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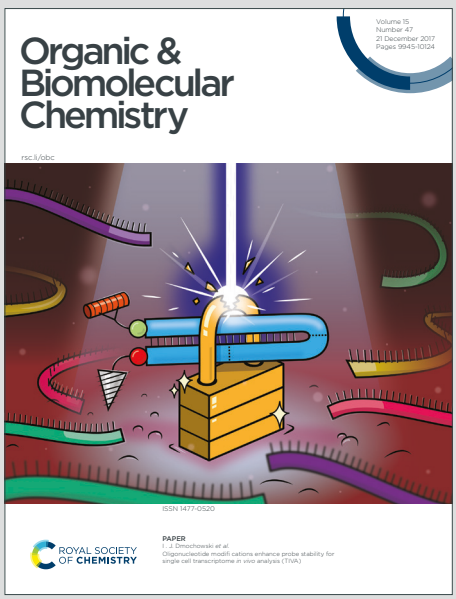

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ARTICLE

MnO_2 as Terminal Oxidant in Wacker Oxidation of Homoallyl Alcohols and Terminal Olefins

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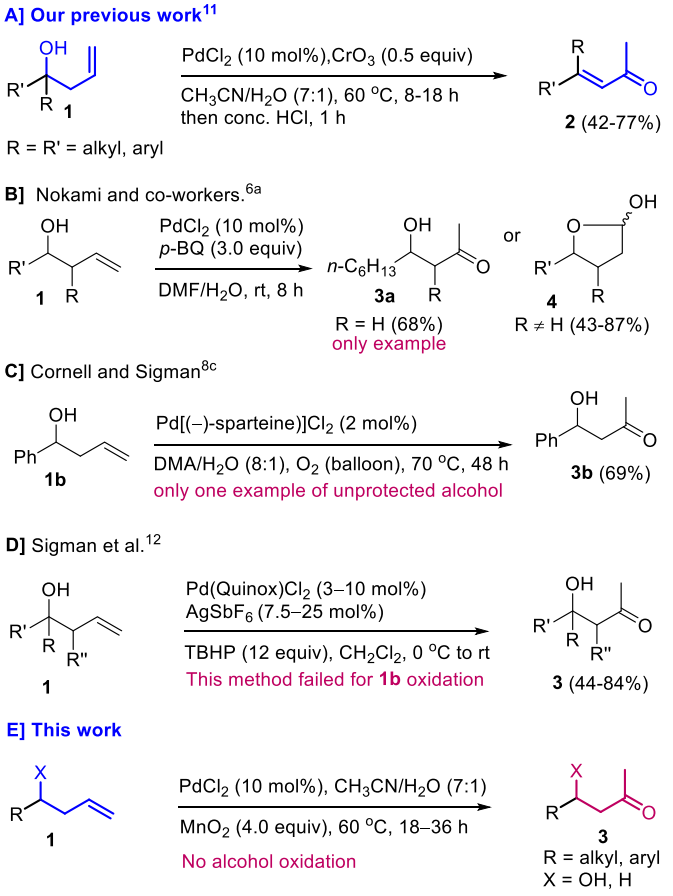
An efficient and mild reaction conditions for Wacker-type oxidation of terminal olefins of less explored homoallyl alcohols to β-hydroxy-methyl ketones has been developed by using Pd(II) catalyst and MnO_2 as co-oxidant. The method involves mild reaction conditions and shows good functional group compatibility along with high regio- and chemoselectivity. While our earlier system of $PdCl_2/CrO_3$/HCl produced α,β-unsaturated ketones from homoallyl alcohols, the present method provided orthogonally the β-hydroxy-methyl ketones. No overoxidation or elimination of benzylic and/or β-hydroxy group was observed. The method could be extended to oxidation of simple terminal olefins as well, to methyl ketones displaying its versatility. A application to the regioselective synthesis of gingerol is demonstrated.

Introduction

β-Hydroxy-keto compounds are key building blocks for 1,3-diketones, 1,3-diols and polyketides present in many natural products, pharmaceuticals, and bioactive compounds.[1] The conventional aldol addition reaction used for the synthesis of β-hydroxy-keto compounds sometimes suffers from substrate scope, selectivity, and a number of by-products formation, especially the self-aldol and aldol condensation products with facile elimination of hydroxy group. The Wacker-type oxidation has been extensively studied for several years to convert terminal olefins to methyl ketones.[2,3] The traditional Cu-mediated Wacker process has limitations, such as corrosive reaction medium, isomerization of the double bond and chlorinated by-products.[4] To overcome this, alternative methods are developed based on solvents (DMF, DMA, sulfolane, CO_2, PEG, ethylene carbonate, etc),[5] organic oxidants,[5a,6] inorganic oxidants,[7] nitrogen-based ligands,[8] nitrates,[9] and organic peroxides.[10] We recently explored the traceless OH-directed Wacker oxidation, one-pot elimination of homoallyl alcohols **1** as an alternative to Wittig olefination/aldol condensation (Scheme 1A).[11] This led to the synthesis of α,β-unsaturated ketones **2**. We visualized an orthogonal chemo selective oxidation of only terminal olefin of homoallyl alcohol by the Wacker process. The selectivity in Wacker oxidation of homoallyl alcohol depends on the substrate and the oxidant.[6a] To the best of our knowledge there exists few reports on such reaction of homoallyl alcohols as substrates for Wacker oxidation.[6a,8c,12,13] In 1988, Nokami and co-workers explored the Wacker oxidation [$PdCl_2$ (10 mol%), *p*-benzoquinone (*p*-BQ, 3.0equiv), DMF-H_2O] of C-3 substituted homoallyl alcohols **1** to result largely in the hemiacetals **4** (aldehyde selective, Scheme 1B).[6a] With no C-3 substituent, the reaction gave methyl ketone (e.g. **3a**, R = H, only example). In 2006, Cornell and Sigman disclosed the use of Pd[(−)-sparteine]Cl_2 (2 mol%)/O_2-based system for ketone-selective Wacker oxidation of homoallyl



Scheme 1 Wacker oxidation of homoallyl alcohols.

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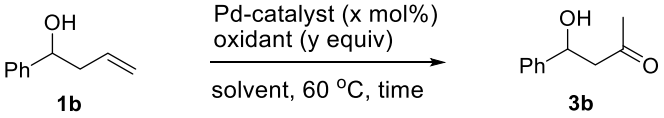
alcohols **1b** (only 1 example of unprotected homoallyl alcohol, Scheme 1C).[8c] In a subsequent report in 2011, Sigman et al.[12] showed Pd(Quinox)Cl_2 (3-10 mol%), $AgSbF_6$ (7.5-25 mol%) and TBHP (12 equiv)-based Wacker oxidation of homoallyl alcohols **1** (Scheme 1D). However, the latter reaction conditions failed for 1-phenyl-but-3-en-ol **1b** and was explored though on limited substrates (only 5 examples). A recent report by Runeberg and Eklund displayed the Wacker oxidation of unprotected carbohydrate-based homoallyl alcohols, unfortunately requiring higher catalyst [$Pd(OAc)_2$ (30 mol%)] and ligand [pyridine (60 mol%)] loading and resulting in product mixtures.[13]

In continuation to our efforts[6b,7f,g] in developing new oxidants for Wacker chemistry, we explored MnO_2 as a terminal oxidant in heterogenous Wacker process. We aimed at orthogonal selectivity with regard to earlier results.[11] MnO_2 and related Mn-based compounds are well recognized oxidant in organic synthesis, used specially in allylic oxidations.[14,15] There has been a report[16] on the use of Mn^{2+} salts of heteropoly acids [$H_{3+x}PMo_{12-x}V_xO_{40}(0 \leq x \leq 3)$] containing $PdCl_2$ and supported on silica for oxidation of ethene. The manganese salts of hetero poly acids were prepared using HPA and $Mn(NO_3)_2$ or $Mn(CO_3)_2$ in aqueous solution. $PdCl_2$ was first supported on silica and then impregnated with hetero poly compounds from aqueous solutions. However, the catalytic activity was affected by the catalyst preparation procedure. The heterogenous reaction also required the presence of molybdenum and vanadium atoms in HPA for the activity. The direct use of MnO_2 is not reported to the best of our knowledge in Wacker process as oxidant for Pd(0) for an excellent oxidation of varied types of homoallyl alcohols **1** to β-hydroxy ketones **3** (X = OH) with a wider substrate scope, generality and milder reaction conditions (Scheme 1E). No competing alcohol oxidation/elimination by MnO_2 was observed under this protocol. This methods was also applicable to both activated and non-activated terminal olefins giving methyl ketones **3** (X = H).

Results and Discussion

We began the investigation by optimizing the reaction conditions using the homoallyl alcohol **1b** as a model substrate (Table 1). Initially we examined various Mn-based oxidants (3 equiv, entries 1-7) along with $PdCl_2$ (10 mol%) to find that MnO_2 was the best giving β-hydroxy ketone **3b** in 67% yield (entry 1). No oxidation of benzylic alcohol by MnO_2 or other oxidants was observed showing a good level of chemoselectivity.[14,15] Similarly, the reaction was also ketone selective and no aldehyde or lactol was detected.[6a] The requirement of 3 equivalents of MnO_2 can be interpreted based on the heterogenous nature of reaction. We next examined the commonest other Pd-catalysts used in Wacker oxidation (entries 8-11), to reveal that $PdCl_2$ was superior. A change in solvent mixtures (entries 12-15) showed MeCN/H_2O in 7:1 ratio was the best. A reaction under nitrogen atmosphere (entry 16) took longer time to complete and gave diminished yield of **3b** (51%). Increasing the amount of MnO_2 (4-6 equiv, entries 17-19) indicated 4 equivalent was optimum giving **3b** in 78% yield. No alcohol oxidation was observed with higher loading of MnO_2 (6 equivalent). Normal MnO_2 is used in superstoichiometric quantity, being heterogenous reaction for allylic and benzylic oxidations.[17] Increase in $PdCl_2$ loading (20 mol%, entry 20) did not affect the yield much (80%). Also, lowering of MnO_2 amount (2-1 equivalent) along with 20 mol% of $PdCl_2$ did not yield superior results. Hence we concluded to have $PdCl_2$ (10 mol%), MnO_2 (4 equiv) in MeCN/H_2O (7:1) at 60 °C as optimum conditions.

Table 1 Optimization of reaction conditions.[a]



1b **3b**

Entry	Pd-catalyst (x mol%)	Oxidant (y equiv)	Solvent (7:1)	Time (h)	Yield[b] **3b** (%)
1	$PdCl_2$ (10)	MnO_2 (3)	MeCN:H_2O	24	67
2	$PdCl_2$ (10)	$Mn(SO_4).4H_2O$ (3)	MeCN:H_2O	30	40
3	$PdCl_2$ (10)	$Mn(SO_4).H_2O$ (3)	MeCN:H_2O	36	35
4	$PdCl_2$ (10)	$KMnO_4$ (3)	MeCN:H_2O	48	18
5	$PdCl_2$ (10)	$Mn(OAc)_2.4H_2O$ (3)	MeCN:H_2O	24	21
6	$PdCl_2$ (10)	$MnCl_2.4H_2O$ (3)	MeCN:H_2O	32	30
7	$PdCl_2$ (10)	$Mn(NO_3)_2.4H_2O$ (3)	MeCN:H_2O	15	58
8	$Pd(OAc)_2$(10)	MnO_2 (3)	MeCN:H_2O	36	53
9	$Pd(OCOCF_3)_2$ (10)	MnO_2 (3)	MeCN:H_2O	22	57
10	$Pd(MeCN)_2$ (10)	MnO_2 (3)	MeCN:H_2O	26	46
11	Pd(dba)$_2$ (10)	MnO_2 (3)	MeCN:H_2O	23	53
12	$PdCl_2$ (10)	MnO_2 (3)	CH_2Cl_2:H_2O	40	36
13	$PdCl_2$ (10)	MnO_2 (3)	DMF:H_2O	36	55
14	$PdCl_2$ (10)	MnO_2 (3)	DMSO:H_2O	48	47
15	$PdCl_2$ (10)	MnO_2 (3)	THF:H_2O	30	38
16[c]	$PdCl_2$ (10)	MnO_2 (3)	MeCN:H_2O	48	51
17	$PdCl_2$ (10)	MnO_2 (4)	MeCN:H_2O	22	78
18	$PdCl_2$ (10)	MnO_2 (5)	MeCN:H_2O	26	79
19	$PdCl_2$ (10)	MnO_2 (6)	CH_3CN:H_2O	26	79
20	$PdCl_2$ (20)	MnO_2 (4)	CH_3CN:H_2O	22	80
21	$PdCl_2$ (20)	MnO_2 (2)	CH_3CN:H_2O	28	74
22	$PdCl_2$ (20)	MnO_2 (1)	CH_3CN:H_2O	32	60

[a]All reactions were carried on 0.5 mmol of olefin **1b** in a closed flask. [b]Isolated yield. [c]Reaction under N_2.

We further investigated the scope of this reaction conditions on various homoallyl alcohols **1** as shown in Scheme 2 to give the β-hydroxy ketones **3** in good yields. Compounds with aryl ring having both electron withdrawing and donating groups like Me, O-alkyl, OH, Cl, NO_2 or Ph at different positions, all worked well giving the β-hydroxy ketones **3b-m** in 61-80% yields. Similarly the anthracene, naphthalene, cinnamyl, and furyl-based substrates **1n-s** gave the β-hydroxy ketones **3n-s** in 68-78% yields. The cinnamyl cases **3p-r** were noteworthy that only the terminal olefin bond was oxidized leaving chemoselectively the internal double bond intact. No allylic alcohol oxidation nor elimination was observed in all cases, which is remarkable in

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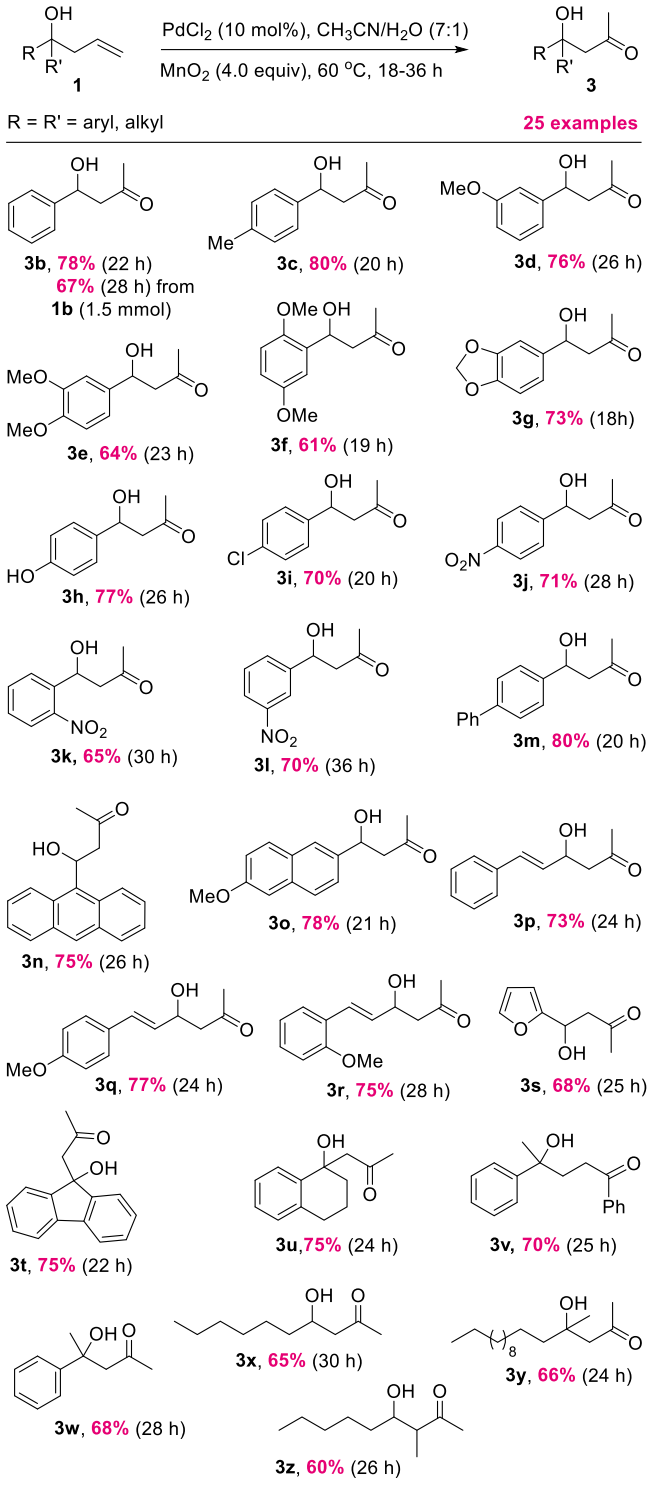
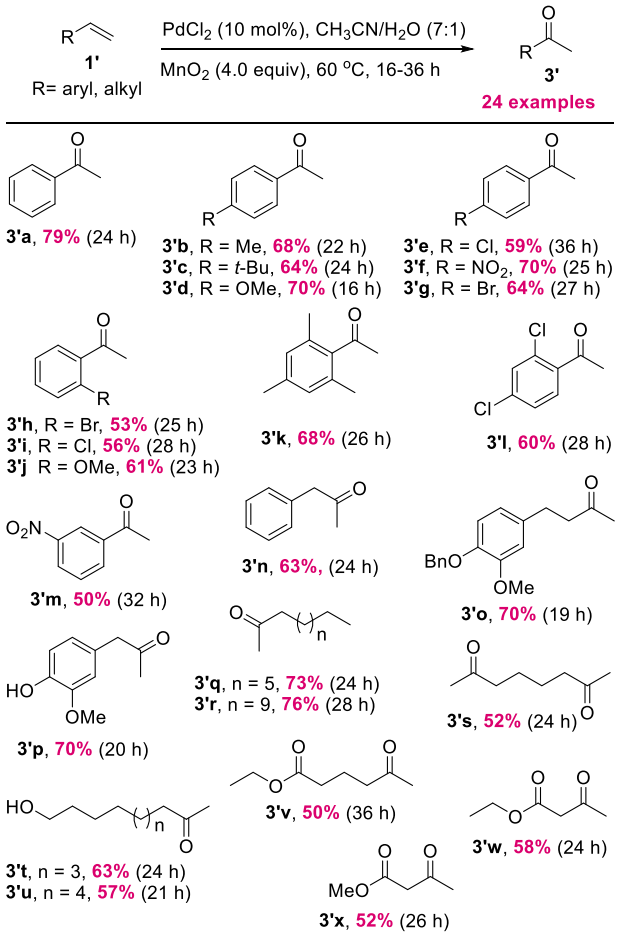
this process knowing that MnO_2 is an oxidant for allylic alcohol oxidation. Also, the tertiary homoallyl alcohols **1t-w** furnished the β-hydroxy ketones **3t-w**, respectively, in 68-75% yields. In case of **3v**, the water addition occurred at the benzylic position considering the stability of benzylic cation giving the γ-hydroxy product regioselectively. Also, no elimination of β-hydroxy group was observed in all cases even though there could be a drive for more substituted double bond formation. Further, the aliphatic secondary and tertiary homoallyl alcohols **1x** and **1y** provided the β-hydroxy ketones **3x** and **3y**, respectively in 65% and 66% yields. The product 2-methyl-β-hydroxy ketone **3z** was selectively obtained in 60% yield unlike the aldehyde selective hemiacetal formation reported in the literature for β-substituted homoallyl alcohols.[6a] Since the substrate homoallyl alcohol **1z** was used as diastereomer mixture, the ketone compound **3z** was obtained as 70:30 diastereomer mixture. A reaction of **1b** at 1.5 mmol scale resulted in **3b** in 67% yield after a 28 h reaction. In all reactions we did not observe the formation of regioisomeric aldehyde and also allylic/benzylic alcohol oxidation products within the detection limit of NMR. The pure products were isolated by chromatographic purification and the remaining material was observed as trail of inseparable and unidentifiable mixtures. The MnO_2 oxidations normally require over 15 equivalents[17] of the oxidants due to heterogenous media. With upto 6 equivalents of MnO_2, no benzylic alcohol oxidation was observed (Table 1, entry 19).



Reaction conditions: **1** (0.5 mmol), $PdCl_2$ (10 mol%), MnO_2 (4.0 equiv) CH_3CN (3.5 mL), H_2O (0.5 mL) at 60 °C.

Scheme 2 Substrate scope for Wacker-type oxidation of homoallyl alcohols.



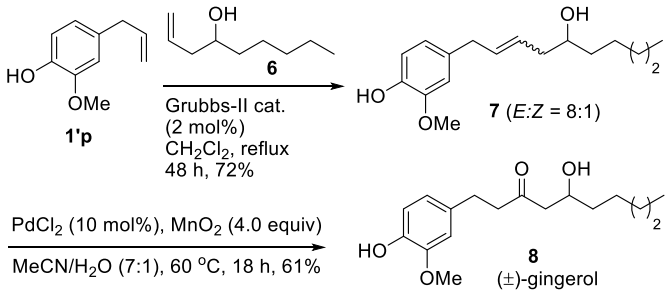
Reaction conditions: **1'** (0.5 mmol), $PdCl_2$ (10 mol%), MnO_2 (4.0 equiv) CH_3CN (3.5 mL), H_2O (0.5 mL) at 60 °C.

Scheme 3 Wacker-type oxidation of styrenes and aliphatic terminal olefins.

The substrate scope was extended to styrenes and unactivated aliphatic terminal olefins (Scheme 3). Thus,

styrenes with electron donating and withdrawing groups all worked well in giving the methyl ketones **3′a-m** in 50-79% yields. No aldehyde products were detected in all cases. The ortho-substituted compounds **3′h-l** were all obtained successfully without any difficulty. The unactivated terminal olefins **1′n-r** and diene **1′s** gave the corresponding methyl ketones **3′n-r** and diketone **3′s** in moderate to good yields. Good functional group compatibility was observed with substrates having free hydroxy or ester groups in obtaining the methyl ketones **3′t-x** in 50-63% yields.

The chemoselective homoallylic Wacker oxidation was applied in the synthesis of the natural product gingerol (**8**)[18] (Scheme 4). The latter was isolated from rhizomes of *Zingiber officinale* by Connell and Sutherland and later by Nakatani *et al.*[19] It shows potent anticancer, antimicrobial, anti-inflammatory, antioxidant, antidiabetic, antiallergic, and antiaging activities.[20] Toward the synthesis of **8**, the cross metathesis of eugenol (**1′p**) with homoallyl alcohol **6**[12] provided the internal homoallyl alcohol **7** in 72% yield as 8:1 (E/Z) mixture. This on Wacker oxidation under present protocol regioselectively gave (±)-gingerol **8** in 61% yield. The enantiopure version of **6** easily obtainable by various asymmetric allylation protocols[21] and also the variation of side chain can lead conveniently to other gingerols and related compounds.[18e]



Scheme 4 Short synthesis of (±)-gingerol (**8**).

Conclusion

In summary, in this paper, we have developed an efficient Wacker-type orthogonal chemoselective oxidation of homoallylic alcohols to β-hydroxy ketones using MnO_2 as co-oxidant in $PdCl_2$ catalysis. Our earlier version led to α,β-unsaturated ketones.[11] Various long-chain terminal olefins, dienes, substituted styrenes have been explored in this paper. A wide spectrum of functional-group tolerance, mild reaction conditions, good regio- and chemo selectivity are key features of the present methodology (50 examples). The presented work gains significance considering not many reports in chemoselective Wacker-type oxidation of homoallyl alcohols selectively to methyl ketones are known. A short synthesis of gingerol using the present Wacker oxidation method has also been achieved.

Experimental Section

General information. Thin-layer chromatography was performed on EM 250 Kieselgel 60 F254 silica gel plates. The spots were visualized by staining with $KMnO_4$ or by using a UV lamp. ^{1}HNMR and ^{13}CNMR were recorded with a spectrometer operating at 400 or 500 and 100 or 125 MHz for proton and carbon nuclei, respectively. The chemical shifts are based on the $CHCl_3$ peak at δ = 7.26 ppm for proton NMR and δ = 77.00 ppm (t) for carbon NMR. IR spectra were obtained on an FT-IR spectrometer by evaporating compounds dissolved in $CHCl_3$ on CsCl pellet or by preparing KBr pellet for solid. HRMS (ESI-TOF) spectra were recorded using positive electrospray ionization by the TOF method.

General Procedure for synthesis of homoallylalcohols: A flame dry round-bottom flask was charged with a solution of requisite allyl bromide (3.50 mmol) in anhydrous THF (5 mL) under argon atmosphere. Zinc dust (0.230 g, 3.50 mmol) was added slowly at 0 °C. The aldehyde (1.0 mmol) dissolved in anhydrous THF (5 mL) was added to the stirring solution. The resulting suspension was stirred for 2 h at 0 °C and then overnight at room temperature. The reaction mixture was quenched with saturated aq. NH_4Cl at 0 °C, the mixture then filtered and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography using petroleum ether/EtOAc (9:1 to 4:1) as an eluent to afford the homoallylalcohols. The known products obtained by this procedure, **1b-d**,[22a] **1e**,[22b] **1f**,[22c] **1g**,[22b] **1h**,[22a] **1i-l**,[22d] **1m**,[22e] **1n**,[22f] **1o**,[22e] **1p**,[22a] **1q**,[22a] **1r**,[22g] **1s**,[22a] **1t**,[22h] **1u**,[22i] **1v**,[22j] **1w**,[22f] **1x**,[22k] **1y**[12] and **1z**[22l] have analytical data consistent with the literature.

Styrenes **1′a-m** and olefins **1′n, 1′p** (eugenol), **1′q-x** were commercially procured (Aldrich Chem. Co.). Preparation of **1′o** is given below.

1-Benzyloxy-4-(but-3-en-1-yl)-2-methoxybenzene (1′o). To the stirred solution of 1-benzyloxy-4-(bromomethyl)-2-methoxybenzene (1 g, 3.26 mmol, 1.0 equiv) in Et_2O (20 mL) was added freshly prepared solution of allyl magnesium bromide (3.6 mL, 3.6 mmol, 1.1 equiv) in Et_2O at 0 °C and the resulting suspension was stirred for 16 h. The reaction was quenched with saturated aq. NH_4Cl and the solution extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography using petroleum ether/EtOAc (19:1) as an eluent to give **1′o** (0.613 g, 70%) as colorless oil. IR ($CHCl_3$): ν_{max}= 3062, 3030, 2923 2856, 1637, 1611, 1582, 1511, 1453, 1381, 1297, 1238, 1175, 1119, 1025, 912, 826, 756, 696, 542 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56–7.16 (m, 5H), 6.96–6.55 (m, 3H), 5.98–5.66 (m, 1H), 5.14 (s, 2H), 5.08–4.98 (m, 2H), 3.89 (s, 3H), 2.66 (t, J = 7.7 Hz, 2H), 2.38–2.33 (m, 2H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 149.5, 146.2, 138.2, 137.5, 135.2, 128.5, 127.8, 127.3, 120.2, 114.9, 114.1, 112.3, 71.2, 56.0, 35.7, 35.0 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{20}NaO_2$ 291.3391; Found 291.3396.

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General procedure for Wacker oxidation of terminal olefins 1 or 1′

To a stirred solution of olefin **1** or **1′** (0.5 mmol) in CH_3CN (3.5 mL) and H_2O (0.5 mL) were added $PdCl_2$ (8.9 mg, 0.05 mmol, 10 mol%) and MnO_2 (174 mg, 2.0 mmol, 4.0 equiv) at room temperature. The reaction mixture was warmed to 60 °C and stirred for specified time in a closed flask. The reaction mixture was then filtered through a small pad of Celite/silica gel and washed with EtOAc and the filtrate concentrated. The residue was purified by silica gel column chromatography using petroleum ether/EtOAc (9:1 to 4:1) as an eluent to afford the methyl ketones **3** or **3′**, respectively.

4-Hydroxy-4-phenylbutan-2-one (3b).[23a] Reaction time = 22 h, colorless oil (64 mg, 78%). IR ($CHCl_3$): ν_{max} = 3444, 3063, 3031, 2928, 1714, 1605, 1495, 1454, 1416, 1361, 1331, 1258, 1165, 1062, 1028, 1000, 941, 916, 701, 541 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 5H), 5.16 (dd, J = 9.0, 3.4 Hz, 1H), 2.92–2.79 (m, 2H), 2.19 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR: (125 MHz, $CDCl_3$): δ = 209.0, 142.7, 128.5, 127.7, 125.6, 69.9, 52.0, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$calcd for $C_{10}H_{12}NaO_2$ 187.0730; Found 187.0740.

4-Hydroxy-4-(*p*-tolyl)butan-2-one (3c).[23b] Reaction time = 20 h, colorless oil (71.3 mg, 80%). IR ($CHCl_3$): ν_{max} = 3437, 3011, 2923 1712, 1666, 1612, 1515, 1420, 1361, 1321, 1307, 1288, 1257, 1179, 1163, 1071, 1020, 980, 948, 821, 759, 600, 568, 542 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.24 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 5.12 (dd, J = 9.3, 3.2 Hz, 1H), 2.88 (dd, J = 17.3, 5.9 Hz, 1H), 2.79 (dd, J = 17.4, 3.2 Hz, 1H), 2.34 (s, 3H), 2.19 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 209.1, 139.8, 137.4, 129.2, 125.6, 69.7, 52.0, 30.7, 21.1 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$calcd for $C_{11}H_{14}NaO_2$ 201.0886; Found 201.0885.

4-Hydroxy-4-(3-methoxyphenyl)butan-2-one (3d).[23a] Reaction time = 26 h, colorless oil (74 mg, 76%). IR ($CHCl_3$): ν_{max} = 3465, 3002, 2933, 2837, 1710, 1602, 1586, 1488, 1436, 1361, 1319, 1288, 1264, 1160, 1044, 953, 870, 782, 756, 699, 665, 552 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.24 (m, 1H), 6.93–6.90 (m, 2H), 6.82–6.80 (m, 1H), 5.13 (dd, J = 9.1, 3.2 Hz, 1H), 3.80 (s, 3H), 2.88 (dd, J = 17.5, 9.3 Hz, 1H), 2.80 (dd, J = 17.5, 2.9 Hz, 1H), 2.19 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125MHz, $CDCl_3$): δ = 209.0, 159.8, 144.4, 129.6, 117.8, 113.2, 111.1, 69.8, 55.2, 51.9, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{14}NaO_3$ 217.0835; Found 217.0835.

4-(3,4-Dimethoxyphenyl)-4-hydroxybutan-2-one(3e).

Reaction time = 23 h, pale yellow solid (72mg, 64%). M.p. 94–98 °C; IR ($CHCl_3$): ν_{max} = 3436, 3002, 2940, 2837, 1713, 1602, 1586, 1543, 1488, 1465, 1456, 1435, 1361, 1318, 1288, 1264, 1159, 1044, 956, 871, 785, 750, 699, 645, 551 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.92 (s, 1H), 6.87–6.81 (m, 2H), 5.10 (dd, J = 9.2, 2.1 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.25 (s, 1H), 2.91 (dd, J = 17.5, 9.3 Hz, 1H), 2.82 (dd, J = 17.5, 2.9 Hz, 1H), 2.19 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 209.1, 149.1, 148.5, 135.4, 117.8, 111.0, 108.8, 69.7, 55.9, 55.8, 52.0, 30.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{16}NaO_4$ 247.0941; Found 247.0938.

4-(2,5-Dimethoxyphenyl)-4-hydroxybutan-2-one(3f).[23c]

Reaction time = 19 h, colorless oil (68.6 mg, 61%). IR ($CHCl_3$): ν_{max}= 3489, 3091, 3081, 3020, 1715, 1602, 1521, 1415, 1163, 1111, 1078, 1014, 973, 922, 857, 698, 668, 627 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$):δ = 7.04 (d, J = 2.5 Hz, 1H), 6.79–6.74 (m, 2H), 5.37 (dd, J = 9.3, 2.8 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 2.92 (dd, J = 17.3, 2.8 Hz, 1H), 2.75 (dd, J = 17.3, 9.4 Hz, 1H), 2.19 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.5, 153.9, 149.9, 132.0, 112.9, 112.3, 111.3, 65.5, 55.8, 55.8, 50.4, 30.6 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{16}NaO_4$ 247.0941; Found 247.0939.

4-(Benzo[1,3]dioxol-5-yl)-4-hydroxybutan-2-one (3g).[23d]

Reaction time = 18 h, white solid (76 mg, 73%). M.p. 53–55 °C; IR ($CHCl_3$): ν_{max} = 3446, 3013, 2902, 1713, 1608,1505, 1488, 1445, 1360, 1249, 1095, 1039, 933, 868, 814, 758, 632, 563 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.86 (d, J = 1.5 Hz, 1H), 6.79–6.74 (m, 2H), 5.93 (s, 2H), 5.05–5.03 (m, 1H), 2.85 (dd, J = 17.3, 9.3 Hz, 1H), 2.75 (dd, J = 17.3, 3.2 Hz, 1H), 2.18 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 209.0, 147.8, 147.0, 136.8, 119.0, 108.1, 106.3, 101.0, 69.7, 52.0, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{12}NaO_4$ 231.0628; Found 231.0633.

4-Hydroxy-4-(4-hydroxyphenyl)butan-2-one (3h). Reaction time = 26 h, colorless oil (69.4 mg, 77%). IR ($CHCl_3$): ν_{max} = 3484, 3017, 2971, 2900, 1713, 1661, 1609, 1592, 1566, 1491, 1406, 1360, 1316, 1257, 1183, 1162, 1092, 1042, 1014, 975, 945, 832, 800, 776, 668, 632, 540 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.14 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 5.05 (dd, J = 9.1, 3.1 Hz, 1H), 3.68 (brs, 1H), 2.89 (dd, J = 17.3, 9.2 Hz, 1H), 2.76 (dd, J = 17.3, 3.2 Hz, 1H), 2.16 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.9, 155.6, 134.1, 127.2, 115.5, 69.7, 51.6, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{12}NaO_3$ 203.0679; Found 203.0685.

4-(4-Chlorophenyl)-4-hydroxybutan-2-one (3i).[23a] Reaction time = 20 h, pale yellow solid (69.5 mg, 70%). M.p. 45–48 °C; IR ($CHCl_3$): ν_{max} = 3483, 3020, 2976, 2915, 2891, 1712, 1661, 1609, 1567, 1492,1406, 1360, 1313, 1186, 1159, 1092, 1014, 975, 928, 877, 823, 667, 626, 540 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 5H), 5.11 (dd, J = 8.6, 3.8 Hz, 1H), 3.00 (br s, 1H), 2.88–2.73 (m, 2H), 2.18 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 208.9, 141.2, 133.3, 128.6, 127.0, 69.1, 51.8, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{11}ClNaO_2$ 221.0340; Found 221.0340.

4-Hydroxy-4-(4-nitrophenyl)butan-2-one (3j).[23a] Reaction time = 28 h, pale yellow solid (74.3 mg, 71%). M.p. 59–64 °C; IR ($CHCl_3$): ν_{max} = 3481, 3019, 2905, 2854, 1712, 1602, 1521, 1413, 1348, 1163, 1109, 1076, 975, 924, 857, 698, 668, 626, 537 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.17 (dd, J = 8.6, 1.8 Hz, 2H), 7.52 (d, J = 8.5 Hz, 2H), 5.24 (t, J = 6.1 Hz, 1H), 2.84 (d, J = 6.7 Hz, 2H), 2.20 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 208.4,

150.0, 147.2, 126.4, 123.7, 68.8, 51.5, 30.6 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{11}NNaO_4$ 232.0580; Found 232.0575.

4-Hydroxy-4-(2-nitrophenyl)butan-2-one (3k).[23a] Reaction time = 30 h, colorless oil (68 mg, 65%). IR ($CHCl_3$): ν_{max} = 3505, 3071, 3013, 2962, 2938, 1677, 1598, 1573, 1466, 1358, 1295, 1249, 1217, 1185, 1154, 1126, 1070, 1044, 1022, 967, 807, 669, 596, 534 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.70 (m, 2H), 7.67–7.61 (m, 1H), 7.48–7.38 (m, 1H), 5.64 (d, *J* = 9.4 Hz, 1H), 3.40 (br s, 1H), 3.06 (d, *J* = 17.6 Hz, 1H), 2.72 (dd, *J* = 17.6, 9.4 Hz, 1H), 2.20 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 208.6, 147.0, 138.5, 133.7, 128.2, 128.1, 124.3, 65.4, 51.1, 30.3 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{11}NNaO_4$ 232.0580; Found 232.0578.

4-Hydroxy-4-(3-nitrophenyl)butan-2-one (3l). Reaction time = 36 h, colorless oil (73.2 mg, 70%). IR ($CHCl_3$): ν_{max} = 3468, 3081, 2926, 2847, 1712, 1583, 1530, 1485, 1351, 1261, 1166, 1095, 1066, 1022, 959, 900, 809, 738, 690 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 2.5 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 5.25 (dd, *J* = 7.6, 4.5 Hz, 1H), 2.87 (d, *J* = 4.7 Hz, 2H), 2.22 (s, 3H)ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 208.6, 148.3, 144.8, 131.8, 129.5, 122.6, 120.7, 68.7, 51.5, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{11}NNaO_4$ 232.0580; Found 232.0574.

4-([1,1'-Biphenyl]-4-yl)-4-hydroxybutan-2-one (3m). Reaction time = 20 h, colorless oil (96 mg, 80%). IR ($CHCl_3$): ν_{max} = 3447, 3020, 2925, 1769, 1485, 1466, 1437, 1415, 1288, 1216, 1156, 1120, 995, 861, 817, 776, 753, 722, 694, 666, 634, 542 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.55 (m, 4H), 7.47–7.41 (m, 4H), 7.34–7.32 (m, 1H), 5.22 (dd, *J* = 8.9, 3.5 Hz, 1H), 2.97–2.84 (m, 2H), 2.22 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.0, 141.7, 140.8, 140.7, 128.8, 127.3, 127.1, 126.1, 69.6, 51.9, 30.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{16}NaO_2$ 263.1043; Found 263.1046.

4-(Anthracen-9-yl)-4-hydroxybutan-2-one (3n). Reaction time = 26 h, pale yellow solid (99 mg, 75%). M.p. 107–109 °C; IR ($CHCl_3$): ν_{max} = 3444, 3050, 3016, 2925, 2854, 1711, 1681, 1593, 1444, 1357, 1329, 1305, 1158, 1085, 931,887, 809, 732, 694, 666, 555cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) : δ = 8.64 (s, 2H), 8.41 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.52–7.43 (m, 4H), 6.79 (dd, *J* = 10.3, 2.6 Hz, 1H), 3.72 (dd, *J* = 18.1, 10.3 Hz, 1H), 2.89 (dd, *J* = 18.1, 2.4 Hz, 1H), 2.24 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.0, 132.6, 131.6, 129.3, 129.1, 128.3, 125.8, 124.8, 66.4, 50.3, 30.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{16}NaO_2$ 287.1043; Found 287.1043.

4-Hydroxy-4-(6-methoxynaphthalen-2-yl)butan-2-one (3o). Reaction time = 21 h, colorless oil (95.3 mg, 78%). IR ($CHCl_3$): ν_{max} = 3469, 3020, 2929, 2857, 1712, 1596, 1490, 1459, 1361, 1288, 1241, 1164, 1112, 1053, 1027, 975, 804, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) : δ = 7.74–7.71 (m, 3H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.16–7.12 (m, 2H), 5.29 (dd, *J* = 9.1, 2.6 Hz, 1H), 3.92 (s, 3H), 2.97 (dd, *J* = 17.5, 9.2 Hz, 1H), 2.89 (dd, *J* = 17.5, 2.9 Hz, 1H), 2.21 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 209.1, 157.7, 137.8, 134.1, 129.4, 128.7, 127.2, 124.3, 119.0, 105.6, 70.0, 55.3, 51.9, 30.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{16}NaO_3$: 267.0992;Found 267.1001

(*E*)-4-Hydroxy-6-phenylhex-5-en-2-one (3p).[24] Reaction time = 24 h, colorless oil (69.4 mg, 73%). IR ($CHCl_3$): ν_{max} = 3450, 3020, 2926, 2855, 1710, 1491, 1405, 1357, 1309, 1092, 1014, 1014, 973, 829, 805, 726, 668, 541 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.24 (m, 5H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 6.1 Hz, 1H), 4.76 (q, *J* = 6.0 Hz, 1H), 2.76 (d, *J* = 6.1 Hz, 2H), 2.21 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.0, 136.4, 130.4, 130.0, 128.5,127.7, 126.4, 68.4, 49.9, 30.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+ H]^+$ calcd for $C_{12}H_{15}O_2$ 191.1067; Found 191.1058.

(*E*)-4-Hydroxy-6-(4-methoxyphenyl)hex-5-en-2-one(3q).[24] Reaction time = 24 h, colorless oil (79.4 mg, 77%). IR ($CHCl_3$): ν_{max} = 3450, 3018, 2927, 2847, 2837, 1711, 1598, 1489, 1465, 1435, 1362, 1291, 1246, 1163, 1105, 1028, 975, 796, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 6.58 (d, *J* = 15.9 Hz, 1H), 6.05 (dd, *J* = 15.9, 6.5 1H), 4.72 (q, *J* = 5.8 Hz, 1H), 3.80 (s, 3H), 2.74 (d, *J* = 5.9 Hz, 2H), 2.20 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 209.0, 159.3, 130.0, 129.2, 127.8, 127.7, 114.0, 68.6, 55.2, 50.1, 30.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{16}NaO_3$ 243.0992; Found 243.0997.

(*E*)-4-Hydroxy-6-(2-methoxyphenyl)hex-5-en-2-one(3r). Reaction time = 28 h, colorless oil (77.3 mg, 75%). IR ($CHCl_3$): ν_{max} = 3446, 3006, 2930, 2854, 1713, 1596, 1490, 1468, 1432, 1368, 1291, 1246, 1168, 1110, 1053, 1025, 976, 726, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 7.6 Hz, 1H), 7.40–7.20 (m, 1H), 7.01–6.85 (m, 3H), 6.23 (dd, *J* = 16.1, 6.4 Hz, 1H), 4.76 (q, *J* = 5.7 Hz, 1H), 3.84 (s, 3H), 2.76 (d, *J* = 6.1 Hz, 2H), 2.21 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.0, 156.8, 130.7, 128.8, 126.9, 125.4, 120.6, 110.8, 69.0, 55.4, 50.1, 30.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{16}NaO_3$ 243.0992; Found 243.1007.

4-(Furan-2-yl)-4-hydroxybutan-2-one (3s).[23d] Reaction time = 25 h, colorless oil (52.4 mg, 68%). IR ($CHCl_3$): ν_{max} = 3442, 3021, 2945, 2861, 1715, 1505, 1413, 1362, 1261, 1164, 1066, 1013, 915, 888, 813, 599 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.22 (m, 1H), 6.32–6.31 (m, 1H), 6.25–6.24 (m, 1H), 5.15 (dd, *J* = 8.9, 3.2 Hz, 1H), 3.05 (dd, *J* = 17.6, 8.9 Hz, 1H), 2.91 (dd, *J* = 17.6, 3.2 Hz, 1H), 2.20 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 208.4, 154.9, 142.1, 110.2, 106.2, 63.7, 48.0, 30.6 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_8H_{10}NaO_3$ 177.0522; Found 177.0518.

1-(9-Hydroxy-9*H*-fluoren-9-yl)propan-2-one (3t). Reaction time = 22 h, colorless oil (89.4 mg, 75%). IR ($CHCl_3$): ν_{max} = 3451, 3065, 3043, 2928, 1775, 1698, 1608, 1588, 1477, 1450, 1421, 1393, 1360, 1329, 1302, 1252, 1234, 1168, 1105, 1088, 1047, 1028, 990, 940, 904, 879, 854, 737, 710, 665, 622, 575 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 7.5 Hz, 2H), 7.54 (d, *J* = 7.5 Hz, 2H), 7.38–7.35 (m, 2H), 7.30–7.26 (m, 2H), 3.05 (s, 2H),

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2.15 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 210.5, 148.0, 139.2, 129.2, 128.1, 123.9, 120.1, 80.5, 51.4, 31.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{16}H_{14}NaO_2$ 261.0886; Found 261.0886.

1-(1-Hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)propan-2-one (3u). Reaction time = 24 h, colorless oil (76.6 mg, 75%). IR ($CHCl_3$): ν_{max} = 3476, 3023, 2931, 2855, 1734, 1486, 1466, 1437, 1378, 1287, 1159, 1120, 1071, 1042, 997, 928, 821, 723, 694, 668, 542 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.9 Hz, 1H), 7.23–7.14 (m, 2H), 7.04 (d, *J* = 7.2 Hz, 1H), 2.94 (s, 2H), 2.88–2.68 (m, 2H), 2.18 (s, 3H), 2.13–2.02 (m, 1H), 2.02–1.87 (m, 2H), 1.79–1.68 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 210.5, 141.0, 136.3, 128.8, 127.3, 126.4, 126.3, 71.8, 53.5, 36.2, 32.1, 29.4, 20.1 ppm. HRMS (ESI-TOF) *m/z*: $[M+K]^+$calcd for $C_{13}H_{16}KO_2$ 243.0782; Found 243.0780.

4-Hydroxy-1,4-diphenylpentan-1-one (3v).[25a] Reaction time = 25 h, colorless oil (89 mg, 70%). IR ($CHCl_3$): ν_{max} = 3469, 3060, 3027, 2975, 2928, 1722, 1683, 1599, 1581, 1494, 1447, 1373, 1278, 1174, 1026, 914, 888, 764, 700, 560 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) : δ = 7.88–7.86 (m, 2H), 7.54–7.51 (m, 1H), 7.47–7.45 (m, 2H), 7.43–7.39 (m, 2H), 7.36–7.33 (m, 3H), 3.03–2.97 (m, 1H), 2.90–2.84 (m, 1H), 2.33–2.24 (m, 2H), 1.63 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 201.2, 147.2, 136.7, 133.1, 128.5, 128.3, 128.1, 126.7, 124.8, 74.2, 37.7, 33.8, 31.3 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{18}NaO_2$ 277.1199;Found 277.1194.

4-Hydroxy-4-phenylpentan-2-one(3w).[12] Reaction time = 28 h, colorless oil (60.6 mg, 68%). ^1H NMR (500 MHz, $CDCl_3$) : δ = 7.50–7.25 (m, 5H), 3.19 (d, *J* = 17.0 Hz, 1H), 2.85 (d, *J* = 17.1 Hz, 1H), 2.08 (s, 3H), 1.52 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 203.7, 140.2, 121.3, 119.7, 117.3,66.3, 46.9, 24.9, 23.7 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$calcd for $C_{11}H_{14}NaO_2$: 201.0886; Found 201.0892.

4-Hydroxydecan-2-one (3x).[23d] Reaction time = 30 h, colorless oil (56 mg, 65%). IR ($CHCl_3$): ν_{max} = 3434, 2959, 2930, 2857, 1712, 1671, 1625, 1530, 1468, 1359, 1163, 1017, 976, 912, 863, 808, 736, 689, 649, 546 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.07–3.99 (m, 1H), 2.64 (dd, *J* = 17.4, 3.4 Hz, 1H), 2.52 (dd, *J* = 17.4, 8.4 Hz, 1H), 2.39 (br s, 1H), 2.19 (s, 3H), 1.53–1.15 (m, 10H), 0.87 (t, *J* = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 210.1, 67.5, 49.9, 36.3, 31.7, 30.7, 29.1, 25.4, 22.5, 14.0 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{20}NaO_2$195.1356; Found 195.1349.

4-Hydroxy-4-methylhexadecan-2-one (3y). Reaction time = 24 h, colorless oil (89.3 mg, 66%). IR ($CHCl_3$): ν_{max}= 3464, 3111, 3019, 2929, 2855, 2796, 1709, 1465, 1408, 1377, 1303, 1128, 1054, 926, 891, 717, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 2.63 (d, *J* = 17.1 Hz, 1H), 2.54 (d, *J* = 17.4 Hz, 1H), 2.19 (s, 3H), 1.41–1.18 (m, 23H), 1.18 (s, 3H), 0.87 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 211.1, 71.6, 52.2, 42.2, 31.9, 30.1, 29.64, 29.62, 29.6, 29.3, 26.7, 24.0, 22.7, 14.1 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$calcd for $C_{17}H_{34}NaO_2$ 293.2451; Found 293.2451.

4-Hydroxy-3-methylnonan-2-one (3z).[12] Reaction time = 26 h, colorless oil (51.7 mg, 60%). Diastereomer mixture (dr = 65:35). Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ = 3.97–3.89 (m, 1H), 2.65–2.51 (m, 1H), 2.19 (s, 3H), 1.51–1.27 (m, 8H), 1.14 (d, *J* = 4.6 Hz, 3H), 0.87 (t, *J* = 6.7 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 214.0, 70.9, 50.8, 34.0, 31.8, 29.3, 26.0, 22.6, 14.1, 9.6. ppm.

Acetophenone (3'a).[6b] Reaction time = 24 h, colorless oil (47.5 mg, 79%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.92 (m, 2H), 7.57–7.51 (m, 1H), 7.48–7.41 (m, 2H), 2.59 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.1, 137.0, 133.0, 128.5, 128.2, 26.5 ppm.

1-(*p*-Tolyl)ethan-1-one (3'b).[9b] Reaction time = 22 h, colorless oil (45.6 mg, 68%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 2.56 (s, 3H), 2.40 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 197.8, 143.8, 134.6, 129.2, 128.4, 26.4, 21.5 ppm; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_9H_{10}ONa$ 157.0624; Found 157.0623 ppm.

1-(4-*tert*-Butylphenyl)ethan-1-one (3'c).[6b] Reaction time = 24 h, colorless oil (56.4 mg, 64%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 2.58 (s, 3H), 1.34 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 197.8, 156.8, 134.6, 128.3, 125.5, 35.1, 31.1, 26.5 ppm; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{17}O$ 177.1274; Found 177.1276.

1-(4-Methoxyphenyl)ethan-1-one (3'd).[6b] Reaction time = 16 h, colorless semi-solid (52.6 mg, 70%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93 (s, 2H), 6.92 (s, 2H), 3.85 (s, 3H), 2.54 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 196.8, 163.4, 130.5, 113.6, 55.4, 26.3 ppm.

1-(4-Chlorophenyl)ethan-1-one (3'e).[9b] Reaction time = 36 h, colorless oil (45.6 mg, 59%). IR ($CHCl_3$): ν_{max} = 3020, 2928, 2855, 1688, 1591, 1572, 1488, 1429, 1398, 1360, 1098, 1013, 958, 832, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.6 Hz, 2H),7.38 (d*J* = 8.7 Hz, 2H), 2.54 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 196.6, 139.4, 135.3, 129.6, 128.7, 26.4 ppm.

1-(4-Nitrophenyl)ethan-1-one (3'f).[6b] Reaction time = 25 h, pale yellow solid (58 mg, 70%). M.p. 77−79 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 2.68 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 196.3, 150.7, 141.6, 129.3, 123.9, 27.0 ppm.

1-(4-Bromophenyl)ethan-1-one (3'g).[9b] Reaction time = 27 h, colorless solid (63.7 mg, 64%). M.p. 46–48 °C; IR ($CHCl_3$): ν_{max} = 3020, 2924, 2857, 1677, 1606, 1573, 1406, 1358, 1309, 1272, 1181, 1122, 1075, 1042, 1018, 954, 927, 878, 841, 817, 772, 668, 637, 591, 567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 2.57 (s, 3H) ppm; $^{13}C\{^1H\}$

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NMR (100 MHz, $CDCl_3$): δ = 197.0, 135.8, 131.8, 129.8, 128.3, 26.5 ppm.

1-(2-Bromophenyl)ethan-1-one (3'h).[26] Reaction time = 25 h, colorless oil (53 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 7.8 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.37 (td, *J* = 7.5, 0.8 Hz, 1H), 7.29 (td, *J* = 7.7, 1.7 Hz, 1H), 2.63 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 201.4, 141.4, 133.8, 131.8, 128.9, 127.4, 118.9, 30.3 ppm. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$calcd for C_7H_8BrNaO 220.9572; Found 220.9567.

1-(2-Chlorophenyl)ethan-1-one (3'i).[9b] Reaction time = 28 h, colorless oil (43.3 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, *J* =7.6 Hz, 1H), 7.41–7.22 (m, 3H), 2.63 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 200.4, 139.0, 131.9, 131.2, 130.6, 129.3, 126.9, 30.6 ppm;

1-(2-Methoxyphenyl)ethan-1-one (3'j).[9b] Reaction time = 23 h, colorless semi-solid (46 mg, 61%). IR ($CHCl_3$): ν_{max} = 3019, 2840, 1676, 1596, 1574, 1485, 1437, 1359, 1294, 1251, 1185, 1071, 1042, 967, 851, 751, 668, 595 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.47–7.42 (m, 1H), 6.97 (dd, *J* = 8.0, 7.6 Hz, 2H), 3.90 (s, 3H), 2.60 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 199.9, 158.8, 133.6, 130.3, 128.1, 120.4, 111.5, 55.4, 31.8 ppm.

1-(2,4,6-Trimethylphenyl)ethan-1-one (3'k). Reaction time = 26 h, colorless oil (55 mg, 68%). IR ($CHCl_3$): ν_{max} = 3019, 2918, 2850, 1698, 1606, 1418, 1353, 1253, 1164, 1058, 1037, 1015, 911, 848, 670, 643, 597 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2H), 2.46 (s, 3H), 2.28 (s, 3H), 2.22 (s, 6H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 208.5, 139.8, 138.2, 132.2, 128.4, 32.1, 20.9, 19.0 ppm; HRMS (ESI-TOF) *m/z*: [M+K]$^+$ calcd for $C_{11}H_{14}KO$: 201.0676; Found 201.0684.

1-(2,4-dichlorophenyl)ethan-1-one (3'l).[9b] Reaction time = 28 h, colorless oil (57 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.3 Hz, 1H), 7.40 (d, *J* = 1.9 Hz, 1H), 7.28 (dd, *J* = 14.3, 12.4 Hz, 1H), 2.61 (s, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.8, 137.6, 137.0, 132.4, 130.6, 130.4, 127.2, 30.6 ppm.

1-(3-Nitrophenyl)ethan-1-one (3'm). Reaction time = 32 h, colorless oil (41.3 mg, 50%). IR ($CHCl_3$): ν_{max} = 3019, 2928, 2850, 1692, 1616, 1534, 1474, 1432, 1353, 1254, 1112, 1019, 910, 848, 670, 597 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 8.0 Hz, 1H), 8.39 (t, *J* = 6.9 Hz, 1H), 8.27 (dd, *J* = 7.0, 1.8 Hz, 1H), 7.69–7.65 (m, 1H), 2.67 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 195.6, 148.4, 138.2, 133.7, 129.9, 127.3, 123.1, 26.6 ppm. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_8H_7NNaO_3$ 188.0318; Found 188.0312.

1-Phenylpropan-2-one (3'n).[25b] Reaction time = 24 h, colorless oil (42.3 mg, 63%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57–7.23 (m, 5H), 3.74 (s, 2H), 2.19 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 206.4, 134.2, 129.3, 128.7, 127.0, 51.1, 29.2 ppm; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_9H_{10}NaO$: 157.0625; Found 157.0624.

4-(4-Benzyloxy-3-methoxyphenyl)butan-2-one (3'o). Reaction time = 19 h, colorless oil (99.5 mg, 70%). IR ($CHCl_3$): ν_{max} = 3019, 2922, 1714, 1666, 1626, 1608, 1591, 1492, 1406, 1359, 1330, 1161, 1091, 1014, 976, 945, 833, 797, 775, 731, 668, 584, 540 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.27 (m, 5H), 6.81–6.73 (m, 2H), 6.65 (d, *J* = 8.1 Hz, 1H), 5.12 (s, 2H), 3.87 (s, 3H), 2.83 (t, *J* = 7.1 Hz, 2H), 2.73 (t, *J* = 7.1 Hz, 2H), 2.13 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 208.1, 149.5, 146.5, 137.3, 134.2, 128.5, 127.7, 127.2, 120.0, 114.2, 112.2, 71.1, 55.9, 45.3, 30.1, 29.3 ppm; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{18}H_{20}NaO_3$ 307.1305; Found 307.1310.

1-(4-Hydroxy-3-methoxyphenyl)propan-2-one (3'p). Reaction time = 20 h, colorless oil (63 mg, 70%). IR ($CHCl_3$): ν_{max} = 3528, 3020, 2979, 2935, 2857, 1708, 1603, 1515, 1468, 1434, 1363, 1268, 1207, 1151, 1120, 1036, 956, 914, 880, 820, 726, 646 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.87 (d, *J* = 7.8 Hz, 1H), 6.71–6.67 (m, 2H), 5.63 (s, 1H), 3.86 (s, 3H), 3.60 (s, 2H), 2.14 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 207.0, 146.6, 144.7, 126.0, 122.2, 114.5, 111.6, 55.9, 50.6, 29.0 ppm; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{10}H_{12}NaO_3$ 203.0679; Found 203.0680.

Decan-2-one (3'q). Reaction time = 24 h, colorless oil (57 mg, 73%). IR ($CHCl_3$): ν_{max} = 3022, 2952, 2921, 1714, 1464, 1400, 1361, 1162, 670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (t, *J* = 7.5 Hz, 2H), 2.13 (s, 3H), 1.54–1.52 (m, 2H), 1.32–1.20 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 209.4, 43.8, 31.8, 29.8, 29.3, 29.1, 29.08, 23.8, 22.6, 14.0 ppm; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{10}H_{20}NaO$ 179.1406; Found 179.1409.

Tetradecan-2-one (3'r). Reaction time = 28 h, colorless oil (81 mg, 76%). IR ($CHCl_3$): ν_{max} = 3020, 2931, 2844, 1717, 1449, 1414, 1361, 1162, 1120, 966, 722, 668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.40 (t, *J* = 7.5 Hz, 2H), 2.12 (s, 3H), 1.61–1.52 (m, 2H), 1.36–1.19 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 209.5, 43.8, 31.9, 29.8, 29.63, 29.61, 29.6, 29.5, 29.4, 29.3, 29.2, 23.9, 22.7, 14.1 ppm; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{14}H_{28}ONa$ 235.2032; Found 235.2030.

Octane-2,7-dione (3's). Reaction time = 24 h, colorless oil (37 mg, 52%). IR ($CHCl_3$): ν_{max} = 3019, 2935, 2853, 1711, 1584, 1462, 1408, 1374, 1301, 1127, 927, 812, 724, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (t, *J* = 2.8 Hz, 4H), 2.11 (s, 6H), 1.53 (t, *J* = 2.8 Hz, 4H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 208.6, 43.3, 29.8, 23.1 ppm. HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_8H_{14}O_2Na$ 165.0886; Found 165.0889.

10-Hydroxydecan-2-one (3't). Reaction time = 24 h, colorless oil (50 mg, 63%). IR ($CHCl_3$): ν_{max} = 3465, 3162, 3013, 2929, 2856, 1711, 1466, 1371, 1299, 1219, 1200, 1120, 1044, 929, 822, 770, 760, 726, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.63 (t, *J* = 6.7 Hz, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 2.13 (s, 3H), 1.60–1.50 (m, 4H), 1.39–1.25 (m, 8H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 209.5, 63.0, 43.8, 32.7, 29.9, 29.4, 29.3, 29.1, 25.7, 23.8 ppm;

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HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_{20}O_2Na$: 195.1356; Found 195.1351.

11-Hydroxyundecan-2-one (3'u). Reaction time = 21 h, colorless oil (53 mg, 57%). IR ($CHCl_3$): ν_{max} = 3416, 2926, 2854, 1711, 1464, 1361, 1171, 1054, 912, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.60 (t, *J* = 6.7 Hz, 2H), 2.39 (t, *J* = 7.4 Hz, 2H), 2.10 (s, 3H), 1.86 (s, 1H), 1.58–1.50 (m, 4H), 1.38–1.20 (m, 10H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.6, 62.9, 43.7, 32.7, 29.8, 29.3, 29.27, 29.2, 29.1, 25.6, 23.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{22}O_2Na$ 209.1512; Found 209.1510.

Ethyl 5-oxohexanoate (3'v). Reaction time = 36 h, colorless oil (39.5 mg, 50%). IR ($CHCl_3$): ν_{max} = 3028., 2945, 2844, 1750, 1718, 1648, 1439, 1363, 1321, 1286, 1202, 1152, 1042, 821, 798, 754, 697, 663, 627, 543 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.12 (q, *J* = 7.1 Hz, 2H), 2.51 (t, *J* = 7.2 Hz, 2H), 2.32 (t, *J* = 7.2 Hz, 2H), 2.14 (s, 3H), 1.89–1.84 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 208.1, 173.2, 60.4, 42.5, 33.2, 29.9, 18.9, 14.2 ppm; HRMS (ESI-TOF) calcd for $C_8H_{14}O_3Na$ 181.0835; Found 181.0840.

Ethyl 3-oxobutanoate (3'w).[6b] Reaction time = 24 h, colorless oil (42 mg, 58%).; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.15 (q, *J* = 7.2 Hz, 2H), 3.41 (s, 2H), 2.23 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.6, 167.0, 61.3, 50.0, 30.0, 14.0 ppm.

Methyl 3-oxobutanoate (3'x).[27] Reaction time = 26 h, colorless oil (30 mg, 52%); ^1H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 3H), 3.42 (s, 2H), 2.21 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.5, 167.5, 52.2, 49.7, 30.0 ppm.

(*E*)-4-(5-Hydroxydec-2-en-1-yl)-2-methoxyphenol (7). To a stirred and degassed solution of phenol **1'p** (100 mg, 0.609 mmol, 1.0 equiv) and homoallyl alcohol **6** (87 mg, 0.609 mmol, 1.0 equiv) in dry CH_2Cl_2 (10 mL) was added Grubbs second-generation catalyst (10.4 mg, 0.0122 mmol, 2 mol%) at room temperature, and the mixture was refluxed for 48 h. The mixture was then cooled and filtered through a small pad of silica gel, and the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography using petroleum ether/EtOAc (5:1) as an eluent to provide (8:1) mixture of (*E*/*Z*)-**7** (122 mg, 72%) as a colorless oil. IR ($CHCl_3$): ν_{max} = 3444, 3054, 2979, 2928, 2857, 1649, 1608, 1514, 1464, 1434, 1374, 1265, 1234, 1208, 1153, 1122, 1036, 971, 912, 888, 822, 733, 705, 651 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 7.9 Hz, 1H), 6.71–6.64 (m, 2H), 5.81 (s, 1H), 5.74–5.59 (m, 1H), 5.58–5.48 (m, 1H), 3.84 (s, 3H), 3.64–3.60 (m, 1H), 3.29 (d, *J* = 6.4 Hz, 2H), 2.30–2.24 (m, 1H), 2.16–2.09 (m, 1H), 1.50–1.42 (m, 2H), 1.32–1.23 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 146.4, 143.8, 133.0, 132.3, 127.2, 120.9, 114.3, 111.0, 71.0, 55.7, 40.4, 38.6, 36.6, 31.8, 25.2, 22.5, 13.9 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{26}NaO_3$ 301.1774;Found 301.1774.

5-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)decan-3-one (±) gingerol (8).[17] The titled compound was prepared from **7** (100 mg, 0.36 mmol) following similar procedure as described for **3** to give **8** (64.6 mg, 48%) as colorless oil. IR ($CHCl_3$): ν_{max} = 3534, 3410, 2959, 2933, 2858, 2252, 1704, 1612, 1215, 1465, 1431, 1369, 1272, 1208, 1153, 1124, 1035, 909, 852, 818, 795, 735, 648, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.79 (d, *J*= 8.0 Hz, 1H), 6.71–6.56 (m, 2H), 5.85 (brs, 1H), 4.02 (d, *J* = 4.0 Hz, 1H), 3.83 (s, 3H), 3.17 (br s, 1H), 2.81 (t, *J* = 6.8 Hz, 2H), 2.71 (t, *J* = 7.0 Hz, 2H), 2.57–2.43 (m, 2H), 1.54–1.19 (m, 8H), 0.87 (t, *J* = 6.7 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 211.4, 146.4, 143.9, 132.5, 120.6, 114.4, 111.0, 67.6, 55.7, 49.2, 45.3, 36.3, 31.6, 29.1, 25.0, 22.5, 13.9 ppm; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{26}NaO_4$ 317.1723; Found 317.1723.

Conflicts of interest

There are no conflicts to declare.

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REFERENCES

1. (*a*) R. Mestres, *Green Chem*. 2004, **6**, 583. (*b*) J. Sukumaran and U. Hanefeld, *Chem. Soc. Rev*. 2005, **34**, 530. (*c*) C. Hertweck, *Angew. Chem., Int. Ed*. 2009, **48**, 4688. (*d*) P. Clapés, W.-D. Fessner, G. A. Sprenger, and A. K. Samland, *Curr. Opin. Chem. Biol.* 2010, **14**, 154.
2. (*a*) J. Smidt, W. Hafner, R. Jira, R. Sieber, J. Sedlmeier, and A. Sabel, *Angew. Chem., Int. Ed.* 1962, **1**, 80. (*b*) J. Tsuji, *Synthesis* 1984, 369. (*c*) J. M. Takacs, and X.-T. Jiang, *Curr. Org. Chem.* 2003, **7**, 369. (*d*) T. V. Baiju, E. Gravel, E. Doris, and I. N. N. Namboothiri, *Tetrahedron Lett.* 2016, **57**, 3993.
3. (*a*) E. Monflier and A. Mortreux, *In Aqueous-Phase Organometallic Catalysis*, 2nd ed. B. Cornils, W. A. Herrmann, Wiley-VHC: Weinheim, Germany, 2004; pp 481–487. (*b*) L. Hintermann, In *Transition Metals for Organic Synthesis*, 2nd ed. M. Beller, and C. Bolm, Wiley-VHC: Weinheim, Germany, 2004; Vol. 2, pp 379. (*c*) R. Jira, *In Applied Homogeneous Catalysis with Organometallic Compounds*, 2nd ed. B. Cornils, W. A. Herrmann, Wiley-VHC: Weinheim, Germany, 2002; Vol. 1, pp 386.
4. J. Aguado, D. P. Serrano, R. Van Grieken, J. M. Escola, R. García, and S. Carretero, *Modified Wacker of Long-chain Terminal Olefins.* In Book of Extended Abstracts of the Fourth World Congress on Oxidation Catalysis; Berlin, Potsdam, Germany, 2001; pp 493.
5. (*a*) W. H. Clement and C. M. Selwitz, *J. Org. Chem.* 1964, **29**, 241. (*b*) D. R. Fahey and E. A. Zuech, *J. Org. Chem.* 1974, **39**, 3276. (*c*) H. Jiang, L. Jia, and J. Li, *Green Chem.* 2000, **2**, 161. (*d*) T. Mitsudome, T. Umetani, N. Nosaka, K. Mori, T. Mizugaki, K. Ebitani, and K. Kaneda, *Angew. Chem., Int. Ed.* 2006, **45**, 481. (*e*) J.-L. Wang, L.-N. He, C.-X. Miao, and Y.-N. Li, *Green Chem.* 2009, **11**, 1317. (*f*) K. Mitsudo, S. Fukunaga, T. Fujita, H. Mandai, S. Suga, and H. Tanaka, *Electrochemistry* 2013, **81**, 347.

6. (*a*) J. Nokami, H. Ogawa, S. Miyamoto, T. Mandai, S. Wakabayasi, and J. Tsuji, *Tetrahedron Lett.* 1988, **29**, 5181. (*b*) D. A. Chaudhari, and R. A. Fernandes, *J. Org. Chem.* 2016, **81**, 2113.
7. (*a*) H. Takayama, T. Koike, N. Aimi, and S. Sakai, *J. Org. Chem.* 1992, **57**, 2173. (*b*) R. A. T. M. van Benthem, H. Hiemstra, and W. N. Speckamp, *J. Org. Chem.* 1992, **57**, 6083. (*c*) N. I. Kuznetsova, M. A. Fedotov, V. A. Likholobov, and Y. I. Yermakov, *J. Mol. Catal.* 1986, **38**, 263. (d) L. Eberson and L. Jönsson, *J. Chem. Soc., Chem. Commun.* 1974, 885. (*e*) K. I. Matveev, *Kinet. Katal.* 1977, **18**, 862. (*f*) R. A. Fernandes, and V. Bethi, *Tetrahedron* 2014, **70**, 4760. (*g*) R. A. Fernandes, and D. A. Chaudhari, *J. Org. Chem.* 2014, **79**, 5787.
8. (*a*) J.-H. Ahn and D. C. Sherrington, *Macromolecules* 1996, **29**, 4164. (*b*) G.-J. Ten Brink, I. W. C. E. Arends, G. Papadogianakis, and R. A. Sheldon, *Appl. Catal. A: General* 2000, **194**, 435. (*c*) C. N. Cornell and M. S. Sigman, *Org. Lett.* 2006, **8**, 4117.
9. (*a*) S. Uchiumi, K. Ataka, and T. Matsuzaki, *J. Organomet. Chem.* 1999, **576**, 279. (*b*) G. Zhang, X. Xie, Y. Wang, X. Wen, Y. Zhao, and C. Ding, *Org. Biomol. Chem.* 2013, **11**, 2947.
10. (*a*) J. Tsuji, H. Nagashima, and K. Hori, *Chem. Lett.* 1980, **9**, 257. (*b*) H. Mimoun, R. Charpentier, A. Mitschler, J. Fischer, and R. Weiss, *J. Am. Chem. Soc.* 1980, **102**, 1047. (*c*) C. N. Cornell, and M. S. Sigman, *J. Am. Chem. Soc.* 2005, **127**, 2796. (*d*) B. W. Michel, A. M. Camelio, C. N. Cornell, and M. S. Sigman, *J. Am. Chem. Soc.* 2009, **131**, 6076.
11. V. Bethi and R. A. Fernandes, *J. Org. Chem*. 2016, **81**, 8577.
12. J. R. McCombs, B. W. Michel, and M. S. Sigman, *J. Org. Chem.* 2011, **76**, 3609.
13. P. A. Runeberg, and P. Eklund, *Org. Lett.* 2019, **21**, 8145.
14. (*a*) A. J. Fatiadi, *Synthesis* 1976, 65. (*b*) A. J. Fatiadi *Synthesis* 1976, 133.
15. (*a*) R. J. K. Taylor, M. Reid, J. Foot, and S. A. Raw, *Acc. Chem. Res.* 2005, **38,** 851. (*b*) C. C. Cosner, P. J. Cabrera, K. M. Byrd, A. M. Adams, and P. Helquist, *Org. Lett.* 2011, **13**, 2071.
16. K. Nowińska, D. Dudko, and R. Golon, *Chem*. *Commun*. 1996, 277.
17. (*a*) T. Aoyama, N. Sonoda, M. Yamauchi, K. Toriyama, M. Anzai, A. Ando, and T. Shioiri, Synlett, 1998, 35. (*b*) S. P. Gholap, D. Jangid, R. A. Fernandes, R. A. *J. Org. Chem*. 2019, **84**, 3537.
18. For recent synthesis see: (*a*) G. Solladié and C. Ziani-Chérif, *J. Org. Chem*. 1993, **58**, 2181. (*b*) S. A. Fleming, C. W. Dyer, and J. Eggington, *Synth. Commun*. 1999, **29**, 1933. (*c*) G. Sabitha, C. Srinivas, T. R. Reddy, K. Yadagiri, and J. S. Yadav, *Tetrahedron: Asymmetry* 2011, **22**, 2124. (*d*) N. V. Kumar, S. C. S. Kumar, P. Srinivas, and B. K. Bettadaiah, *Org. Prep. Proc. Int.* 2015, **47**, 443. (*e*) S. Paladhi, I.-S. Hwang, E. J. Yoo, D. H. Ryu, and C. E. Song, *Org. Lett*. 2018, **20**, 2003.
19. (*a*) D. W. Connell and M. D. Sutherland, *Aust. J. Chem*. 1969, **22**, 1033. (*b*) H. Kikuzaki, S.-M. Tsai, and N. Nakatani, *Phytochemistry* 1992, **31**, 1783.
20. R. B. Semwal, D. K. Semwal, S. Combrinck, and A. M. Viljoen, *Phytochemistry* 2015, **117**, 554.
21. (*a*) H. C. Brown, and P. K. Jadhav, *J. Am. Chem. Soc.* 1983, **105**, 2092. (*b*) W. R. Roush, A. E. Walts, and L. K. Hoong, *J. Am. Chem. Soc*. 1985, **107**, 8186. (*c*) U. S. Racherla, and H. C. Brown, *J. Org. Chem.* 1991, **56**, 401. (*d*) G. E. Keck, K. H. Tarbet, and L. S. Geraci, *J. Am. Chem. Soc*. 1993, **115**, 8467. (*e*) K. Kubota, J. L. Leighton, *Angew. Chem., Int. Ed.* 2003, **42**, 946.
22. (*a*) Z. Du, Y. Li, F. Wang, W. Zhou, and J.-X. Wang, *Synth. Commun.* 2011, **41** , 1664. (*b*) S. C. Cosgrove, S. Hussain, N. J. Turner, and S. P. Marsden, *ACS Catal.* 2018, **8,** 5570. (*c*) M. S. Reddy, M. Narender, Y. V. D. Nageswar, and K. R. Rao, *Synth. Commun*. 2007, **37**, 1983. (*d*) R. Tomifuji, S. Masuda, T. Kurahashi, and S. Matsubara, *Org. Lett*. 2019, **21**, 3834. (*e*) T. Hamaguchi, Y. Takahashi, H. Tsuji, and M. Kawatsura, *Org. Lett*. 2020, **22**, 1124. (*f*) J.-X. Wang, X. Jia, T. Meng, and L. Xin, *Synthesis* 2005, 2838. (*g*) T. Naicker, P. I. Arvidsson, H. G. Kruger, G. E. M. Maguire, and T. Govender, *Eur. J. Org. Chem*. 2011, 6923. (*h*) K. Takenaka, Y. D. Dhage, and H. Sasai, *Chem. Commun*. 2013, **49**, 11224. (*i*) R. S. Vasconcelos, L. F. Silva Jr, and A. Giannis, *J. Org. Chem*. 2011, **76**, 1499. (*j*) L.-M. Zhao, H.-S. Gao, D.-F. Li, J. Dong, L.-L. Sang, and J. Ji, *Org. Biomol. Chem*. **2017**, *15*, 4359. (*k*) B. Das, D. B. Shinde, B. S. Kanth, A. Kamle, and C. G. Kumar, *Eur. J. Med. Chem*. 2011, **46**, 3124. (*l*) K.-T. Tan, S.-S. Chng, H.-S. Cheng, and T.-P. Loh, *J. Am. Chem. Soc*. 2003, **125**, 2958.
23. (*a*) R. Fernandez-Lopez, J. Kofoed, M. Machuqueiro, and T. Darbre, *Eur. J. Org. Chem*. 2005, 5268. (*b*) V. Ashokkumar, C. Chithiraikumar, and A. Siva, *Org. Biomol. Chem*. 2016, **14**, 9021. (*c*) P. S. Mainkar, V. Chippala, R. Chegondi, and S. Chandrasekhar, *Synlett* 2016, 1969. (*d*) V. Maslak, Z. Tokic-Vujosevic, Z. Ferjancic, and R. N. Saicic, *Tetrahedron Lett*. 2009, **50**, 6709.
24. H. Shulman, C. Makarov, A. K. Ogawa, F. Romesberg, and E. Keinan, *J. Am. Chem. Soc.* 2000, **122**, 10743.
25. (*a*) E. Speckmeier, P. J. W. Fuchs, and K. Zeitler, *Chem*. *Sci*. 2018, **9**, 7096. (*b*) J.-L. Wang, H.-J. Li, H.-S. Wang, and Y.-C. Wu, *Org. Lett*. 2017, **19**, 3811.
26. N. Schröder, J. Wencel-Delord, and F. Glorius, *J. Am. Chem. Soc.* 2012, **134**, 8298.
27. B. Wahl, H. Bonin, A. Mortreux, S. Giboulot, F. Liron, G. Poli, and M. Sauthier, *Adv. Synth. Catal*. 2012, **354**, 3105.

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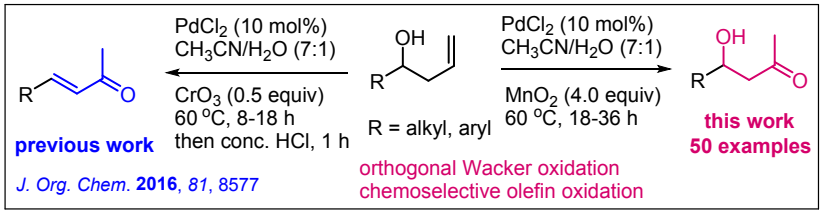
Abstract



An efficient and mild reaction conditions for Wacker-type oxidation of terminal olefins of less explored homoallyl alcohols to β-hydroxy-methyl ketones has been developed by using Pd(II) catalyst and MnO_2 as co-oxidant.