3] Late stage alcohol deoxygenation provide also a useful handle for the fine-tuning of key properties including lipophilicity, solubility or hydrogen-bonding. Most dehydroxylation processes are based on a two-step procedure and/or require stoichiometric amount of metallic reagents that may be toxic, expensive or difficult to remove from the deoxygenated product formed.[4] Barton-McCombie radical deoxygenation is an emblematic example of such processes since a thionoester generated in a first step is reduced by a stannane reagent in a second step. One-pot deoxygenation reactions of hydroxyl groups activated by a vicinal carbonyl group have been also described (Scheme 1).

Hydroxyl groups in α-position to ketones or esters are for example reductively cleaved with SmI_2 in the presence of a proton source.[5,6] However, the main drawbacks associated with this approach are the stoichiometric use of costly samarium metal and the possible reduction of functional groups sensitive to SmI_2. The list includes nitriles, alkyl halides and α,β-unsaturated ketones.[7] Dehydroxylation in α-position to esters may require the use of toxic HMPA to increase the reduction potential of SmI_2.[7]

In 1998, Rauter *et al.* reported an interesting iodide-mediated deoxygenation of α-hydroxy sugar esters or ketones in the presence of Ph_3P and imidazole.[8,9] Despite an ever-growing interest for the use of molecular iodine as an environmentally benign, nontoxic and inexpensive reagent,[10] this metal-free deoxygenation method, surprisingly, has been thus far almost overlooked. The use of large amounts of reagents (up to 4 equivalents) and the fact that only carbohydrate substrates were used to evaluate the reaction scope may explain, in part, this apparent lack of interest in the synthetic chemist community at large.



Scheme 1. One-pot deoxygenation reactions of hydroxyl groups activated by a vicinal electron-withdrawing group.

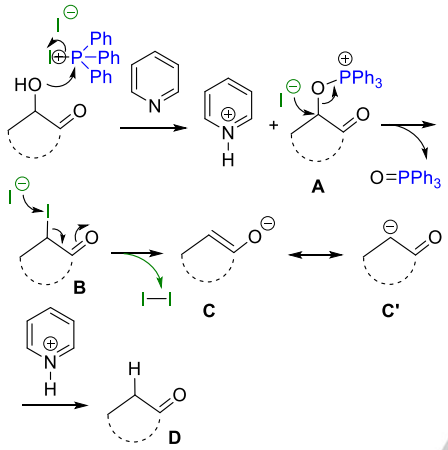
In this context and regarding the economic and environmental interest of metal-free methods, we decided to explore the feasibility of a dehydroxylation process that would make use of sub-stoichiometric amount of molecular iodine. From mechanistic considerations, it was indeed anticipated that catalytic amount of I_2 would be theoretically sufficient to convert alcohols into the corresponding deoxygenated products in the presence of triphenylphosphine (Ph_3P) and a base (*vide infra*). Furthermore, our objective was to expand the reaction scope beyond carbohydrate substrates and ketone/ester activating groups. Herein, we wish to describe the full details of this synthetic and mechanistic study that provided a simple, metal-free dehydroxylation procedure using sub-stoichiometric amount of molecular iodine.

Laboratoire d'Innovation Moléculaire et Applications
Univ. de Strasbourg | Univ. de Haute-Alsace | CNRS | LIMA (UMR 7042)
Equipe de Synthèse Organique et Molécules Bioactives (SYBIO), ECPM
25 Rue Becquerel, 67087 Strasbourg, France
Tel.: (+33) 3-6885-2792; fax: (+33) 3-6885-2754
Email : philippe.compain@unistra.fr

Supporting information for this article is given via a link at the end of the document.

Results and Discussion

Optimization studies were carried out under a variety of reaction conditions from 3,5-dibenzyl-D-xylono-1,4-lactone (**1**) as a model substrate, obtained in one step from commercially available (3*R*,4*R*)-3,5-di-*O*-benzyl-tetrahydrofuran-1,2-diol (Table 1). First attempts were guided by mechanistic considerations and focused on the amount of iodine reagent necessary to achieve a complete conversion of the starting material. According to the tentative mechanism proposed in Scheme 2, molecular iodine is expected to be indeed regenerated along with the formation of a key enolate intermediate. Sub-stoichiometric amount of I_2 would be therefore sufficient for the reaction to proceed to completion.

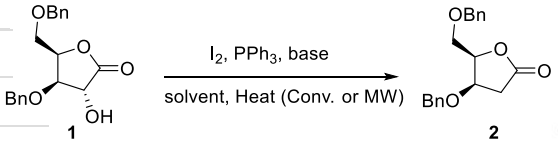


Scheme 2. Tentative mechanism for the iodine-mediated deoxygenation.

The first steps of the process are expected to be similar to the Garegg-Samuelsson reaction leading to the conversion of hydroxyl groups into iodo groups using the I_2-Ph_3P-imidazole reagent.[11] Formation of iodotriphenylphosphonium iodide followed by nucleophilic attack of the hydroxyl group would provide phosphonium salt **A**. Nucleophilic displacement of the phosphonium leaving group by iodide ion would then afforded the α-iodo carbonyl intermediate **B** and triphenylphosphine oxide. Further attack of an iodide ion on the iodo group in **B** would produce α-deoxy carbonyl product **D** *via* enolate **C**. Such reduction of carbon-halogen bonds in α-position to carbonyl groups by iodide ion have been postulated to account for the dehalogenation of haloketone using sodium iodide and an acid (5% aqueous H_2SO_4).[12]

The reaction was first studied in pyridine with the I_2/PPh_3 system. Treatment with 1 equiv. of I_2 and 1.5 equiv. of PPh_3 provided the expected 2-deoxyxylonolactone **2**[13] in 80% yields after 7 hours at 60°C (entry 1). The use of 0.5 equiv. of I_2 was found to slightly decrease the efficiency of the process and a longer reaction time was required but, satisfactorily, product **2** could be obtained in 70% yields after 20 hours (entry 2). The yield could be significantly increased to 91% in only 3 hours by using microwave irradiation (entry 3). The amount of I_2 could nevertheless not be lowered further since the use of 0.25 or 0.4 equivalent led to the recovery of more than 70% of the starting material (entries 4-6). Reactions performed at room temperature, even with a stoichiometric amount of I_2, were unsuccessful with incomplete conversion of the starting material (entry 7). The reaction was then performed in toluene with conventional heating or under microwave irradiation by treatment with 0.5 equiv. of I_2 and 1.5 equiv. of PPh_3 using stoichiometric amount of pyridine. Pleasingly, 2-deoxyxylonolactone **2** could be obtained in high yields under these conditions (entries 8-10). No improvement was observed when the solvent was switched from toluene to THF, chloroform or DMF (entries 11-14). The addition of 0.5 equiv. of TMSI was found to drastically reduce the yield of the deoxygenation process (entry 15). No conversion was observed in the absence of base or when pyridine was replaced by Et_3N, K_2CO_3 or imidazole in toluene at 60°C (entries 16-19). Similarly, the reaction did not proceed when I_2 was replaced by TBAI, as a source of iodide (entry 20).

Table 1. Optimization of the alcohol deoxygenation.



Entry	PPh_3 (equiv.)	I_2 (equiv.)	Additive[a]	Temp (°C)	Base[a]	Solvent	Time (h)	Yield[c] (%)
1	1.5	1.0	-	60	-	Pyridine	7	80
2	1.5	0.5	-	60	-	Pyridine	20	70
3	1.5	0.5	-	60[b]	-	Pyridine	3	91
4	1.25	0.25	-	90	-	Pyridine	20	LC
5	1.25	0.4	-	90	-	Pyridine	20	LC
6	1.5	0.4	-	60	-	Pyridine	20	LC
7	1.7	1.5	-	25	-	Pyridine	20	-[d]
8	1.5	0.5	-	100[b]	Pyr. (5)	Toluene	3	97
9	1.5	0.5	-	100[b]	Pyr (1.1)	Toluene	3	95
10	1.5	0.5	-	Δ	Pyr. (1.1)	Toluene	4.5	93
11	1.5	0.5	-	60[b]	Pyr. (10)	Toluene	3	80
12	1.5	0.5	-	60[b]	Pyr. (10)	$CHCl_3$	3	NR
13	1.5	0.5	-	60[b]	Pyr. (10)	DMF	3	NR
14	1.5	0.5	-	Δ	Pyr. (5)	THF	6	76
15	1.5	0.5	TMSI (0.5)	60[b]	Pyr. (10)	Toluene	3	17
16	1.5	0.5	-	60[b]	Et_3N (10)	Toluene	3	NR
17	1.5	0.5	-	60[b]	K_2CO_3 (10)	Toluene	3	NR
18	1.5	0.5	-	60[b]	Imidazole (10)	Toluene	3	NR
19	1.5	0.5	-	60[b]	-	Toluene	3	NR
20	1.5	-	TBAI (0.5)	60[b]	Pyr. (10)	Toluene	3	NR

[a] Number of equivalent in parentheses. [b] Reaction performed under microwave irradiations. [c] Isolated yield. [d] 64% of 1 recovered after 20h. Conv=conventional, TBAI= tetrabutylammonium iodide. LC = low conversion (more than 70% of starting material recovered/isolated). NR = no reaction

The deoxygenation process was then evaluated with conventional heating on a series of alcohols under the optimized reaction conditions requiring the least amount of pyridine [I_2 (0.5 equiv.), PPh_3 (1.5 equiv), pyridine (1.1 equiv.) in refluxing toluene]. We wished to explore the scope of the reaction with the double objective of going beyond carbohydrate substrates and of evaluating different types of activating electron-withdrawing groups.

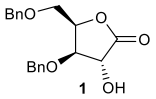
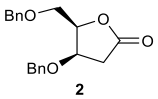
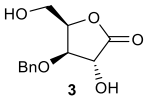
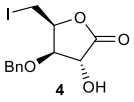
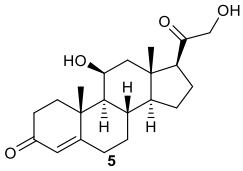
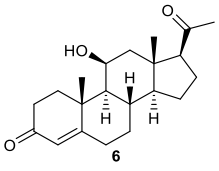
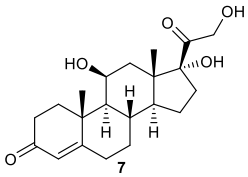
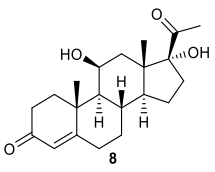
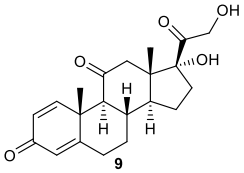
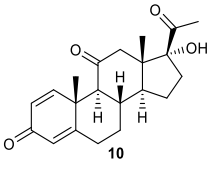
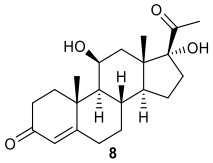
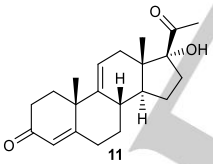
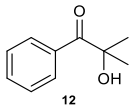
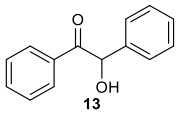
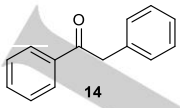
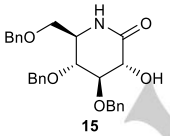
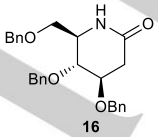
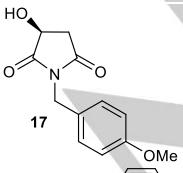
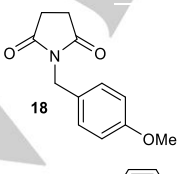
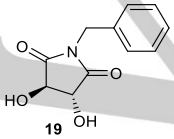
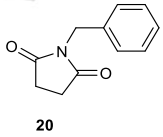
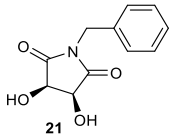
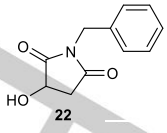
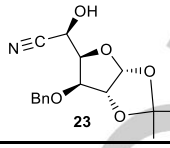
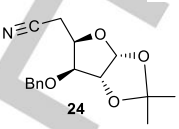
We first tested the stability of primary hydroxyl groups under deoxygenation conditions using diol lactone **3**[14], the mono-protected analogue of our test substrate **1** (entries 1 and 2). Not surprisingly, the Garegg-Samuelsson reaction leading to the corresponding iodide **4** occurred, blocking the formation of the targeted α-deoxygenated lactone. Pleasingly, under our optimized conditions, the desired deoxygenation could be however performed in high yields in the presence of a secondary alcohol as shown by the conversion of the commercially available α-cetol **5** to give the steroid derivative **6** (entry 3).[15]

Quite remarkably, tertiary alcohols in α-position to a ketone group remained untouched under the optimized reaction conditions leading to highly regioselective deoxygenation of the primary alcohols in **7** and **9** (entries 4-5). Further attempts to remove the tertiary OH group in **8** afforded only the dehydration of the C11 hydroxyl group to generate in low yields the corresponding steroid derivative **11** with a double bond positioned at C9-C11 (entry 6). The non-reactivity of tertiary alcohols under our deoxygenation conditions was further confirmed with 2-hydroxy-2-methylpropiophenone (Entry 7).

It is noteworthy that the enone group is compatible with the deoxygenation protocols which represents an advantage compared to the competing SmI_2-mediated deoxygenation reaction (entries 4-6).[5-8]

The conversion of benzoin (**13**) proceeded quantitatively to give the corresponding deoxy ketone **14** (entry 8).[16] For the latter example, the reaction was performed with polymer-bound, triphenyl phosphine-supported reagent to facilitate the

Table 2. Substrate scope[a]

Entry	Substrate	Product	Yield[b] (%)
1	 **1**	 **2**	93
2	 **3**	 **4**	50
3	 **5**	 **6**	85
4	 **7**	 **8**	79
5	 **9**	 **10**	76
6	 **8**	 **11**	12
7	 **12**	-	-[c]
8[d]	 **13**	 **14**	Quant.
9	 **15**	 **16**	81
10	 **17**	 **18**	81
11[e]	 **19**	 **20**	71
12[e]	 **21**	 **22**	51
13	 **23**	 **24**	51

[a] Deoxygenation conditions: (substrate/I_2/PPh_3/Pyridine 1:0.5:1.5:1.1, Δ, 5-8h). [b] Isolated yield. . [c] No conversion observed. [d] Reaction performed with triphenylphosphine-supported reagent (see experimental part). [e] 3 equiv. of PPh_3 and 2 equiv of pyridine were used.

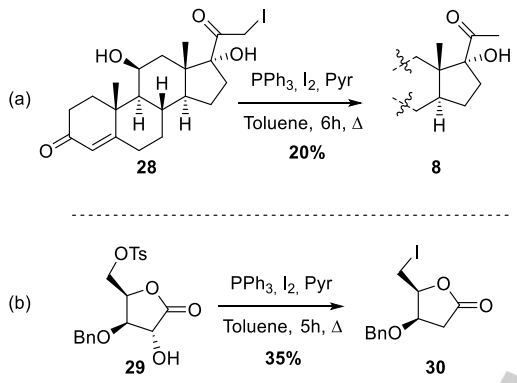
purification process by removing the triphenylphosphine oxide formed during the deoxygenation reaction before column chromatography.

Further screening revealed that the scope of the reaction could be further extended to other carbonyl-based electron-withdrawing groups including amides (substrate **15**[17]) (entry 9) and imides (substrate **17**[18])(entries 10-12). Interestingly, as shown with the conversion of *trans*-3,4-dihydroxypyrrolidine-2,5-dione derivative **19**[19] to the corresponding succinimide **20**,[20] double deoxygenation may be performed in good yields using 0.5 equiv. of I_2 (entry 11). According to the tentative mechanism proposed scheme 2, the amount of PPh_3 and pyridine has however to be doubled compared to the optimized protocol used for mono-deoxygenation. In sharp contrast, under the exactly same conditions, 3,4-dihydroxypyrrolidine-2,5-dione **21**,[21] the *cis* diastereomer of **19**, gave the racemic mono-deoxygenated product **22** in 51 % yield, the fully dehydroxylated product **20** being obtained in only 8% yield (entry 12). The impact of diol relative configuration on the deoxygenation reaction outcome is an interesting observation that is however difficult to rationalize at this stage. Dehydroxylation could be also achieved in α-position to a nitrile group. Acetal-protected cyanohydrin **23**[22] reacted with I_2 and PPh_3 to provide the expected cyano deoxy-sugar **24**[23] in 51% yield (entry 13). This result showed that the dehydroxylation process may be extended to systems based on electron-withdrawing groups other than carbonyls.

The impact of reversing the order of addition of reactants was evaluated on three representative substrates. Mixed results were obtained when the alcohol was added after the preformation of the key iodotriphenylphosphonium iodide intermediate (Scheme 2).[24,25] A slightly better yield (86%) was obtained for **10**, whereas no improvement was observed for the deoxygenation of secondary alcohol **15**. Conversion of diol **19** led mainly to degradation products and only small amount of monodeoxygenated product **22** could be identified based on crude NMR.

Control experiments were undertaken to probe the main steps of the tentative mechanism proposed in scheme 2. First, no deoxygenation was found to occur in the absence of PPh_3 or a base (entry 19, Table 1) and the reaction proceeds with sub-stoechiometric amounts of I_2 even for diol double deoxygenation

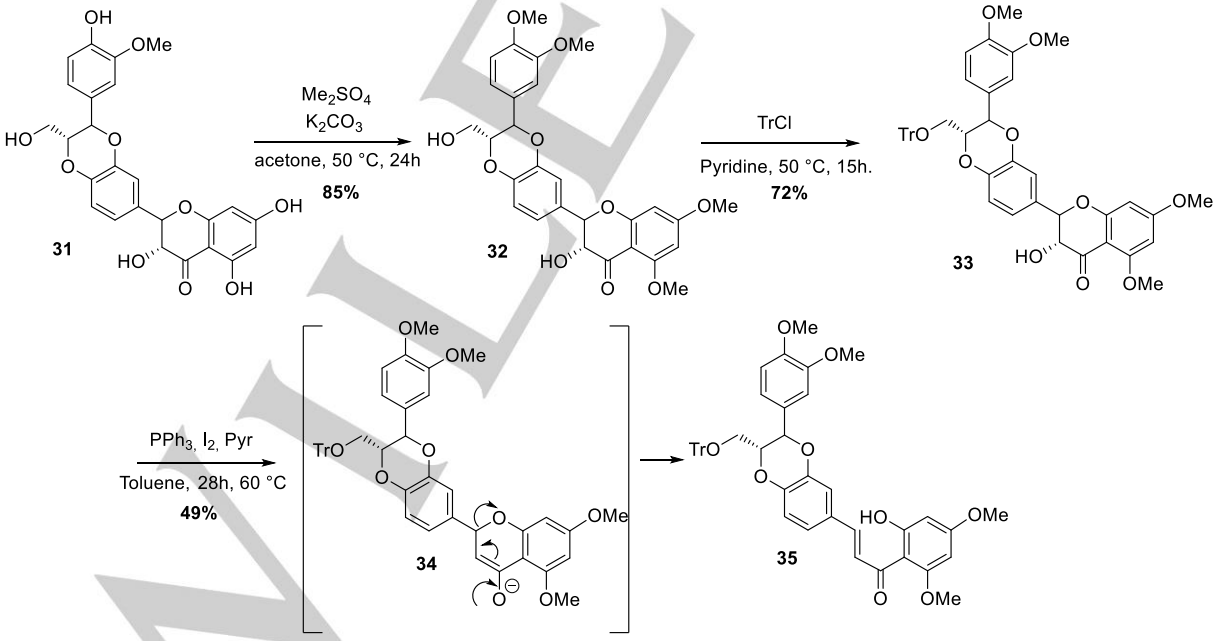
(entries 11-12, Table 2). To demonstrate that iodide **B** was an intermediate in the deoxygenated product formation, the iodo steroid **28** was prepared in two steps from the corresponding alcohol **7**.[26] Under typical deoxygenation conditions, the iodide derivative **28** afforded the expected ketone **8** in 20% yield (Scheme 3a), providing a good support that an α-iodo carbonyl derivative **28** is an intermediate in the mechanistic pathway. The lower yield observed may be explained by the fact that, in this case, **28** is not a transient species as in the conversion of alcohol **7**, but is present since the beginning of the process. To trap the iodide anion intermediate, the deoxygenation process was applied to tosylate **29** (Scheme 3b). The expected formation of iodide derivative **30** resulting from dehydroxylation at C2 and nucleophilic displacement at C5 occurred in a good yield of 35% considering the initial amount of I_2 (0.5 equiv.).



Scheme 3. Conversion of mechanistic probes under typical deoxygenation conditions (substrate/I_2/PPh_3/Pyr 1:0.5:1.5:1.1).

Next, we examined the possible formation of the enolate intermediate **C** via the attack of iodine ion onto the iodo group in α-position to the carbonyl group, a process that has been postulated to explain the iodide-mediated dehalogenation of haloketone.[12]

The formation of an enolate intermediate was supported by the conversion of the trityl-protected silibinin derivative **33** obtained in two steps from commercially available **31**. Chroman-4-one systems are known to be prone to retro-Michael reaction after formation of the corresponding enolate by deprotonation with a base.[27] Treatment of **33** under deoxygenation conditions provided in 49% yield the expected phenol **35** (Scheme 4). This ring-opening product may result from the formation of transient enolate **34** that is somehow trapped and engaged into a retro-Michael reaction.



Scheme 4. Synthesis and conversion of mechanistic probe **33** under typical deoxygenation conditions (substrate/I_2/PPh_3/Pyr 1:0.5:1.5:1.1).

Conclusions

In conclusion, the one-pot deoxygenation of primary and secondary alcohols activated by a vicinal electron-withdrawing group using sub-stoichiometric amount of molecular iodine in the presence of Ph_3P and pyridine has been developed. This metal-free process was found to proceed well with a variety of activating electron-withdrawing groups including ketones, esters, amides, imides and nitrile groups. The deoxygenation protocol is compatible with free secondary and tertiary hydroxyl groups and provides the dehydroxylated products with chemoselectivity that compares favorably with the related commonly used SmI_2-mediated reductive cleavage. Studies directed toward the extension of the reaction scope to systems with non-carbonylated activating groups are underway in our laboratory.

Experimental Section

General methods and remarks

Commercially available starting materials were purchased from commercial suppliers and were used without further purification. When specified, anhydrous solvents were required. Tetrahydrofuran (THF) was distilled over sodium/benzophenone under argon. Dimethylformamide (DMF) was purchased anhydrous over molecular sieves. Toluene was distilled over CaH_2, pyridine was distilled over KOH and both of them were stored over molecular sieves 3Å under argon. All reactions were carried out in standard glassware or in vials adapted to a Biotage Initiator® microwave reactor. Crude mixtures were purified by flash chromatography on silica gel 60 (230-400 mesh, 0.040-0.063 mm). Reaction monitoring and primary characterization of products were achieved by Thin Layer Chromatography (TLC) on aluminum sheets coated with silica gel 60 F254. Eluted TLC's were revealed under UV (254 nm) and with 12-molybdophosphoric acid or potassium permanganate. Nuclear Magnetic Resonance (NMR) spectra were recorded on 300 MHz, 400 MHz or 500 MHz spectrometers with non deuterated solvent peaks as reference. Chemical shifts are given in part per million (ppm) on the delta scale. Data are presented as followed: chemical shift, multiplicity (s = singlet, d =doublet, t = triplet, q = quadruplet, m = multiplet), coupling constants (*J* in Hz), integration and assignment. Carbon multiplicities were assigned by Distortionless Enhancement by Polarization Transfer (DEPT) experiments. ^{1}H and ^{13}C signals were assigned by correlation spectroscopy (COSY), Heteronuclear Single Quantum Correlation (HSQC), Heteronuclear Multiple-Bond Correlation spectroscopy (HMBC) and Nuclear Overhauser Effect Spectroscopy (NOESY) when required. Infrared (IR) spectra (cm^{-1}) were recorded neat. ESI-TOF high resolution mass spectra (HRMS) were carried out on a MicroTOF spectrometer. Specific rotations were determined on a polarimeter with sodium lamp (λ = 589 nm).

General Procedure

The substrate (1 eq.) was solubilized in dry toluene (40 eq.). Then, PPh_3 (1.5 eq.), dry pyridine (1 eq.) and finally iodine (0.5 eq.) were added. The mixture was heated under reflux for 5 to 8 h (depending on the substrate) under argon atmosphere. After completion, the reaction was cooled to room temperature and diluted with toluene. The solution was washed with $Na_2S_2O_3$ sat. solution and the aqueous and the organic phase were separated. Brown residue, if remaining in the flask, was dissolved in DCM and this new organic phase was then washed with $Na_2S_2O_3$ sat. solution. Aqueous phases were gathered and extracted three times with DCM. Organic phases were gathered and dried with Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography (SiO_2) to afford the deoxygenated product.

3,5-Di-*O*-benzyl-D-xylono-1,4-lactone (1): (3*R*,4*R*)-3,5-di-*O*-benzyl-tetrahydrofuran-1,2-diol (1 eq., 8.20 g, 24.8 mmol) was dissolved in dioxane (74.5 mL). H_2O (40 mL) and K_2CO_3 (3 eq., 10.3 g, 74.5 mmol) were added. The mixture was cooled to 0 ºC and Br_2 (3 eq., 11.9 g, 3.83 mL, 74.5 mmol) was added dropwise. The reaction was allowed to warm to room temperature and was stirred for 16 h. A saturated solution of $Na_2S_2O_3$ was added and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Petroleum Ether/ EtOAc 8:2 to 6:4) and compound **1** was obtained in 39% yield (3.195 g). The analytical data of compound **1** were in accordance with those reported in literature.[28]

2-Deoxy-3,5-bis-*O* -benzyl- γ -lactone (2): General procedure was followed starting from **1** (1.0 eq., 80.4 mg, 0.245 mmol) with a reaction time of 4.5 h. The residue was purified by flash column chromatography on silica gel (Petroleum Ether/ EtOAc 9:1) affording **2** (70.8 mg, 0.227 mmol, 93%) as an oil. Analytical data were in accordance with those reported in literature.[13]

3-*O*-benzyl-5-iodo-5-deoxy-D-xylono-1,4-lactone (4): General procedure was followed starting from **3** (1 eq., 61.3 mg, 0.257 mmol) with a reaction time of 6 h. The residue was purified by flash column chromatography on silica gel (Petroleum Ether/ EtOAc 7:3 to 4:6) affording **4** (44.8 mg, 0.129 mmol, 50%). Experimental data were in accordance with those reported in literature.[28]

11β-Hydroxy-4-pregnene-3,20-dione (6): General procedure was followed starting from **5** (1.01 eq., 100 mg, 0.287 mmol) with a reaction time of 6 h. The brown crude residue was purified by column chromatography on silica gel (Petroleum Ether/ EtOAc 4:6) affording **6** (80.4 mg, 0.243 mmol, 85%) as a white solid. **Mp=** 180 °C. **^{1}H-NMR (300 MHz, $CDCl_3$):** δ 0.85 (s, 3H, H18), 0.96 (dd, *J* = 11.0, 2.9 Hz, 1H, H14), 1.00–1.17 (m, 2H, H9, H6β), 1.21 (s, 1H, OH), 1.25–1.35 (m, 1H, H15α), 1.41 (s, 3H, H19), 1.57–1.76 (m, 3H, H12α, H16β, H15β), 1.82 (td, *J* = 13.4, 4.5 Hz, 1H, H1α), 1.89–2.03 (m, 2H, H8, H6α), 2.08 (s, 3H, H21), 2.11–2.24 (m, 4H, H16α, H1β, H12β, H7α), 2.30 (dt, *J* = 16.6, 4.2 Hz, 1H, H2α), 2.36–2.50 (m, 3H, H17, H7β, H2β), 4.38 (s, 1H, H11), 5.63 (s, 1H, H4). **^{13}C-NMR (75 MHz, $CDCl_3$):** δ 15.9 (C18), 21.0 (C19), 22.6 (C16), 24.4 (C15), 31.3 (C21), 31.4 (C8), 32.1 (C7), 32.6 (C6), 33.9 (C2), 35.0 (C1), 39.3 (C10), 43.1 (C13), 48.1 (C12), 56.4 (C14), 57.5 (C9), 63.9 (C17), 68.0 (C11), 122.3 (C4), 172.4 (C5), 199.7 (C3), 209.2 (C20).

11β,17α-Dihydroxypregn-4-ene-3,20-dione (8) : General procedure was followed using commercially available hydrocortisone **7** (1 eq., 198.5 mg, 0.55 mmol). The reaction was heated under reflux for 6 h. The obtained residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc 4:6) to afford **8** (149 mg, 0.431 mmol, 79 %) as a white solid. **Mp =** 226 °C. **Optical rotation** $[\alpha]_D^{20}$ = +127 (c 1, $CHCl_3$). **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 1.00 (s, 3H, H18), 1.03 (d, *J* = 3.2 Hz, 1H, H9), 1.12 (dd, *J* = 13.3, 4.4 Hz, 1H, H7α), 1.21 (m, 1H, OH-C11), 1.43 (s, 3H, H19), 1.46 (d, *J* = 6.1 Hz, 1H, H15α), 1.52 (dd, *J* = 14.0, 2.4 Hz, 1H, H12α), 1.55–1.63 (m, 1H, H16α), 1.64–1.75 (m, 1H, H14), 1.79–1.91 (m,

2H, H15β, H1α), 1.93–2.06 (m, 3H, H12β, H8, H7β), 2.17 (dt, *J* = 13.3, 4.6 Hz, 1H, H1β), 2.20–2.24 (m, 1H, H6α), 2.27 (s, 3H, H21), 2.34 (dt, *J* = 16.6, 4.2 Hz, 1H, H2α), 2.40–2.53 (m, 2H, H2β, H6β), 2.64–2.75 (m ,1H, H16β), 2.94 (s, 1H, OH-C17), 4.43–4.49 (m, 1H, H11), 5.66 (s, 1H, H4). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 18.1 (C18), 21.1 (C19), 24.1 (C15), 28.1 (C21), 31.4 (C8), 32.2 (C6), 32.8 (C7), 33.5 (C16), 33.9 (C2), 35.1 (C1), 39.3 (C10), 39.9 (C12), 47.7 (C13), 51.6 (C14), 56.1 (C9), 68.5 (C11), 89.6 (C17), 122.5 (C4), 172.3 (C5), 199.7 (C3), 211.8 (C20).

17-Hydroxypregna-1,4-diene-3,11,20-trione (10) : General procedure was followed using commercially available prednisone **9** (1 eq., 141 mg, 0.387 mmol). The reaction was heated under reflux for 6 h. The crude residue was purified by chromatography column on silica gel (Petroleum Ether/EtOAc 4:6) to afford product **10** (100 mg, 0.294 mmol, 76 %) as a white solid. **Mp** = 241–244 °C. **Optical rotation** $[\alpha]_D^{20}$ = +165 (c 1.2, $CHCl_3$) **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 0.69 (s, 3H, H18), 1.19–1.37 (m, 1H, H7α), 1.42 (s, 3H, H19), 1.45 (qd, *J* = 12.2, 6.1 Hz, 1H, H15β), 1.73 (ddd, *J* = 14.9, 9.6, 6.0 Hz, 1H, H16α), 1.88–2.04 (m, 3H, H8, H9, H15α), 2.04–2.17 (m, 2H, H7β, H12β), 2.23 (s, 3H, H21), 2.32–2.44 (m, 2H, H6α, H14), 2.51 (tdd, *J* = 13.6, 5.0, 1.5 Hz, 1H, H6β), 2.76 (ddd, *J* = 15.1, 11.7, 3.3 Hz, 1H, H16β), 2.85 (d, *J* = 12.3 Hz, 1H, H12α), 3.84 (s, 1H, OH), 6.06 (s, 1H, H4), 6.19 (dd, *J* = 10.2, 2.0 Hz, 1H, H2), 7.68 (d, *J* = 10.2 Hz, 1H, H1). **^{13}C-NMR (100MHZ, $CDCl_3$):** 16.2 (C18), 18.9 (C19), 23.5 (C15), 27.5 (C21), 32.3 (C7), 33.7 (C6), 33.8 (C16), 36.1 (C8), 42.5 (C10), 49.4 (C14), 49.9 (C12), 51.3 (C13), 60.1 (C9), 88.7 (C17), 124.5 (C4), 127.5 (C2), 155.7 (C1), 167.2 (C5), 186.6 (C3), 209.6 (C11), 210.5 (C20). **IR ($CHCl_3$)** ν_{max} **:** 3411, 2957, 1704, 1657, 1619, 1353, 1241, 897, 754 cm^{-1}. **HRMS** *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{26}O_4$ 343.1904; Found 343.1916.

2-Phenylacetophenone (14): Benzoin **13** (1 eq., 97.1 mg, 0.448 mmol) was solubilized in toluene (1.91 mL) at room temperature. Polymer-bound PPh_3 (CAS Number: 39319-11-4, purchased from Sigma-Aldrich, ~3 mmol/g triphenylphosphine loading) (1.5 eq., 0.224 g, 0.673 mmol of PPh_3) , pyridine (1 eq., 35.5 mg, 0.036 mL, 0.448 mmol) and then iodine (0.504 eq., 57.4 mg, 0.226 mmol) were added to the mixture. The reaction was then heated under reflux for 7 h. The mixture was diluted with toluene and filtered. The polymer-bound PPh_3 was then swelled and rinsed with CH_2Cl_2 and MeOH, and the filtrate was evaporated to dryness. The residue was then diluted with CH_2Cl_2 and washed with $Na_2S_2O_3$. The organic phase was dried with Na_2SO_4, filtered and evaporated to dryness. 2-Phenylacetophenone (88 mg, 0.448 mmol, 100 %) was obtained as a white solid. Analytical data were in accordance with the commercially available product **14**.

3,4,6-Tri-*O*-benzyl-D-glucono-1,5-lactam (16): General procedure was followed using **15** (1.0 eq., 60.6 mg, 0.135 mmol). The reaction was heated under reflux for 6 h. The obtained residue was purified by column chromatography on silica gel (Petroleum Ether/AcOEt 4:6) to afford **16** (47.1 mg, 0.1091 mmol, 81 %) as a white solid. Analytical data are in accordance with those reported in literature.[17]

1-(4-Methoxybenzyl)pyrrolidine-2,5-dione (18): General procedure was followed using **17** (1 eq., 156 mg, 0.647 mmol). The reaction was heated under reflux for 5 h. The obtained residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc 1:1) to afford **18** (114 mg, 0.523 mmol, 81 %) as a white solid. Analytical data are in accordance with those reported in literature.[20]

1-Benzylpyrrolidine-2,5-dione (20): (3*R*,4*R*)-1-Benzyl-3,4-dihydroxypyrrolidine-2,5-dione **19** (1 eq., 115 mg, 0.521 mmol) was solubilized in dry toluene (2.22 mL) at room temperature. Then, PPh_3 (3 eq., 410 mg, 1.56 mmol), dry pyridine (2 eq., 82.4 mg, 0.0842 mL, 1.04 mmol) and iodine (0.512 eq., 67.7 mg, 0.267 mmol) were added. The solution was heated under reflux for 6 h. The mixture was diluted with toluene and $Na_2S_2O_3$ was added. Organic and aqueous phase were separated. The organic phase was dried over Na_2SO_4, filtered and evaporated to dryness. The obtained crude was purified by column chromatography on silica gel (EtOAc/Petroleum Ether 4:6). 1-Benzylpyrrolidine-2,5-dione **20** (69.6 mg, 0.368 mmol, 71 %) was obtained as a white solid. Analytical data are in accordance with those reported in literature.[20]

***N*-Benzylmalimide (22):** Following the same procedure than for the synthesis of compound **20**, starting from **21** (1 eq., 94.7 mg, 0.428 mmol), the reaction was heated under reflux for 7 h. The obtained residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc 6:4 to 5:5) to afford **22** (45.2 mg, 0.22 mmol, 51 %). Analytical data are in accordance with those reported in literature.[29]

α-D-*xylo*-Hexofuranurononitrile, 5-deoxy-1,2-*O*-(1-isopropylidene)-3-*O*-benzyl (24): General procedure was followed using **23** (1 eq., 74.6 mg, 0.244 mmol). The reaction was heated under reflux for 5 h. The obtained residue was purified by column chromatography on silica gel (Petroleum Ether/AcOEt 85:15) to afford product **24** (36 mg, 0.124 mmol, 51 %). Analytical data are in accordance with those reported in literature.[23]

3-*O*-Benzyl-5-*O*-tosyl-D-xylono-1,4-lactone (29): 3-*O*-Benzyl-D-xylono-1,4-lactone (1 eq., 462 mg, 1.938 mmol) was diluted in dry pyridine (1.5 mL), the solution was cooled to 0 °C then TsCl (1.1 eq., 411.1 mg, 2.135 mmol) was added and the reaction mixture was stirred for 2 h at 0 °C and then allowed to reach room temperature and stirred for 20 h. The reaction mixture was treated with water (1.6 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The organic phase was dried with Na_2SO_4 and concentrated under reduced pressure. The crude was co-evaporated three times with toluene to remove traces of pyridine. The residue was purified by column chromatography on silica gel (Petroleum Ether/ EtOAc 7:3). Product **29** was obtained (307.4 mg, 0.783 mmol, 40 %) in presence of 20 % of a side product which is supposed to be the tosylated product at OH 2, with free OH group in position 5, as indicate NMR and Mass analyses. A second purification by column chromatography on silica gel (Petroleum Ether/ EtOAc 7:3) on the mixture of **29** and the side product allowed us to isolate compound **29** as pure product in the early fractions. **Optical rotation** $[\alpha]_D^{20}$ = +45 (c 0.8, $CHCl_3$). **^{1}H-NMR (400 MHz, MeOD):** δ 2.43 (s, 3H, CH_3), 3.30 (s, 1H, OH), 4.25 (dd, *J* = 11.1, 3.6 Hz, 1H, H5a), 4.31 (dd, *J* = 11.2, 2.7 Hz, 1H, H5b), 4.37 (t, *J* = 7.8 Hz, 1H, H3), 4.6 (d, *J* = 12.0 Hz, 1H, OCH_2Ph), 4.62−4.67 (m, 2H, H2, H4), 4.77 (d, *J* = 11.9 Hz, 1H, OCH_2Ph), 7.25−7.40 (m, 7H, H_{Ar}), 7.75 (d, *J* = 8.1 Hz, 2H, H_{Ar}(OTs)). **^{13}C-NMR (100MHz, $CDCl_3$):** δ 21.8 (CH_3), 66.8 (C5), 72.0 (C2), 72.8 (OCH_2Ph), 75.5 (C4), 79.4 (C3), 128.0, 128.1, 128.3, 128.7, 130.1 (C^{III}_{Ar}), 132.2, 136.9, 145.4 ($3xC^{IV}_{Ar}$), 174.3 (C1). **IR (neat)** ν_{max} : 3486, 2924, 1792, 1598, 1455, 1363, 1190, 1175, 1095, 1066, 965, 739, 663, 553. **HRMS** *m/z* $[M+Na]^+$ Calcd for $C_{19}H_{20}NaO_7S$ 415.0818; Found 415.0822.

3-*O*-Benzyl-5-iodo-2,5-dideoxy-D-xylono-1,4-lactone (30): General procedure was followed using **29** (1 eq., 53 mg, 0.13 mmol). The reaction was heated under reflux for 5 h. The obtained residue was purified by column chromatography on silica gel (Petroleum Ether/AcOEt 8:2) to afford product **30** (19 mg, 0.06 mmol, 44 %). **Optical rotation** $[\alpha]_D^{20}$ = -87 (c 1, $CHCl_3$). **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 2.67 (dd, *J* = 17.7, 5.0 Hz, 1H, H2a), 2.77 (dd, *J* = 17.7, 1.0 Hz, 1H, H2b), 3.42 (dd, *J* = 9.5, 5.4 Hz, 1H, H5a), 3.51 (t, *J* = 9.5 Hz, 1H, H5b), 4.36 (ddd, *J* = 5.0, 4.0, 1.0 Hz, 1H, H3), 4.50 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.60 (d, *J* = 11.3 Hz, 1H, OCH_2Ph), 4.65 (ddd, *J* = 9.5, 5.4, 4.0 Hz, 1H, H4), 7.30−7.40 (m, 5H, H_{Ar}). **^{13}C-NMR (100MHz, $CDCl_3$):** δ -1.5 (C5), 36.2 (C2), 72.2 (OCH_2Ph), 74.5 (C3), 83.2 (C4), 128.1, 128.3, 128.7 ($5C^{III}_{Ar}$), 136.8 (C^{IV}_{Ar}), 174.4 (C1). **IR (neat)** ν_{max} : 1777, 611 cm^{-1}. **HRMS** m/z $[M+Na]^+$ Calcd for $C_{12}H_{13}IO_3Na$ 354.9802 ; Found 354.9801.

(3*R*)-2-(3-(3,4-Dimethoxyphenyl)-2-((trityloxy)methyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-3-hydroxy-5,7-dimethoxychroman-4-one (33): **32** (1 eq., 297 mg, 0.567 mmol) was coevaporated three times with anhydrous THF and dissolved in anhydrous pyridine (2.14 mL). Triphenylmethyl chloride (1.68 eq., 270 mg, 0.952 mmol) was added to the solution and the solution was then heated at 50 °C for 15 h. The reaction was monitored by TLC (EtOAc/Petroleum Ether 9:1). The mixture was then diluted with MeOH and concentrated under reduced pressure. The crude was next purified on a silica gel column eluting with EtOAc/Petroleum Ether 6:4 in the presence of 1% of Et_3N to EtOAc/Petroleum Ether 8:2 + 1% of Et_3N , affording **33** (314 mg, 0.41 mmol, 72 %) as a pale amorphous solid. **Mp =** 139-142 °C. **Optical rotation** $[\alpha]_D^{20}$ = -4 (c 0.9, $CHCl_3$). **^{1}H- NMR (400 MHz, $CDCl_3$):** δ 2.76 (dd, *J* = 10.6, 2.9 Hz, 1H, H19a), 3.56 (dd, *J* = 10.6, 2.1 Hz, 1H, H19b), 3.70 (s, 3H, H27), 3.80 (s, 3H, H1), 3.86 (s, 3H, H25), 3.93 (s, 3H, H5), 4.05−4.13 (m, 2H, H18, OH), 4.47 (ddd, *J* = 12.2, 5.7, 1.3 Hz, 1H, H10), 4.98 (d, *J* = 12.2 Hz, 1H, H11), 5.29 (d, *J* = 8.6 Hz, 1H, H20), 6.08−6.15 (m, 2H, H8, H3), 6.69 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 6.81−6.87 (m, 2H, H_{Ar}), 7.13 (d, *J* = 3.5 Hz, 2, H_{Ar}), 7.17−7.30 (m, 10H, H_{Ar}), 7.43 (d, *J* = 8.1 Hz, 6H, H_{Ar}). **^{13}C- NMR (100 MHz, $CDCl_3$):** δ 55.9 (C25, C27), 56.1, 56.4 (C1, C5), 63.1 (C19), 72.8 (C10), 76.7 (C20), 77.9 (C18), 83.1 (C11), 86.7 (C29), 93.4, 93.8 (C3, C8), 103.1 (C6), 110.4 (C17), 110.1 (C14), 116.6 (C13), 117.5 (C^{III}_{Ar}), 120.4 (C^{III}_{Ar}), 121.2 (C^{III}_{Ar}), 123.9 (C12), 127.2, 127.9, 128.8 (C^{IV}_{Ar} Trityl), 129.6 (C21), 143.8 (C30, C31, C32), 144.1 (C^{IV}_{Ar}), 144.7 (C^{IV}_{A}), 149.1 (C26), 149.4 (C24), 162.3 (C^{IV}_{Ar}), 165.1 (C7), 167.1 (C^{IV}_{Ar}), 191.0 (C9). **IR ($CHCl_3$)** ν_{max} : 3439, 2935, 1674, 1608, 1574, 1508, 1449, 1259, 1215, 1158, 1109, 1027, 912, 816, 730, 703, 633 $^{cm-1}$. **HRMS** *m/z* $[M+H]^+$ calcd for $C_{47}H_{43}O_{10}$ 767.2851; Found 767.2807.

(*E*)-3-(3-(3,4-Dimethoxyphenyl)-2-((trityl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-(2-hydroxy-4,6-dimethoxyphenyl)prop-2-en-1-one (35): Compound **33** (1 eq., 95.2 mg, 0.124 mmol) was solubilized in dry toluene (0.53 mL). PPh_3 (1.53 eq., 49.7 mg, 0.189 mmol), pyridine (1 eq., 0.01 mL, 0.124 mmol) and iodine (0.524 eq., 16.5 mg, 0.065 mmol) were successively added. The solution was heated to 60 °C for 28 h. After completion, the reaction was cooled to room temperature and diluted with toluene. The mixture was washed with a $Na_2S_2O_3$ saturated aqueous solution and aqueous and organic phase were separated. Brown residue was dissolved with CH_2Cl_2 and this new organic phase was then washed with $Na_2S_2O_3$ sat. solution. Aqueous phases were gathered and extracted three times with CH_2Cl_2. Organic phases were gathered and dried with Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/Petroleum Ether 3:7 +1% Et_3N) to afford deoxygenated product **35** (45.5 mg, 0.0606 mmol, 49 %) as a yellow foam. **Mp =** 155-160 °C **Optical rotation** $[\alpha]_D^{20}$ **=** -2 (c 0.8, $CHCl_3$). **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 2.80 (dd, *J* = 10.8, 3.2 Hz, 1H, H19a), 3.55 (dd, *J* = 10.8, 2.4 Hz, 1H, H19b), 3.70 (s, 3H, OMe), 3.83 (s, 3H, H1), 3.87 (s, 3H, OMe), 3.90 (s, 3H, H5), 4.17 (dt, *J* = 8.0, 2.6 Hz, 1H, H18), 5.27 (d, *J* = 8.1 Hz, 1H, H20), 5.96 (d, *J* = 2.3 Hz, 1H, H3), 6.11 (d, *J* = 2.3 Hz, 1H, H8), 6.74 (d, *J* = 8.5 Hz, 1H, H23), 6.85−6.90 (m, 2H, H28, H22), 7.08 (d, *J* = 8.4 Hz, 1H, H14), 7.20−7.24 (m, 4H, H13, H_{para}), 7.25−7.29 (m, 6H, H_{ortho}), 7.30 (d, *J* = 2.0 Hz, 1H, H17), 7.40−7.45 (m, 6H, H_{meta}), 7.76 (d, *J* = 15.5Hz, 1H, H11 or H10), 7.80 (d, *J* = 15.5 z, 1H, H10 or H11), 14.39 (s, 1H, OH). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 55.7, 55.9, 56.0, 56.1 (C1, C5, C25, C27), 63.0 (C19), 76.9 (C20), 78.2 (C18), 86.8 (C29), 91.3 (C3), 93.9 (C8), 106.5 (C6), 110.6 (C28), 111.2 (C23), 116.6 (C17), 117.6 (C14), 120.3 (C22), 123.3 (C13), 125.8 (C10), 127.2 (C_{para}), 127.9 (C_{ortho}), 128.4 (C21), 128.7 (C_{meta}), 129.3 (C12), 142.6 (C11), 143.7 (C30, C31, C32), 144.2 (C16), 145.9 (C15), 149.1 (C24), 149.6 (C26), 162.6 (C4), 166.2 (C2), 168.5 (C7), 192.6 (C9). **IR ($CHCl_3$)** ν_{max} **:** 2933, 1618, 1581, 1558, 1503, 1263, 1217, 1157, 1114, 1029, 817, 749, 701, 632 cm^{-1}. **HRMS** *m/z* $[M+H]^+$ calcd for $C_{47}H_{43}O_9$ 751.2902; Found 751.2902.

Acknowledgements

This work was supported by the CNRS and the University of Strasbourg. MMP and FS thank the French Ministry of research for a PhD fellowship and L. G. A.-M the Erasmus program. Robin Weiss is acknowledged for assistance with synthetic work. The authors express their gratitude to Jean-Marc Weibel for fruitful discussions.

Keywords: alcohol deoxygenation • molecular iodine • transition metal-free • carbohydrates • steroids

[1] J. Rohr, *Bioorganic Chemistry Deoxysugars, Polyketides and Related Classes: Synthesis, Biosynthesis, Enzymes*, Springer Berlin Heidelberg, Berlin, Heidelberg, **1997**.

[2] C. Mendez, A. Luzhetskyy, A. Bechthold, J. Salas, *Curr. Top. Med. Chem.* **2008**, *8*, 710–724.

[3] R. Madsen, in *Glycoscience* (Eds.: B.O. Fraser-Reid, K. Tatsuta, J. Thiem), Springer Berlin Heidelberg, Berlin, Heidelberg, **2008**, pp. 179–225.

[4] For selected reviews see: a) J. M. Herrmann, B. König, *Eur. J. Org. Chem.* **2013**, 7017–7027; b) W. Hartwig, *Tetrahedron* **1983**, *39*, 2609-2645.

[5] a) G. A. Molander, *Chem. Rev.* **1992**, *92*, 29–68; b) J.A. Soderquist, *Aldrichimica Acta* **1991**, *24*, 15-23.

[6] a) G. A. Molander, G. Hahn, *J. Org. Chem.* **1986**, *51*, 1135–1138; b) S. Hanessian, C. Girard, *Synlett* **1994**, 861-864.

[7] *Organic Synthesis Using Samarium Diiodide: A Practical Guide*, Royal Society Of Chemistry, Cambridge, **2009**.

[8] A. P. Rauter, A. C. Fernandes, J. A. Figueiredo, *J. Carbohydr. Chem.* 1998, *17*, 1037–1045.

[9] For some examples of related α-ketols deoxygenation using 2.5 equivalents of iodotrimethylsilane see : T.-L. Ho, *Synth. Commun.* **1979**, *9*, 665–668.

[10] P. T. Parvatkar, P. S. Parameswaran, S. G. Tilve, *Chem. - Eur. J.* **2012**, *18*, 5460–5489.

[11] P. J. Garegg, T. Regberg, J. Stawiński, R. Strömberg, *J. Chem. Soc. Perkin Trans. 2* **1987**, 271–274.

[12] A. L. Gemal, J. L. Luche, *Tetrahedron Lett.* **1980**, *21*, 3195–3198.

[13] M. P. Doyle, J. S. Tedrow, A. B. Dyatkin, C. J. Spaans, D. G. Ene, *J. Org. Chem.* **1999**, *64*, 8907–8915.

[14] F. Stauffert, J. Serra-Vinardell, M. Gómez-Grau, H. Michelakakis, I. Mavridou, D. Grinberg, L. Vilageliu, J. Casas, A. Bodlenner, A. Delgado, et al., *Org Biomol Chem* **2017**, *15*, 3681–3705.

[15] a) G. Rosenkranz, J. Pataki, C. Djerassi, *J. Org. Chem.* **1952**, *17*, 290–293; b) A. Christy Hunter, K. R. Watts, C. Dedi, H. T. Dodd, *J. Steroid Biochem. Mol. Biol.* **2009**, *116*, 171–177

[16] S. E. Denmark, Y. Fan, *J. Org. Chem.* **2005**, *70*, 9667–9676.

[17] F. Stauffert, M. L. Lepage, M. M. Pichon, D. Hazelard, A. Bodlenner, P. Compain, *Synthesis* **2016**, *48*, 1177–1180.

[18] P. Q. Huang, Q. F. Chen, C. L. Chen, H. K. Zhang, *Tetrahedron Asymmetry* **1999**, *10*, 3827–3832.

[19] M. Arslan, M. Şentürk, İ. Fidan, O. Talaz, D. Ekinci, S. Coşgun, C. T. Supuran, *J. Enzyme Inhib. Med. Chem.* **2015**, *30*, 896–900.

[20] J. Zhang, M. Senthilkumar, S. C. Ghosh, S. H. Hong, *Angew. Chem. Int. Ed.* **2010**, *49*, 6391–6395.

[21] E. S. Dremina, X. Li, N. A. Galeva, V. S. Sharov, J. F. Stobaugh, C. Schöneich, *Anal. Biochem.* **2011**, *418*, 184–196.

[22] S. U. Hansen, M. Baráth, B. A. B. Salameh, R. G. Pritchard, W. T. Stimpson, J. M. Gardiner, G. C. Jayson, *Org. Lett.* **2009**, *11*, 4528–4531.

[23] G. W. J. Fleet, D. R. Witty, *Tetrahedron Asymmetry* **1990**, *1*, 119–136.

[24] C. W. Cheung, P. Ren, X. Hu, *Org. Lett*. **2014**, *16*, 2566-2569.

[25] L. C. Dias, G. Diaz, A. A. Ferreira, P. R. R. Meira, E. Ferreira, *Synthesis* **2003**, *4*, 603-622.

[26] J. Anthes, K. Mccormick, J. Hey, R. Aslanian, P. Biju, M. Berlin, D. Solomon, H. Wang, Y.-H. Lim, Y. J. Lee, et al., *C20-C21 Substituted Glucocorticoid Receptor Agonists*, **2009**, WO2009085879 (A2).

[27] a) C. E. Anson, C. S. Creaser, A. V. Malkov, L. Mojovic, G. R. Stephenson, *J. Organomet. Chem.* **2003**, *668*, 101–122; b) M. Majewski, N. M. Irvine, G. W. Bantle, *J. Org. Chem.* **1994**, *59*, 6697–6702; c) M. R. Jirousek, S. M. Mazza, R. G. Salomon, *J. Org. Chem.* **1988**, *53*, 3688–3695.

[28] D. R. Witty, G. W. J. Fleet, K. Vogt, F. X. Wilson, Y. Wang, R. Storer, P. L. Myers, C. J. Wallis, *Tetrahedron Lett.* **1990**, *31*, 4787–4790.

[29] K. L. Bhat, D. M. Flanagan, M. M. Joullié, *Synth. Commun.* **1985**, *15*, 587–598.

10.1002/ejoc.201800051

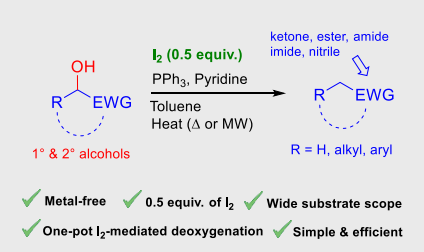
WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

The use of sub-stoichiometric amount of molecular iodine in the presence of PPh_3 and pyridine effects a direct deoxygenation of primary and secondary alcohols in α-position to a variety of activating electron-withdrawing groups.



Synthetic Methods

*Maëva M. Pichon, Fabien Stauffert, Luis G. Addante-Moya, Anne Bodlenner, Philippe Compain**

Page No. – Page No.

Metal-Free Iodine-mediated Deoxygenation of Alcohols in α-Position to Electron-withdrawing Groups