DOI: 10.1002/ejoc.201500829

MnO_2/TBHP: A Versatile and User-Friendly Combination of Reagents for the Oxidation of Allylic and Benzylic Methylene Functional Groups

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Keywords: Heterogeneous catalysis / Manganese / Oxidation / Peroxides / Enones

In the presence of activated MnO_2, *tert*-butyl hydroperoxide (TBHP) in CH_2Cl_2 is able to oxidize the allylic and benzylic methylene groups of different classes of compounds. I describe a one-pot oxidation protocol based on two sequential steps. In the first step, carried out at low temperature, MnO_2 catalyses the oxidation of the methylene group. This is followed by a second step where reaction temperature is increased, allowing MnO_2 both to catalyse the decomposition of unreacted TBHP and to oxidize allylic alcohols that could possibly be formed. The proposed oxidation procedure is generally applicable, although its efficiency, regioselectivity, and chemoselectivity are strongly dependent on the structure of the substrate.

Introduction

The oxidation of the allylic and benzylic methylene groups to the corresponding conjugated carbonyl derivatives is a transformation of great synthetic interest. This kind of reaction is considered to be one of the fundamental methods for C–H functionalization, and is accompanied by a significant increase in the synthetic and/or commercial value of the target molecules.[1] The required starting materials are often readily available, as they are cheap bulk chemicals such as terpenes and their derivatives,[2] or products from the petrochemical industry. As a consequence, allylic oxidation is a particularly attractive synthetic approach, especially for industrial processes.

Classically, the direct oxidation of methylene groups to the corresponding carbonyl derivatives is carried out with stoichiometric amounts of chromium- or selenium-based reagents. Otherwise, lengthy multistep procedures, involving halogenation, substitution of the halogen atom with a hydroxyl group, and finally oxidation, have also been extensively used.

Due to the high toxicity of the chromium and selenium waste inherent in these processes, as well as to the unsatisfactory atom economy, the latter approaches do not comply with the fundamental principles of green chemistry,[3] and are no longer acceptable in modern industrial chemistry.

As a consequence, during the last thirty years, a number of greener methods have been developed. More specifically, the use of catalytic oxidants combined with environmentally friendly oxidants such as organic and inorganic peroxides have given very good results.[4–12] In this way, the overall amount of heavy metals involved in the oxidation processes has been decreased, while still allowing the direct oxidation of the methylene group.

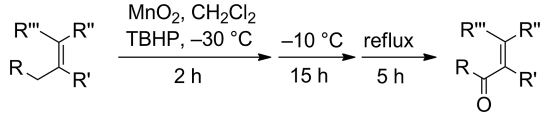
In this area, *tert*-butyl hydroperoxide (TBHP) has proved to be the most versatile peroxide, as it has good solubility in both organic solvents and water, as well as having a good thermal stability. Moreover, TBHP is able to oxidize allylic and benzylic methylene groups in combination with different catalysts, including transition metal derivatives (Cr,[4] Cu,[5] Co,[6] Ru,[7] Rh,[8] Pd,[9] Mn[10]), periodinanes,[11] and other substances.[12]

In this context, I have recently developed a new oxidation process based on the use of TBHP in combination with manganese dioxide.[13] The method allows the synthesis of the high-value flavour compound nootkatone by regioselective oxidation of the sesquiterpene valencene.

Since it has been claimed that other oxidation procedures that use TBHP and catalytic manganese salts are of great synthetic interest,[10a] I decided to investigate the general applicability of this method.

Results and Discussion

According to the procedure I propose, manganese dioxide has a triple function: it catalyses the oxidation of the methylene group that is carried out by TBHP, it catalyses the decomposition of the unreacted TBHP, and it oxidizes allylic alcohols that may have been formed during the reaction (Scheme 1). In this way, this approach can overcome



Scheme 1. MnO_2/TBHP allylic oxidation protocol.

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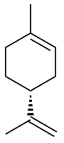
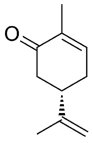
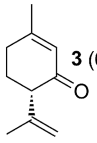
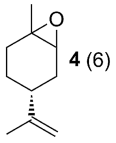
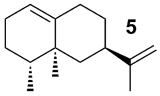
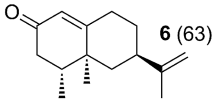
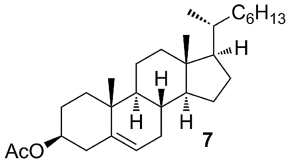
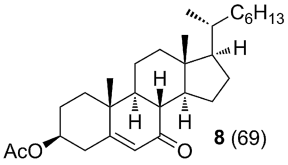
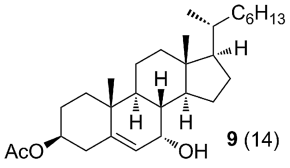
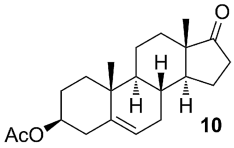
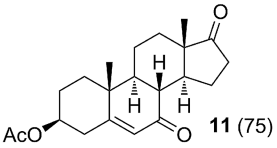
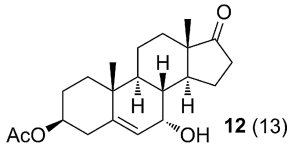
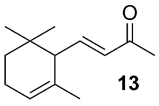
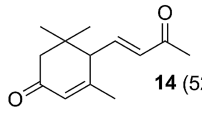
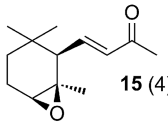
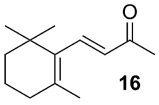
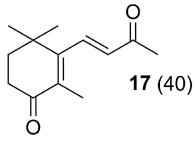
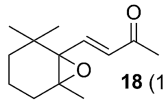
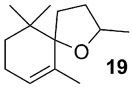
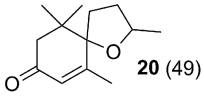
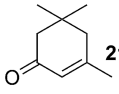
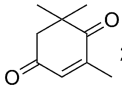
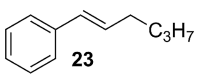
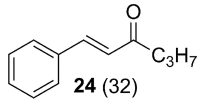
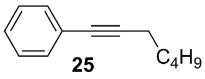
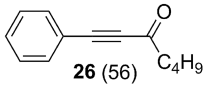
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500829.

some of the issues related to the use of TBHP, such as the removal of unreacted hydroperoxide, and the separation of allylic alcohols that could be formed in addition to the desired α,β-unsaturated ketone.

I observed that in CH_2Cl_2 and in the presence of activated manganese dioxide, TBHP is able to oxidize the allylic methylene group of different classes of compounds. The oxidation proceeds efficiently at temperatures ranging from –40 to 0 °C. Heating the TBHP solution in the presence of activated MnO_2 at temperatures above 30 °C results in the rapid decomposition of the peroxide with concomitant evolution of oxygen.

Finally, for the sake of completeness, it should be mentioned that a suspension of activated MnO_2 in CH_2Cl_2 is

Table 1. MnO_2/TBHP oxidation[a] of compounds with allylic or propargylic methylene groups.

Entry	Substrates	Unreacted substrates %[b]	Products, yields %[b]	Other oxidation products, yields %[b]
1	 **1**	26	 **2** (22)  **3** (6)	 **4** (6)
2	 **5**	4	 **6** (63)	
3	 **7**	8	 **8** (69)	 **9** (14)
4	 **10**	6	 **11** (75)	 **12** (13)
5	 **13**	25	 **14** (52)	 **15** (4)
6	 **16**	3	 **17** (40)	 **18** (19)
7	 **19**	35	 **20** (49)	
8	 **21**	66	 **22** (28)	
9	 **23**	1	 **24** (32)	
10	 **25**	39	 **26** (56)	

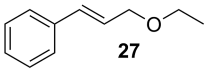
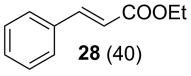
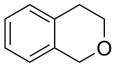
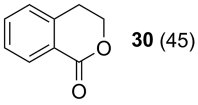
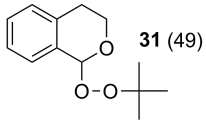
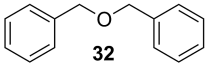
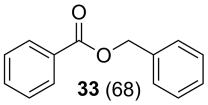
[a] Reaction conditions as described in the general procedure. [b] Yields of isolated products after chromatography.

able to oxidize different kinds of allylic alcohols. All these aspects were exploited in the one-pot experimental procedure shown in Scheme 1. Thus, a stirred mixture of the compound containing allylic methylene group(s), CH_2Cl_2, and activated MnO_2 (ca. 8 equiv.) was treated with the commercially available aqueous solution of TBHP (70 wt.-%; 2.4 equiv.). The experimental conditions illustrated in Scheme 1 gave a mixture of the desired α,β-unsaturated ketone, the unreacted olefin, and other oxidation products such as allylic alcohols or epoxides. The recovered MnO_2 was found to be still active,[14] and it could be reused again for the same reaction.

To check the effectiveness of the process, I investigated the oxidation of a number of different compounds, using the same experimental conditions for each experiment (Tables 1, 2, and 3). Although the aforementioned conditions are not optimized, and the yields of the ketones could be improved, the decision to use uniform conditions helps to describe the relative reactivity and regioselectivity of the oxidation procedure for the classes of compounds investigated. Accordingly, I first studied the reactivity of different compounds with allylic or propargylic methylene groups (Table 1).

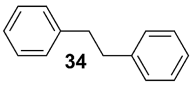
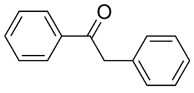
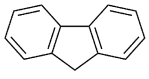
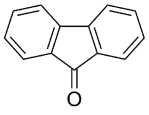
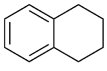
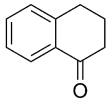
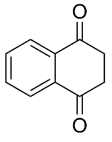
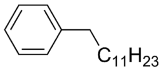
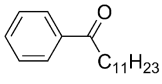
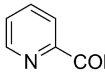
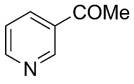
The results indicate a very complex reactivity that is strongly dependent on the substrates used. For example, the oxidation of limonene (**1**) didn't proceed to completion, and gave carvone (**2**), its isomer isopiperitenone (**3**), and epoxy derivative **4** as the major products, as well as a number of

Table 2. MnO_2/TBHP oxidation[a] of compounds with a methylene group linked to both a double bond and an alkoxy group.

Entry	Substrates	Unreacted substrates %[b]	Products, yields %[b]	Other oxidation products, yields %[b]
1	 **27**	0	 **28** (40)	
2	 **29**	0	 **30** (45)	 **31** (49)
3	 **32**	5	 **33** (68)	

[a] Reaction conditions as described in the general procedure. [b] Yields of isolated products after chromatography.

Table 3. MnO_2/TBHP oxidation[a] of compounds with benzylic methylene groups.

Entry	Substrates	Unreacted substrates %[b]	Products, yields %[b]	Other oxidation products, yields %[b]
1	 **34**	75	 **35** (15)	
2	 **36**	2	 **37** (93)	
3	 **38**	7	 **39** (55)	 **40** (5)
4	 **41**	70	 **42** (21)	
5	 **43**	79	 **44** (16)	
6	 **45**	67	 **46** (23)	

[a] Reaction conditions as described in the general procedure. [b] Yields of isolated products after chromatography.

overoxidation products. Conversely, (+)-valencene (**5**) was effectively oxidized to give (+)-nootkatone (**6**) in good yield and with very good regioselectively. Similarly, both cholesterol acetate (**7**) and prasterone acetate (**10**) were oxidized very efficiently and with almost complete regioselectivity.

It is worth noting that for these last two reactions, allylic alcohols **9**[15] and **12**[16] were also isolated as single isomers. Most probably, the last step of the oxidation protocol is not able to convert them completely into ketones **8** and **11**, respectively, as demonstrated by confirmatory experiments.[17]

Very different behaviour was observed for compounds containing a 2,6,6-trimethylcyclohexenic framework. Although the oxidation of α-ionone (**13**) didn't proceed to completion, the process gave keto-derivative **14** in a good overall yield, along with a marginal amount of *cis*-epoxy-α-ionone (**15**). On the other hand, β-ionone was oxidized almost completely, but the expected ketone (i.e., **17**) was isolated in a lower yield, along with a considerable amount of epoxy-β-ionone (**18**) and other overoxidation products.

Theaspirane (**19**) and isophorone (**21**) showed reactivity similar to that described for α-ionone, giving the relevant flavour compound theaspirone (**20**) and keto-isophorone (**22**), respectively, with good regio- and chemoselectivity. This latter ketone was obtained in a low yield, most probably because of the combined effect of the electron-withdrawing keto group and the steric hindrance around the methylene group. Lastly, I report the case of acyclic compounds **23** and **25**. Cinnamyl derivative **23** was oxidized very efficiently to give ketone **24**, benzaldehyde, benzoic acid, cinnamaldehyde, and further overoxidation products. On the other hand, the reaction of alkyne derivative **25** was less effective, but did give the expected ketone (i.e., **26**) in good yield, and with high chemoselectivity.

Next, I examined the reactivity of the compounds with a methylene group linked both to a double bond and to an alkoxy group (Table 2).

Surprisingly, all three of the substrates tested were transformed very efficiently to give the expected ester derivatives, along with other oxidation products. Cinnamol ethyl ether (**27**) was completely oxidized to give a complex mixture made up of ethyl cinnamate (**28**), benzaldehyde, benzoic acid, cinnamaldehyde, and other unidentified products. Conversely the oxidation of isochroman (**29**) quantitatively gave a mixture of only two products, namely isochromanone (**30**) and peroxide **31**.[18] Most probably, the intermediate benzylic radical is highly stabilized by the vicinal oxygen atom, and the abstraction of the allylic hydrogen by the *tert*-butoxy radicals is favoured when the methylene group is part of a ring.[19] Together, these effects allowed the complete transformation of the substrate, and also increased the stability of *tert*-butylhydroperoxide **31**, which was isolated and characterized without noticeable degradation. Similarly, dibenzyl ether (**32**) was almost completely oxidized to give benzyl benzoate (**33**) along with a mixture of benzaldehyde and benzoic acid.

The last class of substrates investigated comprises compounds with a benzylic methylene group (Table 3). As was found for the compounds with allylic methylene groups, the reactivity of these compounds in the oxidation was also found to be strongly dependent on their chemical structure. Biphenyl **34** and the linear alkyl benzene **41** reacted poorly, albeit with good chemoselectivity, to give ketones **35** and **42**, respectively. Similarly, 2-ethylpyridine (**43**) and 3-ethylpyridine (**45**) gave the corresponding acetylpyridines (i.e., **44** and **46**) in low yield. It is worth noting that neither the presence of the heteroatom nor the position of the chain on the aromatic ring seemed to affect the reactivity trend.

A very different outcome was observed when the benzylic methylene group was part of a ring. Fluorene (**36**) and tetrahydronaphthalene (**38**) were oxidized almost completely. In addition, compound **36** gave fluorenone (**37**) in nearly quantitative yield, indicating the complete chemoselectivity of the reaction. Conversely, the oxidation of compound **38** gave ketone **39** as the major product, along with quinone **40** and a number of unidentified oxidation products.

It is worth nothing that the described reactivity, and especially the isolation of peroxide **31**, point to a reaction mechanism involving the formation of the *t*BuOO$^{\cdot}$ radical, as described previously for different metal-catalysed TBHP oxidation procedures.[8,10a,12b] MnO_2 can catalyse the decomposition of TBHP to give HO$^{\cdot}$ and *t*BuO$^{\cdot}$ radicals. The latter intermediate can react with TBHP to produce *t*BuOO$^{\cdot}$, which is able to abstract an allylic hydrogen atom from the substrate to produce the allylic radical. This allylic radical can then react with a further molecule of *t*BuOO$^{\cdot}$ to give the corresponding *tert*-butyl peroxyether, whose decomposition gives *tert*-butanol and the expected enone. Concurrently, the reaction of the HO$^{\cdot}$ radical with TBHP produces *t*BuOO$^{\cdot}$ and water. This latter step probably occurs on the MnO_2 surface, where the metal atom can coordinate the oxygen atom of the HO$^{\cdot}$ radical intermediate.

Overall, the yields and selectivities of the oxidation are affected by the factors that influence both the formation and the stability of the intermediate allylic radical. For this reason, reaction conditions such as the temperature and the amount of the oxidant could be specifically modified in order to improve the yields in the cases of compounds that give overoxidation products (for example, compounds **24** and **28**), or to increase the conversion of substrates that reacted poorly (for example, compounds **34**, **41**, **43**, and **45**).

Conclusions

In conclusion, I have described a simple and user-friendly synthetic procedure for the oxidation of allylic and benzylic methylene groups to the corresponding conjugated carbonyl derivatives. The proposed oxidation protocol is based on the combined use of MnO_2 and TBHP, and is generally applicable, although its efficiency, regioselectivity, and chemoselectivity are strongly dependent on the chemical structure of the substrate. A comprehensive rationalization of the reactivity of this combination of oxidants is still lacking. Further studies on this topic are underway, and the results will be reported in due course.

Experimental Section

General Remarks: All air- and moisture-sensitive reactions were carried out using dry solvents under an atmosphere of nitrogen. All solvents and reagents were of commercial quality. (+)-Limonene, (+)-valencene, α-ionone, β-ionone, racemic theaspirane, isophorone, isochroman, dibenzyl ether, bibenzyl, fluorene, 1,2,3,4-tetrahydronaphthalene, 2-ethylpyridine, and 3-ethylpyridine were purchased from Aldrich. Cholesterol acetate was prepared from commercially sourced cholesterol (Aldrich) by acetylation with acetic anhydride and pyridine; prasterone acetate was prepared from commercially sourced prasterone by acetylation with acetic anhydride and pyridine. (*E*)-(3-Ethoxyprop-1-enyl)benzene (**27**), (*E*)-hex-1-enylbenzene (**23**), hept-1-ynylbenzene (**25**), and *n*-dodecylbenzene (**41**), were prepared starting from cinnamyl alcohol, cinnamyl acetate, phenylacetylene, and undecyl bromide, respectively, according to the procedures described in the Supporting Information.

TLC: Merck silica gel 60 F_{254} plates. Column chromatography (CC): silica gel. GC–MS analysis: HP-6890 gas chromatograph equipped with a 5973 mass detector, using a HP-5MS column (30 m × 0.25 mm, 0.25 μm film thickness; Hewlett–Packard) with the following temp. program: 60 °C (1 min) – 6 °C/min – 150 °C (1 min) – 12 °C/min – 280 °C (5 min); carrier gas: He; constant flow: 1 mL/min; split ratio 1:30; t_R given in min: t_R(**2**) = 12.27, t_R(**3**) = 12.90, t_R(**4**) = 9.61 and 9.73, t_R(**6**) = 23.43, t_R(**14**) = 20.51, t_R(**15**) = 18.58, t_R(**17**) = 20.69, t_R(**18**) = 17.66, t_R(**20**) = 19.97 and 20.13, t_R(**22**) = 9.91, t_R(**23**) = 14.14, t_R(**24**) = 18.83, t_R(**25**) = 16.51, t_R(**26**) = 19.70, t_R(**27**) = 14.54, t_R(**28**) = 17.24, t_R(**30**) = 17.59, t_R(**33**) = 21.94, t_R(**35**) = 21.46, t_R(**37**) = 21.76, t_R(**39**) = 15.25, t_R(**40**) = 15.92, t_R(**41**) = 23.40, t_R(**42**) = 24.95, t_R(**44**) = 7.35, t_R(**46**) = 9.12. Mass spectra of compounds **8**, **9**, **11**, **12**, and **31** were recorded with a Bruker ESQUIRE 3000 PLUS spectrometer (ESI detector). Optical rotations: Jasco DIP-181 digital polarimeter. ^{1}H and ^{13}C NMR spectra and DEPT experiments: $CDCl_3$ solutions at room temp. using a Bruker AC-400 spectrometer at 400, 100, and 100 MHz, respectively; chemical shifts in ppm relative to internal $SiMe_4$ (δ = 0 ppm). Melting points were measured with a Reichert apparatus, equipped with a Reichert microscope.

General Procedure for Allylic and Benzylic Oxidation: A solution of TBHP (70% wt. in water; 120 mmol) was added dropwise to a vigorously stirred mixture made up of the compound to be oxidized (50 mmol), activated MnO_2 (400 mmol), and CH_2Cl_2 (100 mL) cooled to –30 °C. After 2 h the reaction was allowed to reach –10 °C, and stirring was continued at that temperature for 15 h. The reaction mixture was then heated at reflux for 5 h, then it was cooled, and the solid MnO_2 was recovered by filtration. The filtrate was concentrated under reduced pressure, and the crude product mixture was purified by chromatography and/or distillation.

Limonene Oxidation: The oxidation of (+)-limonene (**1**; 10 g, 73.4 mmol) according to the general procedure gave a complex mixture whose chromatographic separation allowed the isolation of unreacted limonene (2.6 g, 26%), limonene 1,2-epoxide **4** (0.67 g, 6%, mixture of *cis* and *trans* isomers), and a carvone/isopiperitenone mixture (3.1 g, 28%, **2**/**3** ratio 79:21, GC analysis). The latter compounds were identified by GC analysis using commercially available **2** and **4** and synthetic **3**[20] as reference standards.

Valencene Oxidation: The oxidation of (+)-valencene (**5**; natural valencene, 67% purity; 15 g, 49.2 mmol) according to the general procedure gave unreacted valencene (0.4 g, 4%) and (+)-nootkatone (**6**; 6.8 g, 63%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[21a]

(+)-Nootkatone (6): Pale yellow oil. $[\alpha]_D^{20}$ = +189.3 (*c* = 2.1, $CHCl_3$); ref.[21b] $[\alpha]_D^{20}$ = +170 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.76 (br. s, 1 H), 4.74 (br. s, 1 H), 4.72 (br. s, 1 H), 2.58–2.46 (m, 1 H), 2.43–2.15 (m, 4 H), 2.08–1.84 (m, 3 H), 1.74 (s, 3 H), 1.35 (qd, *J* = 12.5, 4.2 Hz, 1 H), 1.20–1.04 (m, 1 H), 1.12 (s, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 170.2, 149.0, 124.7, 109.2, 44.0, 42.1, 40.5, 40.3, 39.3, 33.0, 31.6, 20.7, 16.8, 14.8 ppm. GC–MS (EI): *m*/*z* (%) = 218 (21) $[M]^+$, 203 (49), 190 (47), 175 (52), 161 (70), 147 (100), 133 (75), 121 (80), 105 (59), 91 (91), 79 (81), 67 (30).

Cholesterol Acetate Oxidation: The oxidation of (+)-cholesterol acetate (**7**; 15 g, 35 mmol) according to the general procedure gave unreacted cholesterol acetate (1.2 g, 8%), 7-oxo-cholest-5-en-3β-yl acetate (**8**; 10.7 g, 69%), and 7α-hydroxycholest-5-en-3β-yl acetate (**9**; 2.17 g, 14%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[10a,15a]

7-Oxo-cholest-5-en-3β-yl Acetate (8): White crystals, m.p. 161–163 °C; ref.[10a] m.p. 154–155 °C. $[\alpha]_D^{20}$ = –101.9 (*c* = 2.1, $CHCl_3$); ref.[10a] $[\alpha]_D^{20}$ = –96.6 (*c* = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.70 (d, *J* = 1.5 Hz, 1 H), 4.77–4.66 (m, 1 H), 2.55 (ddd, *J* = 13.9, 5.1, 1.9 Hz, 1 H), 2.51–2.45 (m, 1 H), 2.45–2.34 (m, 1 H), 2.23 (t, *J* = 11.1 Hz, 1 H), 2.08–1.84 (m, 4 H), 2.05 (s, 3 H), 1.75–1.45 (m, 5 H), 1.44–0.97 (m, 13 H), 1.21 (s, 3 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 0.87 (d, *J* = 6.6 Hz, 3 H), 0.88 (d, *J* = 6.6 Hz, 3 H), 0.68 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.8, 170.2, 163.7, 126.7, 72.2, 54.8, 50.0, 49.8, 45.4, 43.1, 39.4, 38.7, 38.3, 37.7, 36.2, 36.0, 35.7, 28.5, 27.9, 27.3, 26.3, 23.8, 22.7, 22.5, 21.2, 21.2, 18.8, 17.2, 11.9 ppm. MS (ESI): *m*/*z* = 465.3 $[M + Na]^+$.

7α-Hydroxycholest-5-en-3β-yl Acetate (9): White crystals, m.p. 138–139 °C; ref.[15a] m.p. 139–140 °C. $[\alpha]_D^{20}$ = –82.5 (*c* = 1, $CHCl_3$); ref.[15b] $[\alpha]_D^{20}$ = –85 (*c* = 0.24, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.62 (d, *J* = 5.1 Hz, 1 H), 4.70–4.59 (m, 1 H), 3.84 (br. s, 1 H), 2.43–2.30 (m, 2 H), 2.09–1.82 (m, 4 H), 2.03 (s, 3 H), 1.78–0.96 (m, 21 H), 1.01 (s, 3 H), 0.93 (d, *J* = 6.6 Hz, 3 H), 0.87 (d, *J* = 6.6 Hz, 3 H), 0.86 (d, *J* = 6.6 Hz, 3 H), 0.69 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3, 145.2, 124.8, 73.4, 65.2, 55.9, 49.4, 42.3, 42.2, 39.5, 39.2, 38.0, 37.6, 37.5, 36.8, 36.2, 35.8, 28.2, 28.0, 27.5, 24.3, 23.8, 22.7, 22.5, 21.3, 20.7, 18.8, 18.2, 11.6 ppm. MS (ESI): *m*/*z* = 467.3 $[M + Na]^+$.

Prasterone Acetate Oxidation: The oxidation of (+)-prasterone acetate (**10**; 12 g, 36.3 mmol) according to the general procedure gave unreacted prasterone acetate (0.72 g, 6%), 7-keto-dehydroepiandrosterone acetate (**11**; 9.4 g, 75%), and 7α-hydroxy-17-oxoandrost-5en-3β-yl acetate (**12**; 1.6 g, 13%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[10a,16]

7-Keto-dehydroepiandrosterone Acetate (11): White crystals, m.p. 186–187 °C; ref.[10a] m.p. 175–178 °C. $[\alpha]_D^{20}$ = –90.1 (*c* = 1.9, $CHCl_3$); ref.[10a] $[\alpha]_D^{20}$ = –85.8 (*c* = 1.7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (d, *J* = 1.9 Hz, 1 H), 4.72 (tt, *J* = 11.6, 4.7 Hz, 1 H), 2.86–2.76 (m, 1 H), 2.60 (ddd, *J* = 14.0, 5.0, 1.9 Hz, 1 H), 2.54–2.35 (m, 3 H), 2.12 (dt, *J* = 19.6, 9.2 Hz, 1 H), 2.07–1.94 (m, 2 H), 2.05 (s, 3 H), 1.90–1.51 (m, 7 H), 1.36–1.19 (m, 2 H), 1.24 (s, 3 H), 0.90 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 219.7, 200.4, 170.0, 164.6, 126.4, 71.9, 50.0, 47.7, 45.7, 44.3, 38.4, 37.8, 35.9, 35.5, 30.7, 27.2, 24.1, 21.0, 20.5, 17.3, 13.7 ppm. MS (ESI): *m*/*z* = 367.1 $[M + Na]^+$.

7α-Hydroxy-17-oxoandrost-5en-3β-yl Acetate (12): White crystals, m.p. 165–167 °C; ref.[16b] m.p. 168–169 °C. $[\alpha]_D^{20}$ = –64.1 (*c* = 2, $CHCl_3$); ref.[16b] $[\alpha]_D^{20}$ = –66 (*c* = 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.66 (d, *J* = 5.0 Hz, 1 H), 4.70–4.57 (m, 1 H), 3.96 (s, 1 H), 2.54–2.30 (m, 3 H), 2.22–2.07 (m, 2 H), 2.03 (s, 3 H), 1.96–

1.77 (m, 4 H), 1.75–1.43 (m, 6 H), 1.40–1.07 (m, 3 H), 1.03 (s, 3 H), 0.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 220.7, 170.3, 145.2, 124.5, 73.1, 64.0, 47.0, 44.9, 42.5, 37.9, 37.5, 37.2, 36.6, 35.7, 31.0, 27.4, 21.8, 21.2, 20.0, 18.1, 13.2 ppm. MS (ESI): m/z = 369.1 $[M + Na]^+$.

α-Ionone Oxidation: The oxidation of racemic α-ionone (**13**; 20 g, 104 mmol) according to the general procedure gave unreacted α-ionone (4.9 g, 25%), 3-keto-α-ionone (**14**; 11.2 g, 52%), and *cis*-α-epoxy-ionone (**15**; 0.85 g, 4%). The ^{1}H and ^{13}C NMR spectra of 3-keto-α-ionone (**14**) were fully consistent with those reported previously,[22a] whereas *cis*-α-epoxy-ionone (**15**) was identified by GC analysis using synthetic **15**[23] as a reference standard.

3-Keto-α-ionone (14): White crystals, m.p. 74–75 °C; ref.[22b] m.p. 75–76.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.67 (dd, J = 15.8, 9.5 Hz, 1 H), 6.19 (d, J = 15.8 Hz, 1 H), 5.98 (s, 1 H), 2.72 (d, J = 9.5 Hz, 1 H), 2.36 (d, J = 16.9 Hz, 1 H), 2.28 (s, 3 H), 2.15 (d, J = 16.9 Hz, 1 H), 1.90 (d, J = 1.1 Hz, 3 H), 1.08 (s, 3 H), 1.01 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 197.3, 158.9, 143.4, 133.7, 126.9, 55.4, 47.3, 36.6, 27.9, 27.5, 27.2, 23.4 ppm. GC–MS (EI): m/z (%) = 206 (1) $[M]^+$, 191 (2), 164 (1), 150 (22), 135 (5), 121 (2), 108 (100), 91 (5), 77 (11).

β-Ionone Oxidation: The oxidation of β-ionone (**16**; 20 g, 104 mmol) according to the general procedure gave unreacted β-ionone (0.55 g, 3%), 3-keto-α-ionone (**17**; 8.5 g, 40%), and β-epoxy-ionone (**18**; 4.1 g, 19%). The ^{1}H and ^{13}C NMR spectra of 4-keto-α-ionone (**17**) were fully consistent with those reported previously,[8a] whereas β-epoxy-ionone (**18**) was identified by GC analysis using synthetic **18**[23] as a reference standard.

4-Keto-β-ionone (17): White crystals, m.p. 52–53 °C; ref.[24] m.p. 53–54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (dq, J = 16.5, 1.1 Hz, 1 H), 6.19 (d, J = 16.5 Hz, 1 H), 2.53 (t, J = 6.9 Hz, 2 H), 2.34 (s, 3 H), 1.89 (t, J = 6.9 Hz, 2 H), 1.80 (d, J = 1.1 Hz, 3 H), 1.19 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 197.2, 157.6, 140.2, 133.5, 131.5, 37.3, 35.5, 34.1, 27.9, 27.3, 13.3 ppm. GC–MS (EI): m/z (%) = 206 (56) $[M]^+$, 191 (13), 177 (4), 163 (100), 149 (24), 135 (28), 121 (44), 107 (14), 91 (20), 77 (11).

Theaspirane Oxidation: The oxidation of racemic theaspirane (**19**; 10 g, 1:1 diastereoisomeric mixture, 51.5 mmol) according to the general procedure gave unreacted theaspirane (3.5 g, 35%), and theaspirone (**20**; 5.3 g, 49%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[25]

Theaspirone (20): Pale yellow oil, 1:1 mixture of diastereoisomers (by GC and NMR analysis). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 and 5.71 (2 m, 1 H), 4.27–4.15 (m, 1 H), 2.48–1.42 (m, 6 H), 1.98 (d, J = 1.3 Hz) and 1.96 (d, J = 1.1 Hz) (3 H), 1.31 and 1.30 (2 d, J = 6.0 Hz, 3 H), 1.07, 1.02, 1.01, and 0.98 (4 s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.7, 197.3, 167.3, 167.3, 124.4, 124.1, 87.8, 87.7, 77.1, 76.8, 49.4, 49.1, 40.8, 39.9, 34.2, 33.5, 31.9, 23.7, 23.6, 22.9, 22.2, 20.5, 19.6, 19.5, 18.1 ppm. GC–MS (EI): m/z (%) = 208 (<1) $[M]^+$, 193 (2), 165 (3), 152 (100), 123 (5), 110 (83), 96 (13), 82 (12), 69 (11), 55 (9).

Oxidation of Isophorone: The oxidation of isophorone (**21**; 20 g, 144.7 mmol) according to the general procedure gave unreacted isophorone (13.2 g, 66%), and 4-oxoisophorone (**22**; 6.1 g, 28%). The latter compound was identified by GC analysis using commercially available **22** as a reference standard.

Oxidation of (*E*)-Hex-1-enylbenzene: The oxidation of (*E*)-hex-1-enylbenzene (**23**; 6 g, 37.4 mmol) according to the general procedure gave unreacted **23** (50 mg, 1%), (*E*)-1-phenylhex-1-en-3-one (**24**; 2.1 g, 32%), and a number of other overoxidation products, including benzaldehyde, cinnamaldehyde, and benzoic acid. The ^{1}H and ^{13}C NMR spectra of isolated **24** were fully consistent with those reported previously.[26]

(*E*)-1-Phenylhex-1-en-3-one (24): Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.20 (m, 5 H), 7.54 (d, J = 16.2 Hz, 1 H), 6.73 (d, J = 16.2 Hz, 1 H), 2.63 (t, J = 7.4 Hz, 2 H), 1.71 (quin, J = 7.4 Hz, 2 H), 0.98 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2, 142.1, 134.7, 130.2, 128.8, 128.1, 126.4, 42.8, 17.8, 13.7 ppm. GC–MS (EI): m/z (%) = 174 (23) $[M]^+$, 146 (7), 131 (100), 115 (3), 103 (41), 77 (19), 51 (4).

Oxidation of Hept-1-ynylbenzene: The oxidation of hept-1-ynylbenzene (**25**; 8 g, 46.5 mmol) according to the general procedure gave unreacted **25** (3.1 g, 39%), and 1-phenylhept-1-yn-3-one (**26**; 4.9 g, 56%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[27]

1-Phenylhept-1-yn-3-one (26): Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.52 (m, 2 H), 7.47–7.32 (m, 3 H), 2.65 (t, J = 7.4 Hz, 2 H), 1.78–1.68 (m, 2 H), 1.46–1.35 (m, 2 H), 0.95 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.9, 132.9, 130.5, 128.5, 120.1, 90.4, 87.9, 45.2, 26.2, 22.1, 13.7 ppm. GC–MS (EI): m/z (%) = 186 (1) $[M]^+$, 185 (4), 171 (2), 158 (5), 144 (23), 129 (100), 115 (4), 102 (16), 75 (10).

Oxidation of (*E*)-(3-Ethoxyprop-1-enyl)benzene: The oxidation of (*E*)-(3-ethoxyprop-1-enyl)benzene (**27**; 5 g, 30.8 mmol) according to the general procedure gave ethyl cinnamate (**28**; 2.2 g, 40%). The latter compound was identified by GC analysis using commercially available **28** as a reference standard.

Oxidation of Isochroman: The oxidation of isochroman (**29**; 10 g, 74.6 mmol) according to the general procedure gave 1-oxo-isochroman (**30**; 5.0 g, 45%) and 1-(*tert*-butylperoxy)isochroman (**31**; 8.1 g, 49%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[8a,18]

1-Oxo-isochroman (30): Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 7.8 Hz, 1 H), 7.53 (td, J = 7.5, 1.3 Hz, 1 H), 7.38 (t, J = 7.8 Hz, 1 H), 7.26 (d, J = 7.5 Hz, 1 H), 4.53 (t, J = 6.0 Hz, 2 H), 3.06 (t, J = 6.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9, 139.5, 133.5, 130.2, 127.5, 127.1, 125.3, 67.2, 27.7 ppm. GC–MS (EI): m/z (%) = 148 (64) $[M]^+$, 118 (100), 90 (68), 77 (4), 63 (11), 51 (7).

1-(*tert*-Butylperoxy)isochroman (31): Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, J = 7.4 Hz, 1 H), 7.30–7.18 (m, 2 H), 7.13 (d, J = 7.4 Hz, 1 H), 6.04 (s, 1 H), 4.22 (td, J = 11.6, 3.3 Hz, 1 H), 3.99 (ddd, J = 11.4, 6.0, 1.4 Hz, 1 H), 3.02 (ddd, J = 16.6, 12.3, 6.0 Hz, 1 H), 2.59 (dd, J = 16.6, 2.6 Hz, 1 H), 1.35 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.6, 130.4, 128.7, 128.6, 128.3, 126.1, 99.2, 80.8, 58.1, 27.8, 26.6 ppm. MS (ESI): m/z = 245.0 $[M + Na]^+$.

Oxidation of Dibenzyl Ether: The oxidation of dibenzyl ether (**32**; 10 g, 50.4 mmol) according to the general procedure gave unreacted **32** (0.5 g, 5%), benzyl benzoate (**33**; 7.3 g, 68%), and a number of other overoxidation products, including benzaldehyde and benzoic acid. Compound **33** was identified by GC analysis using commercially available benzyl benzoate as a reference standard.

Oxidation of Bibenzyl: The oxidation of bibenzyl (**34**; 10 g, 54.9 mmol) according to the general procedure gave unreacted **34** (7.5 g, 75%), and phenylbenzyl ketone (**35**; 1.65 g, 15%). The latter compound was identified by GC analysis using commercially available **35** as a reference standard.

Oxidation of Fluorene: The oxidation of fluorene (**36**; 10 g, 60.2 mmol) according to the general procedure gave unreacted **36**

(0.2 g, 2%), and fluorenone (**37**; 10.1 g, 93%). The latter compound was identifed by GC analysis using commercially available **37** as a reference standard.

Oxidation of Tetralin: The oxidation of 1,2,3,4-tetrahydronaphthalene (**38**; 10 g, 75.7 mmol) according to the general procedure gave unreacted **38** (0.72 g, 7%), α-tetralone (**39**; 6.1 g, 55%), 1,2,3,4-tetrahydronaphthalene-1,4-dione (**40**; 0.6 g, 5%), and a number of unidentified overoxidation products. Compounds **39** and **40** were identified by GC analysis using commercially available **39** and **40** as reference standards.

Oxidation of Dodecylbenzene: The oxidation of dodecylbenzene (**41**; 10 g, 40.6 mmol) according to the general procedure gave unreacted **41** (7 g, 70%), and 1-phenyldodecan-1-one (**42**; 2.2 g, 21%), whose ^{1}H and ^{13}C NMR spectra were fully consistent with those reported previously.[28a]

1-Phenyldodecan-1-one (42): White crystals, m.p. 44–45 °C; ref.[28b] m.p. 43–45 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.92 (m, 2 H), 7.57–7.50 (m, 1 H), 7.48–7.40 (m, 2 H), 2.95 (t, J = 7.3 Hz, 2 H), 1.73 (quin, J = 7.3 Hz, 2 H), 1.43–1.20 (m, 16 H), 0.88 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.5, 137.3, 132.8, 128.5, 128.0, 38.6, 31.9, 29.6, 29.5, 29.5, 29.4, 29.3, 24.4, 22.7, 14.0 ppm. GC–MS (EI): *m/z* (%) = 260 (11) $[M]^+$, 189 (1), 133 (13), 120 (100), 105 (70), 91 (2), 77 (23), 55 (4).

Oxidation of 2-Ethylpyridine and 3-Ethylpyridine: The oxidation of 2-ethylpyridine (**43**; 10 g, 93.4 mmol) or 3-ethylpyridine (**45**; 5 g, 46.7 mmol) according to the general procedure gave unreacted **43** (7.85 g, 79%), and 2-acetylpyridine (**44**; 1.82 g, 16%), or unreacted **45** (3.35 g, 67%), and 3-acetylpyridine (**46**; 1.31 g, 23%), respectively. The ^{1}H and ^{13}C NMR spectra of the products were fully consistent with those reported previously.[29]

2-Acetylpyridine (44): Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.68 (d, J = 4.8 Hz, 1 H), 8.03 (dt, J = 7.8, 0.9 Hz, 1 H), 7.82 (td, J = 7.8, 1.8 Hz, 1 H), 7.45 (ddd, J = 7.8, 4.8, 1.2 Hz, 1 H), 2.72 (d, J = 0.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.9, 153.7, 148.9, 136.7, 126.9, 121.5, 25.6 ppm. GC–MS (EI): *m/z* (%) = 121 (89) $[M]^+$, 106 (7), 93 (54), 79 (100), 51 (29), 43 (23).

3-Acetylpyridine (46): Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.17 (s, 1 H), 8.78 (d, J = 4.9 Hz, 1 H), 8.22 (dt, J = 8.0, 2.0 Hz, 1 H), 7.41 (dd, J = 8.0, 4.9 Hz, 1 H), 2.63 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 153.4, 149.9, 135.3, 132.4, 123.5, 26.5 ppm. GC–MS (EI): *m/z* (%) = 121 (53) $[M]^+$, 106 (100), 78 (81), 51 (23), 43 (13).

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Received: June 25, 2015
Published Online: August 26, 2015

