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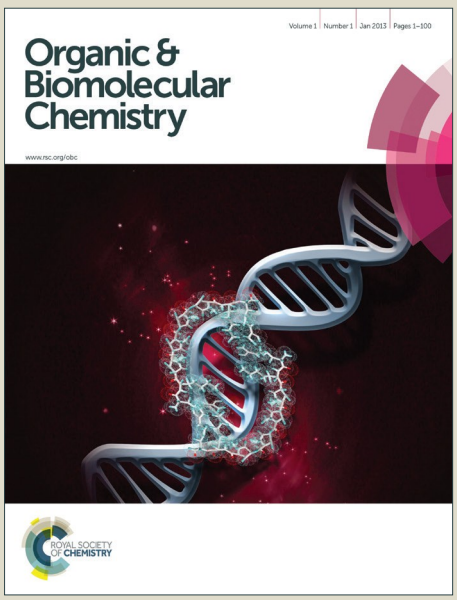

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PAPER

Green organocatalytic α-hydroxylation of ketones

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An efficient and green method for the α-hydroxylation of substituted ketones has been developed. This method includes the *in situ* conversion of various ketones into the corresponding silyl enol ethers and their oxidation to the corresponding α-hydroxy ketones. Two protocols have been established leading either to protected α-hydroxy carbonyls or free α-hydroxy ketones. Both procedures are easy to follow and lead to good to high yields for a variety of ketones.

Introduction

The α-hydroxy ketone subunit is an important motif found in a diverse range of biologically relevant molecules and constitutes a valuable synthetic target. It is also a flexible intermediate in the synthesis of many pharmaceuticals,[1,2] as well as for the synthesis of depsipeptides and natural products of biological importance.[3] The construction of the C-O bond is crucial not only because its biological functions, but also because this architecture is useful for directing further stereoselective elaboration. The classical method for the preparation of α-hydroxy carbonyl compounds involves substitution of α-amino or α-halo carbonyls with hydroxides. In literature, the synthesis of α-hydroxy ketones can also be performed by the reduction of diketones[4] or via enolisation of α-methylene carbonyl compounds and reaction with an electrophilic oxygen source like organic peracids,[5] singlet oxygen,[6] osmium tetroxide,[7] and ozonolysis.[8] Among several synthetic protocols, the Rubbotom oxidation, which involves the epoxidation of silyl enol ethers to generate silyl-protected α-hydroxy ketones, has been one of the most widely used methods.[5a,9] α-Hydroxy ketones can also prepared by the oxidation of epoxides and aziridines.[10] Direct methods for the preparation of α-hydroxy ketones involve iodine reagents[11] and metal-based procedures utilizing Pd,[12a] Sn[12b] and Ru.[12c,d] Finally, a number of α-hydroxylation procedures of carbonyl compounds have been developed in organocatalysis.[13]

In recent years, our interest lies on developing novel organocatalytic methodologies that can lead to useful organic intermediates. Along these lines, we have developed an organocatalytic α-amination of branched aldehydes.[14] More recently, we turned our attention on the organocatalytic activation of hydrogen peroxide. Since hydrogen peroxide by itself is a poor oxidant for organic oxidations, it has to be coupled with a catalyst or a reagent to create a reactive intermediate that will carry out the oxidation. A couple of years ago, we have introduced 2,2,2-trifluoroacetophenone, among a number of activated ketones, as an efficient organocatalyst for the oxidation of silanes to silanols,[15a] tertiary amines and azines to *N*-Oxides[15b] and alkenes to epoxides.[15c] Also, the same protocol was extended in the oxidation of *N*-allyl tertiary amines, followed by a Meisenheimer rearrangement leading to O-allyl hydroxyl amines.[15d] In general, this oxidation protocol is environmentally friendly, as the only byproduct is water.

Herein, our design plan involves the successful employment of this organocatalytic oxidative protocol on enol ethers to afford α-hydroxy ketones. Our final target would be the synthesis of the silyl enol ethers from the corresponding ketone and the *in situ* oxidation of the enolate to the corresponding α-hydroxy ketones.

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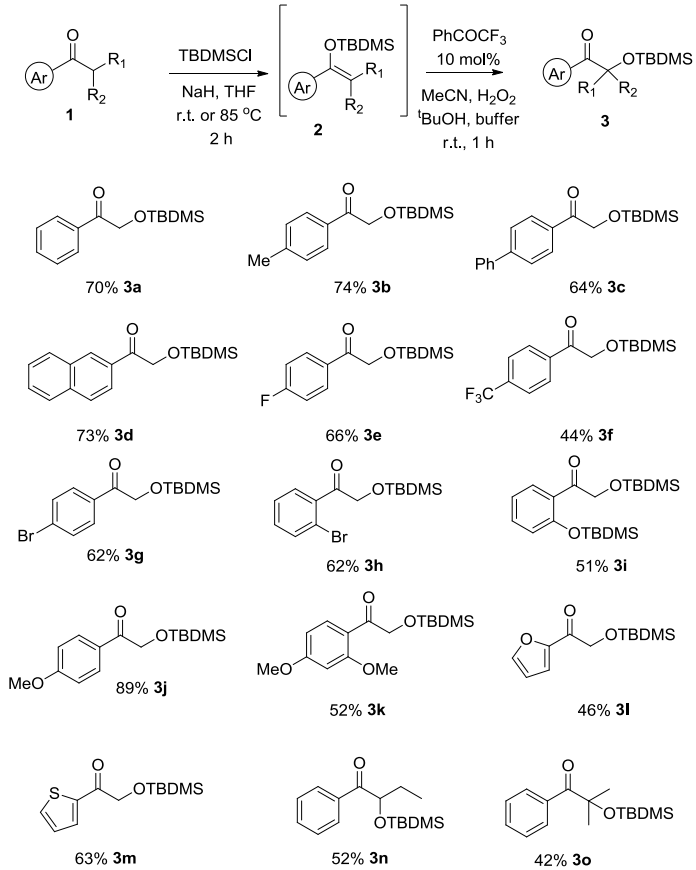
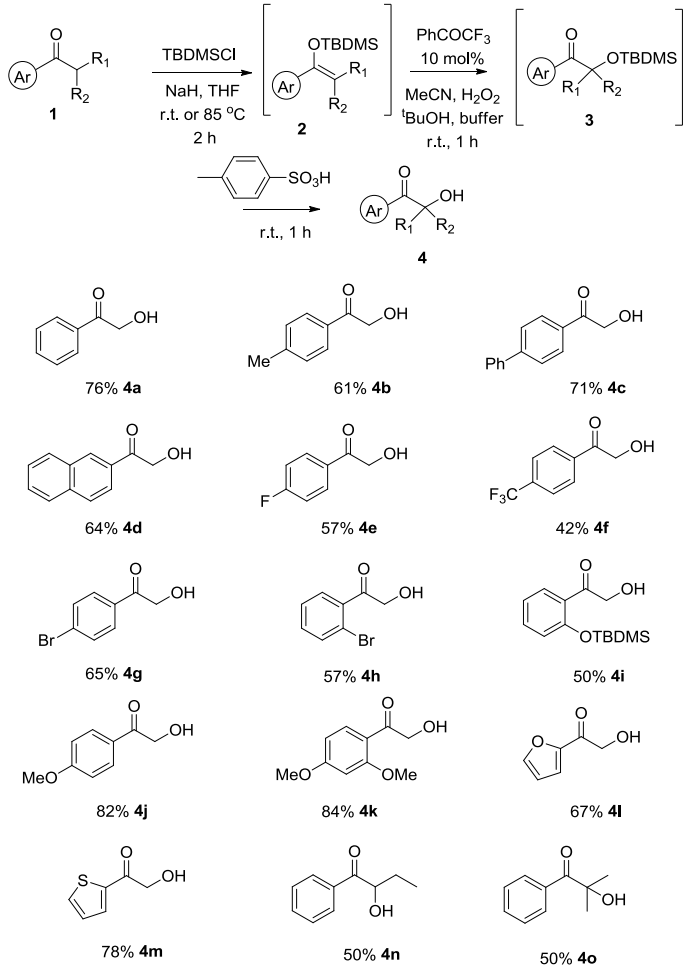
Results and discussion

Our initial concern whether the TBDMS-enol ether of acetophenone could be oxidized under our previously-developed oxidative reaction conditions were readily answered by preparing the silyl enol ether and subjecting it in the oxidative reaction conditions, leading to a quantitative conversion of TBDMS-protected alcohol **3a**. We then turned our attention in developing an *in situ* protocol. Indeed, it is possible to perform both the silyl enol ether formation and the Rubottom-type oxidation in a single operation leading to 70% yield of protected alcohol **3a** (Scheme 1). Filtration through a Florisil plug and evaporation of THF before the oxidation was proven to be necessary in order to maintain the yield of the reaction. Among a variety of protecting groups that were tested (TES, TMS, TIPS etc), TBDMS led to the best isolated yields of products. Finally, the optimum reaction conditions were studied and identified. A variety of substituted ketones were then tested, leading to a number of TBDMS-protected α-hydroxy ketones (Scheme 1). Alkyl-substituted aryl methyl ketones were used successfully leading to good to high yields (**3b-d**). Halogen substituents were also well tolerated either at *para*- or *ortho*-position, leaving room for further synthetic manipulations on the aromatic ring (**3e-h**). Substrates bearing free hydroxyl groups on the aromatic ring can also be employed leading to a double protection (**3i**). Electron rich aromatic rings and heterocyclic aromatic methyl ketones led also to good to high yields (**3j-m**). Substrates with larger stereochemical hindrance led to slightly lower yields, but even tertiary alcohol are possible to be formed by this method (**3n, 3o**). In these cases, the corresponding products were obtained after silica treatment, as the corresponding epoxides were more stable.

In an attempt to further extend this protocol, our focus turned on one-pot deprotection of the silyl-group (Scheme 2). This was found to be possible just by addition of *p*-toluenesulfonic acid in the reaction mixture for 1 h. Starting from acetophenone, the α-hydroxy ketone **4a** was isolated in 76% yield. Alkyl-substituted



Scheme 1 Organocatalytic synthesis of TBDMS-protected α-hydroxy ketones



Scheme 2 Organocatalytic synthesis of α-hydroxy ketones

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aromatic methyl ketones were also employed succefully (**4b-d**). Halogen-containing aromatics led to slightly lower yields, while ortho-substituted aromatics were well tolerated (**4e-h**). It has to be noted that selective deprotection of the alcohol in the presence of the phenol was also possible (**4i**). In this case, electron rich aromatic methyl ketones afforded the highest yields (**4j**, **4k**), while ketones bearing heterocyclic aromatic moieties led also to the desired product in good yield (**4l**, **4m**). Substrates with further substitution on the alkyl side chain led again to slightly worse yields (**4n**, **4o**). Again, it has to be highlighted that tertiary alcohols were successfully generated with this protocol.

Conclusions

In conclusion, a highly versatile and green protocol was developed for the conversion of ketones into protected α-hydroxy ketones using H_2O_2 as the oxidant. This method was further extended in the synthesis of free α-hydroxy ketones. This method provides an effective entry for the installation of α-hydroxy moieties into ketones, a non-trivial task as appeared in literature. A variety of substituted aromatic ketones, heteroaromatic ketones were employed successfully leading to high to excellent yields in both cases. When the alkyl chain was changed from methyl to higher members of alkyl substituents, the protocol led to lower yields, but it was still successful. Thus, these protocols can be extended in the synthesis of both secondary and tertiary α-hydroxy ketones.

Experimental

General methods

Chromatographic purification of products was accomplished using forced-flow chromatography on Merck Kieselgel 60 F254 230-400 mesh. Thin-layer chromatography (TLC) was performed on aluminum backed silica plates (0.2 mm, 60 F254). Visualization of the developed chromatogram was performed by fluorescence quenching using phosphomolybdic acid, anisaldehyde or potassium permanganate stains. Melting points were determined on a Buchi 530 hot stage apparatus and are uncorrected. Mass spectra (ESI) were recorded on a Finningan Surveyor MSQ LC-MS spectrometer. HRMS spectra were recorded on Bruker Maxis Impact QTOF spectrometer. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Varian Mercury (200 MHz, 50 MHz and 188 MHz respectively), and are internally referenced to residual solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b s = broad signal, b s m = broad signal multiplet), coupling constant and assignment. Data for ^{13}C and ^{19}F NMR are reported in terms of chemical shift (δ ppm). Mass spectra and conversions of the reactions were recorded on a Shimadzu GCMS-QP2010 Plus Gas Chromatograph Mass Spectrometer utilizing a MEGA column (MEGA-5, F.T: 0.25µm, I.D.: 0.25mm, L: 30m, Tmax: 350 ^{o}C, Column ID 11475).

Representative procedure for 3a-3b, 3e, 3g-3i

Substituted acetophenone (1.00 mmol) and *tert*-butylchlorodimethylsilane (196 mg, 1.30 mmol) were placed in an oven-dried round bottom flask sealed with a septum, under Ar atmosphere, and dissolved in dry THF (4.0 mL). The solution was cooled down to -78 ^{o}C and NaH (60% in oil, 160 mg, 4.00 mmol) was added. The reaction mixture was stirred for 2 hours at room temperature, filtered using florisil and the solvent removed under vacuum. ^{t}BuOH (0.5 mL), 2,2,2-trifluoro-1-phenylethanone (17.4 mg, 0.10 mmol), aqueous buffer solution (0.5 mL, 0.6M K_2CO_3 - 4x10^{-5}M EDTA tetrasodium salt), acetonitrile (0.15 mL, 3.00 mmol) and 30% aqueous H_2O_2 (0.36 mL, 3.00 mmol) were added consecutively. After the addition, stirring was continued for another 1 hour at room temperature. The crude product was purified using flash column chromatography (Pet. Ether) to afford the desired product.

Representative procedure for 3c-3d, 3f, 3j-3o

Substituted ketone (1.00 mmol) and *tert*-butylchlorodimethylsilane (196 mg, 1.30 mmol) were placed in an oven-dried round bottom flask sealed with a septum, under Ar atmosphere, and dissolved in dry THF (4.0 mL). The solution was cooled down to -78 ^{o}C and NaH (60% in oil, 160 mg, 4.00 mmol) was added. The reaction mixture was stirred for 30 minutes at room temperature, heated under reflux for 2 hours at 85 ^{o}C, filtered using florisil and the solvent removed under vacuum. ^{t}BuOH (0.5 mL), 2,2,2-trifluoro-1-phenylethanone (17.4 mg, 0.10 mmol), aqueous buffer solution (0.5 mL, 0.6M K_2CO_3 - 4x10^{-5}M EDTA tetrasodium salt), acetonitrile (0.15 mL, 3.00 mmol) and 30% aqueous H_2O_2 (0.36 mL, 3.00 mmol) were added consecutively. After the addition, stirring was continued for another 1 hour at room temperature. The crude product was

purified using flash column chromatography (Pet. Ether) to afford the desired product.

2-((*tert*-Butyldimethylsilyl)oxy)-1-phenylethanone (3a).[16] Colorless oil. 70% yield; ^{1}H NMR ($CDCl_3$) δ: 7.90 (2H, dt, J = 6.9 and 1.8 Hz, ArH), 7.58-7.35 (3H, m, ArH), 4.91 (2H, s, OCH_2), 0.92 (9H, s, 3 x CH_3), 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 197.2, 134.7, 133.2, 128.5, 127.7, 67.3, 25.7, 18.4, -5.4; MS (ESI) 251 ($M+H^+$, 67%).

2-((*tert*-Butyldimethylsilyl)oxy)-1-(p-tolyl)ethanone (3b). White solid. Mp 39-41 ^{o}C; 74% yield; ^{1}H NMR ($CDCl_3$) δ: 7.81 (2H, d, J = 8.1 Hz, ArH), 7.22 (2H, d, J = 8.1 Hz, ArH), 4.86 (2H, s, OCH_2), 2.37 (3H, s, CH_3), 0.92 (9H, s, 3 x CH_3), 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 196.9, 144.0, 132.2, 129.2, 127.9, 67.3, 25.7, 21.6, 18.4, -5.4; HRMS calcd for $C_{15}H_{24}NaO_2Si$ $[M+Na]^+$ 287.1438; found: 287.1443.

1-([1,1'-Biphenyl]-4-yl)-2-((*tert*-butyldimethylsilyl)oxy)ethanone (3c). White solid. Mp 89-91 ^{o}C; 64% yield; ^{1}H NMR ($CDCl_3$) δ: 8.01 (2H, d, J = 8.3 Hz, ArH), 7.75-7.56 (4H, m, ArH), 7.51-7.37 (3H, m, ArH), 4.96 (2H, s, OCH_2), 0.95 (9H, s, 3 x CH_3), 0.15 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 197.0, 145.9, 139.8, 133.5, 128.9, 128.4, 128.2, 127.2, 127.2, 67.5, 25.8, 18.5, -5.3; HRMS calcd for $C_{20}H_{26}NaO_2Si$ $[M+Na]^+$ 349.1594; found: 349.1603.

2-((*tert*-Butyldimethylsilyl)oxy)-1-(naphthalen-2-yl)ethanone (3d).[17] Colorless oil. 73% yield; ^{1}H NMR ($CDCl_3$) δ: 8.47 (1H, s, ArH), 8.12-7.79 (4H, m, ArH), 7.70-7.47 (2H, m, ArH), 5.05 (2H, s, OCH_2), 0.96 (9H, s, 3 x CH_3), 0.16 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 197.4, 135.6, 132.3, 132.0, 129.5, 129.4, 128.4, 127.7, 126.8, 123.6, 67.6, 25.8, 18.5, -5.3 ; MS (ESI) 301 ($M+H^+$, 82%).

2-((*tert*-Butyldimethylsilyl)oxy)-1-(4-fluorophenyl)ethanone (3e).[17] White solid. Mp 37-39 ^{o}C; 66% yield; ^{1}H NMR ($CDCl_3$) δ: 8.09-7.91 (2H, m, ArH), 7.19-7.05 (2H, m, ArH), 4.86 (2H, s, OCH_2), 0.92 (9H, s, 3 x CH_3), 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 196.2, 166.2 (d, J_{CF} = 255.2 Hz), 132.8 (d, J_{CF} = 9.6 Hz), 130.6 (d, J_{CF} = 3.9 Hz), 115.7 (d, J_{CF} = 22.1 Hz), 67.4, 25.6, 18.4, -5.4; ^{19}F NMR ($CDCl_3$) δ: -24.7; MS (ESI) 269 ($M+H^+$, 75%).

2-((tert-Butyldimethylsilyl)oxy)-1-(4-(trifluoromethyl)phenyl)ethanone (3f).[17] Yellow solid. Mp 40-42 ^{o}C; 44% yield; ^{1}H NMR ($CDCl_3$) δ: 8.04 (2H, d, J = 8.4 Hz, ArH), 7.72 (2H, d, J = 8.4 Hz, ArH), 4.90 (2H, s, OCH_2), 0.92 (9H, s, 3 x CH_3), 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 196.8, 137.5, 134.5 (q, J = 32.8 Hz), 128.4, 125.6 (q, J = 3.6 Hz), 123.5 (q, J = 272.7 Hz), 67.7, 25.7, 18.4, -5.4; ^{19}F NMR ($CDCl_3$) δ: 16.2; MS (ESI) 319 ($M+H^+$, 61%).

1-(4-Bromophenyl)-2-((*tert*-butyldimethylsilyl)oxy)ethanone (3g).[18] White viscous oil. 62% yield; ^{1}H NMR ($CDCl_3$) δ: 7.81 (2H, d, J = 8.4 Hz, ArH), 7.59 (2H, d, J = 8.4 Hz, ArH), 4.85 (2H, s, OCH_2), 0.91 (9H, s, 3 x CH_3), 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 196.7, 133.5, 131.9, 129.6, 128.1, 67.3, 25.7, 18.4, -5.4; MS (ESI) 330 ($M+H^+$, 55%).

1-(2-Bromophenyl)-2-((*tert*-butyldimethylsilyl)oxy)ethanone (3h). Yellow oil. 62% yield; ^{1}H NMR ($CDCl_3$) δ: 7.60-7.51 (1H, m, ArH), 7.44-7.35 (1H, m, ArH), 7.33-7.28 (2H, m, ArH), 4.69 (2H, s, OCH_2), 0.85 (9H, s, 3 x CH_3), 0.09 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 202.4, 139.3, 133.2, 131.5, 128.5, 127.1, 118.7, 68.8, 25.6, 18.2, -5.5; HRMS calcd for $C_{14}H_{21}BrNaO_2Si$ $[M+Na]^+$ 351.0386; found: 351.0390.

2-((*tert*-Butyldimethylsilyl)oxy)-1-(2-((*tert*-butyldimethylsilyl)oxy)phenyl)ethanone (3i). Yellow oil. 51% yield; 2.6 equiv. TBDMSCl were added; ^{1}H NMR ($CDCl_3$) δ: 7.81-7.66 (1H, m, ArH), 7.41-7.29 (1H, m, ArH), 7.07-6.80 (2H, m, ArH), 4.84 (2H, s, OCH_2), 1.00 (9H, s, 3 x CH_3), 0.92 (9H, s, 3 x CH_3), 0.31 (6H, s, 2 x CH_3) 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 199.9, 154.9, 133.1, 130.5, 128.3, 121.2, 119.6, 70.7, 29.7, 25.8, 22.7, 18.6, -3.8, -5.3; HRMS calcd for $C_{20}H_{36}NaO_3Si$ $[M+Na]^+$ 403.2095; found: 403.2101.

2-((*tert*-Butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)ethanone (3j).[19] Colorless oil. 89% yield; ^{1}H NMR ($CDCl_3$) δ: 7.90 (2H, d, J = 9.0 Hz, ArH), 6.90 (2H, d, J = 9.0 Hz, ArH), 4.85 (2H, s, OCH_2), 3.83 (3H, s, OCH_3), 0.91 (9H, s, 3 x CH_3), 0.10 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 195.9, 163.4, 130.1, 127.7, 113.6, 67.2, 55.3, 25.7, 18.4, -5.4; MS (ESI) 281 ($M+H^+$, 72%).

2-((*tert*-Butyldimethylsilyl)oxy)-1-(2,4-dimethoxyphenyl)ethanone (3k). Yellow viscous oil. 52% yield; ^{1}H NMR ($CDCl_3$) δ: 7.93 (1H, d, J = 8.7 Hz, ArH), 6.54 (1H, dd, J = 8.7 and 1.9 Hz, ArH), 6.43 (1H, d, J = 1.9 Hz, ArH), 4.81 (2H, s, OCH_2), 3.87 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 0.93 (9H, s, 3 x CH_3), 0.11 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ:

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197.0, 164.6, 160.9, 132.8, 118.4, 105.4, 98.0, 71.0, 55.5, 55.4, 25.9, 18.6, -5.3; HRMS calcd for $C_{16}H_{26}NaO_4Si$ $[M+Na]^+$ 333.1494; found: 333.1499.

2-((*tert*-Butyldimethylsilyl)oxy)-1-(furan-2-yl)ethanone (3l).[19] Colorless oil. 46% yield; ^{1}H NMR ($CDCl_3$) δ: 7.61-7.54 (1H, m, ArH), 7.36-7.29 (1H, m, ArH), 6.54-6.51 (1H, m, ArH), 4.73 (2H, s, OCH_2), 0.91 (9H, s, 3 x CH_3), 0.10 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 187.0, 150.8, 146.3, 118.0, 112.1, 67.1, 25.8, 18.5, -5.4; MS (ESI) 241 ($M+H^+$, 77%).

2-((tert-butyldimethylsilyl)oxy)-1-(thiophen-2-yl)ethanone (3m). Yellow oil. 63% yield; ^{1}H NMR ($CDCl_3$) δ: 7.90-7.85 (1H, m, ArH), 7.65-7.62 (1H, m, ArH), 7.14-7.09 (1H, m, ArH), 4.72 (2H, s, OCH_2), 0.93 (9H, s, 3 x CH_3), 0.12 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 191.1, 140.5, 133.8, 132.5, 127.8, 68.0, 25.8, 18.4, -5.4; HRMS calcd for $C_{12}H_{20}NaO_2SSi$ $[M+Na]^+$ 279.0845; found: 279.0851.

2-((*tert*-Butyldimethylsilyl)oxy)-1-phenylbutan-1-one (3n). Colorless oil. After the oxidation, silica (250 mg, 70-230 mesh) was added and the reaction mixture was left stirring for 1 hour at room temperature; 52% yield; ^{1}H NMR ($CDCl_3$) *δ*: 8.05 (2H, d, *J* = 6.9 Hz, ArH), 7.59-7.36 (3H, m, ArH), 4.67 (1H, dd, *J* = 7.4 and 5.6 Hz, OCH), 1.91-1.67 (2H, m, CH_2), 1.00 (3H, t, *J* = 7.4 Hz, CH_3), 0.87 (9H, s, 3 x CH_3), 0.04 (3H, s, CH_3), -0.03 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$) *δ*: 201.6, 135.0, 132.9, 129.2, 128.3, 79.3, 29.1, 25.7, 18.6, 10.2, -5.2; HRMS calcd for $C_{16}H_{26}NaO_2Si$ $[M+Na]^+$ 301.1594; found: 301.1599.

2-((*tert*-Butyldimethylsilyl)oxy)-2-methyl-1-phenylpropan-1-one (3o). Yellow oil. After the oxidation, silica (250 mg, 70-230 mesh) was added and the reaction mixture was left stirring for 1 hour at room temperature; 42% yield; ^{1}H NMR ($CDCl_3$) *δ*: 8.17-8.01 (2H, m, ArH), 7.56-7.28 (3H, m, ArH), 1.58 (6H, s, 2 x CH_3), 0.80 (9H, s, 3 x CH_3), 0.05 (3H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) *δ*: 203.9, 132.1, 130.2, 128.3, 127.7, 80.4, 29.0, 25.8, 18.1, -2.2; HRMS calcd for $C_{16}H_{26}NaO_2Si$ $[M+Na]^+$ 301.1594; found: 301.1601.

Representative procedure for 4a-4b, 4e, 4g-4i

Substituted ketone (1.00 mmol) and *tert*-butylchlorodimethylsilane (196 mg, 1.30 mmol) were placed in an oven-dried round bottom flask sealed with a septum, under Ar atmosphere, and dissolved in dry THF (4.0 mL). The solution was cooled down to -78 °C and NaH (60% in oil, 160 mg, 4.00 mmol) was added. The reaction mixture was stirred for 2 hours at room temperature, filtered using florisil and the solvent removed under vacuum. ^{t}BuOH (0.5 mL), 2,2,2-trifluoro-1-phenylethanone (17.4 mg, 0.10 mmol), aqueous buffer solution (0.5 mL, 0.6M K_2CO_3 - 4x10^{-5}M EDTA tetrasodium salt), acetonitrile (0.15 mL, 3.00 mmol) and 30% aqueous H_2O_2 (0.36 mL, 3.00 mmol) were added consecutively. After the addition, stirring was continued for another 1 hour at room temperature. Subsequently, *p*-toluenesulfonic acid (350 mg, 2.00 mmol) was added and the reaction mixture was left stirring for 1 hour at room temperature. The crude product was purified using flash column chromatography (10% EtOAc in Pet. Ether) to afford the desired product.

Representative procedure for 4c-4d, 4f, 4j-4o

Substituted ketone (1.00 mmol) and *tert*-butylchlorodimethylsilane (196 mg, 1.30 mmol) were placed in an oven-dried round bottom flask sealed with a septum, under Ar atmosphere, and dissolved in dry THF (4.0 mL). The solution was cooled down to -78 °C and NaH (60% in oil, 160 mg, 4.00 mmol) was added. The reaction mixture was stirred for 30 minutes at room temperature, heated under reflux for 2 hours at 85 °C, filtered using florisil and the solvent removed under vacuum. ^{t}BuOH (0.5 mL), 2,2,2-trifluoro-1-phenylethanone (17.4 mg, 0.10 mmol), aqueous buffer solution (0.5 mL, 0.6M K_2CO_3 - 4x10^{-5}M EDTA tetrasodium salt), acetonitrile (0.15 mL, 3.00 mmol) and 30% aqueous H_2O_2 (0.36 mL, 3.00 mmol) were added consecutively. After the addition, stirring was continued for 1 hour at room temperature. Subsequently, *p*-toluenesulfonic acid (350 mg, 2.00 mmol) was added and the reaction mixture was left stirring for 1 hour at room temperature. The crude product was purified using flash column chromatography (10% EtOAc in Pet. Ether) to afford the desired product.

2-Hydroxy-1-phenylethanone (4a).[20] White solid. Mp 86-89 °C, 76% yield; ^{1}H NMR ($CDCl_3$) *δ*: 7.92 (2H, d, *J* = 7.1 Hz, ArH), 7.64 (1H, t, *J* = 7.1 Hz, ArH), 7.51 (2H, t, *J* = 7.1 Hz, ArH), 4.88 (2H, s, OCH_2), 3.38 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) *δ*: 198.3, 134.1, 133.2, 128.8, 127.5, 65.3; MS (ESI) 137 ($M+H^+$, 81%).

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2-Hydroxy-1-(p-tolyl)ethanone (4b).[21] White solid. Mp 72-74 °C, 61% yield; ^{1}H NMR ($CDCl_3$) δ: 7.78 (2H, d, J = 8.2 Hz, ArH), 7.26 (2H, d, J = 8.2 Hz, ArH), 4.82 (2H, s, OCH_2), 3.67 (1H, br s, OH), 2.39 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ: 197.8, 145.2, 130.7, 129.5, 127.6, 65.2, 21.7; MS (ESI) 151 ($M+H^+$, 69%).

1-([1,1'-Biphenyl]-4-yl)-2-hydroxyethanone (4c).[22] White solid. Mp 125-127 °C, 71% yield; ^{1}H NMR ($CDCl_3$) δ: 7.97 (2H, d, J = 8.4 Hz, ArH), 7.69 (2H, d, J = 8.4 Hz, ArH), 7.61 (2H, dd, J = 8.0 and 1.5 Hz, ArH), 7.52-7.38 (3H, m, ArH), 4.89 (2H, s, OCH_2), 3.63 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ: 197.8, 146.8, 139.4, 131.9, 128.9, 128.4, 128.2, 127.4, 127.2, 65.2; MS (ESI) 213 ($M+H^+$, 72%).

2-Hydroxy-1-(naphthalen-2-yl)ethanone (4d).[23] White solid. Mp 108-110 °C, 64% yield; ^{1}H NMR ($CDCl_3$) δ: 8.28 (1H, s, ArH), 7.92-7.65 (4H, m, ArH), 7.59-7.38 (2H, m, ArH), 4.96 (2H, s, OCH_2); ^{13}C NMR ($CDCl_3$) δ: 196.3, 135.8, 132.0, 130.2, 129.4, 129.4, 128.8, 128.6, 127.6, 126.8, 122.7, 65.3; MS (ESI) 187 ($M+H^+$, 57%).

1-(4-Fluorophenyl)-2-hydroxyethanone (4e).[21] White solid. Mp 109-111 °C, 57% yield; ^{1}H NMR ($CDCl_3$) δ: 8.03-7.86 (2H, m, ArH), 7.16 (2H, t, J = 8.6 Hz, ArH), 4.84 (2H, s, OCH_2), 3.65 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ: 196.8, 166.1 (d, J_{CF} = 254.8 Hz), 132.7 (d, J_{CF} = 9.5 Hz), 129.7 (d, J_{CF} = 3.7 Hz), 115.6 (d, J_{CF} = 22.0 Hz), 65.2; MS (ESI) 155 ($M+H^+$, 67%).

2-Hydroxy-1-(4-(trifluoromethyl)phenyl)ethanone (4f).[24] Yellow solid. Mp 110-112 °C, 42% yield; ^{1}H NMR ($CDCl_3$:CD_3OD 4:1) δ: 7.99 (2H, d, J = 8.2 Hz, ArH), 7.72 (2H, d, J = 8.2 Hz, ArH), 4.87 (2H, s, OCH_2), 3.35 (1H, br s, OH); ^{13}C NMR ($CDCl_3$:CD_3OD 4:1) δ: 197.7, 136.0, 128.0, 127.6 (q, J = 29.9 Hz), 125.9 (q, J = 3.7 Hz), 123.0 (q, J = 248.2 Hz), 65.6; ^{19}F NMR ($CDCl_3$) δ: 15.6; MS (ESI) 205 ($M+H^+$, 71%).

1-(4-Bromophenyl)-2-hydroxyethanone (4g).[25] Colorless solid. Mp 103-104 °C, 65% yield; ^{1}H NMR (DMSO) δ: 7.81 (2H, d, J = 8.5 Hz, ArH), 7.68 (2H, d, J = 8.5 Hz, ArH), 4.74 (2H, s, OCH_2), 3.36 (1H, br s, OH); ^{13}C NMR (DMSO) δ: 198.5, 133.5, 131.8, 129.6, 127.4, 65.3; ^{19}F NMR ($CDCl_3$) δ: -23.1; MS (ESI) 216 ($M+H^+$, 48%).

1-(2-Bromophenyl)-2-hydroxyethanone (4h).[21] White low melting solid. 57% yield; ^{1}H NMR ($CDCl_3$) δ: 7.69-7.56 (1H, m, ArH), 7.55-7.43 (1H, m, ArH), 7.42-7.27 (2H, m, ArH), 4.75 (2H, s, OCH_2), 3.29 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ: 201.4, 136.6, 134.2, 132.8, 129.2, 127.4, 119.6, 67.7; MS (ESI) 216 ($M+H^+$, 45%).

1-(2-((*tert*-Butyldimethylsilyl)oxy)phenyl)-2-hydroxyethanone (4i). Yellow oil. 2.6 equiv. of TBDMSCl were added; 50% yield; ^{1}H NMR ($CDCl_3$) δ: 7.92 (1H, dd, J = 7.9 and 1.9 Hz, ArH), 7.41 (1H, ddd, J = 8.3, 7.9 and 1.9 Hz, ArH), 7.10-6.83 (2H, m, ArH), 4.81 (1H, d, J = 16.8 Hz, OC*H*H), 4.68 (1H, d, J = 16.8 Hz, OC*H*H), 0.99 (9H, s, 3 x CH_3), 0.34 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 199.5, 156.4, 134.6, 130.8, 125.4, 121.2, 119.8, 69.5, 25.9, 18.7, -3.4; HRMS calcd for $C_{14}H_{22}NaO_3Si$ $[M+Na]^+$ 289.1230; found: 289.1236.

2-Hydroxy-1-(4-methoxyphenyl)ethanone (4j).[22] Pale yellow solid. Mp 104-107 °C, 82% yield; ^{1}H NMR ($CDCl_3$) δ: 7.83 (2H, d, J = 9.0 Hz, ArH), 6.90 (2H, d, J = 9.0 Hz, ArH), 4.77 (2H, s, OCH_2), 3.82 (3H, s, OCH_3); ^{13}C NMR ($CDCl_3$) δ: 196.6, 164.1, 129.8, 126.1, 113.9, 64.8, 55.4; MS (ESI) 167 ($M+H^+$, 77%).

1-(2,4-Dimethoxyphenyl)-2-hydroxyethanone (4k). Yellow solid. Mp 127-129 °C, 84% yield; ^{1}H NMR ($CDCl_3$) δ: 7.99 (1H, d, J = 8.8 Hz, ArH), 6.51 (1H, d, J = 8.8 Hz, ArH), 6.39 (1H, s, ArH), 4.65 (2H, s, OCH_2), 3.85 (3H, s, OCH_3), 3.82 (3H, s, OCH_3); ^{13}C NMR ($CDCl_3$) δ:197.1, 165.7, 162.1, 132.8, 116.0, 105.9, 97.7, 69.2, 55.5, 55.3; HRMS calcd for $C_{10}H_{12}NaO_4$ $[M+Na]^+$ 219.0628; found: 219.0637.

1-(Furan-2-yl)-2-hydroxyethanone (4l).[26] Yellow solid. Mp 83-85 °C, 67% yield; ^{1}H NMR ($CDCl_3$) δ: 7.65-7.57 (1H, m, ArH), 7.29-7.25 (1H, m, ArH), 6.60-6.54 (1H, m, ArH), 4.71 (2H, s, OCH_2), 3.38 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ:187.6, 149.9, 147.0, 117.9, 112.5, 65.0; MS (ESI) 127 ($M+H^+$, 65%).

2-Hydroxy-1-(thiophen-2-yl)ethanone (4m).[27] Brown oil. 78% yield; ^{1}H NMR ($CDCl_3$:CD_3OD 4:1) δ: 7.76-7.67 (2H, m, ArH), 7.14-7.06 (1H, m, ArH), 4.74 (2H, s, OCH_2); ^{13}C NMR ($CDCl_3$:CD_3OD 4:1) δ: 191.7, 139.6, 134.8, 132.4, 128.7, 65.6; MS (ESI) 143 ($M+H^+$, 59%).

2-Hydroxy-1-phenylbutan-1-one (4n).[28] Colorless oil. 50% yield; After the oxidation silica (250 mg, 70-230 mesh) was added and the reaction mixture was left stirring for 1 hour at room temperature; ^{1}H NMR ($CDCl_3$) δ: 7.90 (2H, d, J = 7.1 Hz, ArH), 7.59 (1H, d, J = 7.1

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Hz, ArH), 7.49 (2H, d, *J* = 7.1 Hz, ArH), 5.05 (1H, dd, *J*= 6.8 and 3.9 Hz, OCH), 3.79 (1H, br s, OH), 2.06-1.81 (1H, m, C*H*H), 1.70-1.49 (1H, m, C*H*H), 0.92 (3H, t, *J* = 7.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ: 202.0, 133.8, 133.7, 128.7, 128.4, 73.8, 28.7, 8.7; MS (ESI) 165 ($M+H^+$, 76%).

2-Hydroxy-2-methyl-1-phenylpropan-1-one (4o).[29] Colorless oil. 50% yield; After the oxidation silica (250 mg, 70-230 mesh) was added and the reaction mixture was left stirring for 1 hour at room temperature; ^{1}H NMR ($CDCl_3$) δ: 8.17-7.92 (2H, m, ArH), 7.63-7.35 (3H, m, ArH), 4.08 (1H, br s, OH), 1.62 (6H, s, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ: 204.6, 133.5, 133.0, 130.1, 128.4, 60.4, 28.3; MS (ESI) 165 ($M+H^+$, 81%).

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