Selective catalytic oxidations by palladium and manganese

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Chapter 6

Manganese catalysed selective oxidation of aliphatic C-H groups and secondary alcohols to ketones with H_2O_2

An efficient and simple method for selective oxidation of secondary alcohols and oxidation of alkanes to ketones is reported. An *in situ* prepared catalyst is employed based on manganese(II) salts, pyridine-2-carboxylic acid and butanedione, which provides good to excellent conversions and yields with high turnover numbers (up to 10,000) with H_2O_2 as oxidant at ambient temperatures. In substrates bearing multiple alcohol groups, secondary alcohols are converted to ketones selectively and in general, benzyl C-H oxidation proceeds in preference to aliphatic C-H oxidation.

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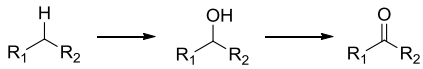
6.1 Introduction

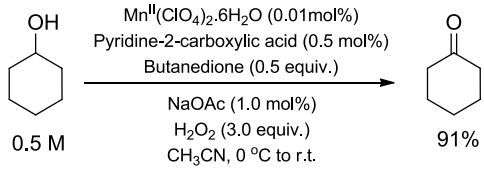
Selective oxidation of alcohols to ketones together with direct conversion of C-H bonds to alcohols and ketones are crucial, yet also highly challenging, processes in synthetic organic chemistry, pharmaceuticals and fine and bulk chemical synthesis (Scheme 1).[1] Traditional methods for achieving such transformations, although in general highly effective, are becoming increasingly undesirable due to increasing demands to reduce the environmental impact, and increase the mass and energy efficiency of processes. Hence the drive to develop benign methods compels us to explore the use of methods employing 1st row transition metals and clean (mass efficient) oxidants.[2] Hydrogen peroxide is a highly favourable oxidant in this regard, second only to oxygen, [3] with water as the sole by-product.[4]



Scheme 1. Oxidation of alcohols and alkanes to ketone.

Several highly effective catalytic methods for the oxidation of alcohols with H_2O_2 have been reported, not least the system of Noyori and coworkers based on tungsten oxide/PTC (where PTC is phase transfer catalyst),[5] Beller and coworkers employing iron catalysts[6] and catalysts based on rhenium, molybdenum and tungsten oxides.[7] However, the use of high temperatures and/or catalyst loadings and potentially toxic PTCs drives the search for alternative methods. Manganese based catalysts are attractive in C-H and alcohol oxidations due to their generally low toxicity, and the often high reaction rates and turnover numbers that can be achieved even at room temperature. Manganese catalysts, based on salen ligands[8] have been employed in oxidation of alcohols with iodosobenzene as oxidant[8a] and catalysed the enantioselective kinetic resolution of secondary alcohols.[8b] Manganese catalysts based on polypyridyl and azacyclononane based ligands,[9, 10,11] as well as porphyrins,[12] have been applied also.[13]

Recently, our group reported an efficient method for the epoxidation and *cis*-dihydroxylation of alkenes catalysed by an *in situ* prepared manganese(II) catalyst which is near stoichiometric in H_2O_2.[14,15,16] This catalytic system consists of a Mn^{II} salt, pyridine-2-carboxylic acid and sub-stoichiometric amounts of ketone and showed good to excellent selectivity, high-turnover numbers (up to 300,000) and high-turnover frequencies (up to 30 s^{-1}) at room temperature, with a wide solvent scope.[16]



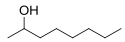
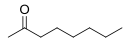
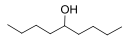
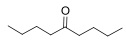
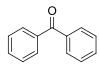
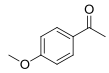
Scheme 2. Oxidation of cyclohexanol to cyclohexanone.

Here, we report the application of this catalytic system to the oxidation of alcohols and alkanes under ambient conditions and low catalyst loadings (Scheme 2). For substrates that do not bear alkene moieties, we show that high-yields and selectivity can be achieved in the oxidation of secondary alcohols with good to excellent selectivity of secondary over primary alcohol oxidation. Furthermore, at higher catalyst loadings (0.1 mol%) selective C-H oxidation at benzylic positions can be achieved as well as C-H oxidation of alkanes.

6.2 Results and discussion

In the present study, initially the oxidation of alcohols was investigated using conditions optimised earlier for alkene oxidation (scheme 2),[16] *i.e.*, substrate (0.5 M), 0.01 mol% manganese perchlorate, 1.0 mol% of sodium acetate and 0.5 mol% of pyridine-2-carboxylic acid as catalyst and 0.5 equiv. of butanedione in acetonitrile with 1.5 equiv. of H_2O_2. With these conditions cyclohexanol was oxidised to cyclohexanone in 73% yield, albeit with incomplete conversion (Table 1, entry 1). With 3.0 equiv. of H_2O_2, full conversion and 91% yield of cyclohexanone was obtained. Importantly, the reactions proceeded without formation of significant amounts of side products (*e.g.*, Baeyer-Villiger oxidation products, double oxidation).

Table 1. Oxidation of secondary alcohols

Entry[a]	Substrate	Conv. [c](%)	Product	Isolated Yield (%)[b]
1		full (73%)		91[c] (73[g])
2[d]		full		78
3[d]		97		88
4[e]		80		72
5		71		68[c]
6		full		95
7		97		90
8		92		77
9		90		80
10		88		75
11[f]		70		64
12		78		76

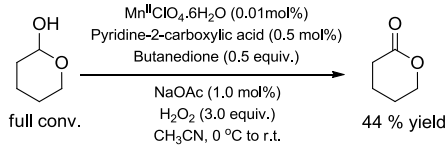
[a] Reaction conditions: 0.5 M substrate (1 mmol), 50 µM $Mn(ClO_4)_2.6H_2O$, 2.5 mM pyridine-2-carboxylic acid, 5.0 mM NaOAc, 0.25 M butanedione and 1.5 M H_2O_2 in acetonitrile. [b] Isolated yield, unless stated otherwise. [c] Conversion and yield, based on substrate, determined by ^1H NMR spectroscopy. [d] 0.4 M substrate (0.8 mmol). [e] In acetone. [f] 0.25 M substrate (0.5 mmol). [g] 0.75 M H_2O_2 (1.5 equiv. w.r.t. substrate) was used.

These conditions were applied to a series of secondary alcohols (Table 1). Cyclic and acyclic aliphatic alcohols were converted cleanly to their corresponding ketone products (Table 1, entries 2-3). For 5-nonanol the conversion achieved was, however, lower which

was ascribed to its lower solubility in acetonitrile compared with the other alcohols examined. The relatively wide solvent scope of the present catalyst system demonstrated previously,[16] allows for the low solubility of 5-nonanol to be overcome by using acetone in place of acetonitrile and provided 5-nonanone in high yield (Table 1, entry 4).

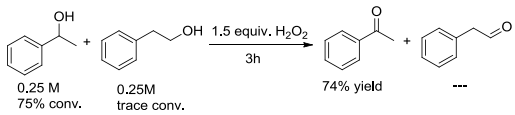
The oxidation of sterically encumbered alcohols was investigated also. 2,4-Dimethyl-pentan-3-ol was converted (71%) with 68% yield to 2,4-dimethyl-pentan-3-one (Table 1, entry 5). Similarly the natural product, isoborneol, was converted to camphor in excellent yield (Table 1, entry 6). The reactions in general were found to be scalable, without significant difference in conversion or yield (see section 6.4.2 for details). Notably, at larger scale complete conversion was achieved by extraction of the product and unreacted starting material from the reaction mixture and subjecting the mixture to the same reaction conditions a second time. In the case of isoborneol at 4 g scale, full conversion and an isolated yield of 87% was achieved.

A series of secondary benzylic alcohols were oxidised to their corresponding ketones under these reaction conditions, in good yields (Table 1). Even bromo-phenyl or oxidatively sensitive methoxy-phenyl bearing substrates proceeded in moderate to good conversion. In general, lower conversion can be overcome by decreasing the initial concentration of the substrate,[16] *e.g.*, as with 1-(4'-methoxyphenyl)ethanol (Table 1, entry 11).



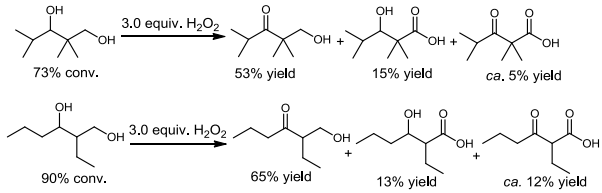
Scheme 3. Oxidation of tetrahydro-*2H*-pyran-2-ol to valero-lactone (yield determined by ^{1}H NMR spectroscopy).

The oxidation of hemiacetals was explored through tetrahydro-*2H*-pyran-2-ol, which can be viewed as a cyclic alcohol with an ether functional group. Full conversion and moderate yield (44%) of valero-lactone was achieved. The moderate yield of the desired product was due primarily to the ring opening to give corresponding carboxylic acid *in situ* (Scheme 3).



Scheme 4. Competition experiment between 1-phenyl- and 2-phenyl-ethanol (for conditions see table 1).

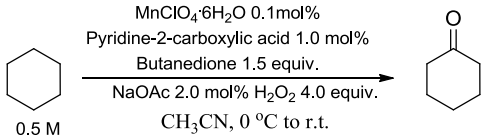
The selective oxidation of secondary aliphatic and aromatic alcohols in the presence of primary alcohols was explored through competition experiments (Schemes 4 and 5). Oxidation of an equimolar mixture of 1- and 2-phenyl-ethanol provided 75% conversion of 1-phenyl-ethanol to acetophenone with only trace conversion of 2-phenyl-ethanol. For substrates bearing both secondary and primary aliphatic alcohol moieties, oxidation of the secondary alcohol proceeded preferentially also (Scheme 5).



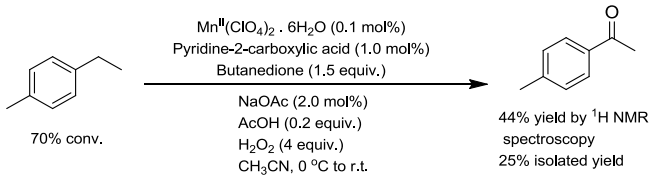
Scheme 5. Chemoselective oxidation of secondary over primary alcohol moieties (for conditions see Table 1).

In addition to the oxidation of secondary alcohols to ketones, the direct oxidation of methylene units to ketones with the present catalytic system was explored.

The direct oxidation of aliphatic compounds such as cyclohexane and cyclooctane proceeded with good conversion and selectivity to the corresponding mono-ketone product. (Table 2, entries 1 and 2). In contrast to alcohol oxidation, however, higher catalyst loadings (0.1 mol%) and up to 4.0 equiv. of H_2O_2 were required (Scheme 6). In addition to the ketone product, the corresponding alcohol, together with a mixture of diketones were observed in amounts that were dependent on the exact reaction conditions.



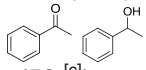
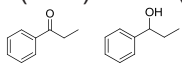
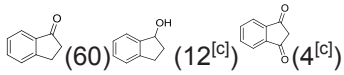
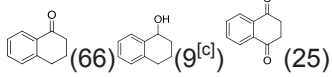
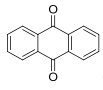
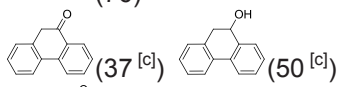
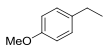
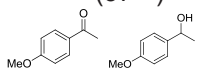
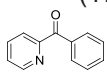
Scheme 6. Oxidation of cyclohexane to cyclohexanone under optimised reaction conditions.



Scheme 7. Oxidation of 1-ethyl-4-methyl-benzene to 4-methyl-acetophenone under optimised reaction conditions.

At catalyst loadings of 0.1 mol%, the oxidation at the benzylic positions for a wide range of alkylated aromatics could be achieved at room temperature (Table 2, entries 3-12). For both ethylbenzene and propylbenzene the corresponding aromatic ketone product was obtained with good selectivity (Table 2, entries 3 and 4). In contrast, oxidation of toluene proceeded with lower conversion (35-40%) and low yield of a mixture of benzyl alcohol (8-10%), benzaldehyde (8-10%) and benzoic acid and a low mass balance due to the formation of an insoluble polymeric material.

Table 2. Oxidation at alkyl and benzylic positions [a]

Entry	Substrate	Conv. (%)	Product/s (isolated yield)[b] (%)
1		63	 (34 [c])
2		60	 (41[c])
3		80	 (50 [c]) (13 [c])
4		50	 (34) (3 [c])
5		full	 (60) (12[c]) (4[c])
6		full	 (66) (9[c]) (25)
7		full	 (99)
8[d]		full	 (76)
9		90	 (37 [c]) (50 [c])
10		75	 (28) (17 [c])
11		25	 (17)
12		80	 (73)
13		83	 (34)

[a] reaction conditions : 0.5 M substrate (1 mmol),, 0.5 mM $Mn(ClO_4)_2 \cdot 6H_2O$, 5 mM pyridine-2-carboxylic acid, 10 mM NaOAc, 0.75 M butanedione and 2.0 M H_2O_2 in acetonitrile. [b] isolated yield, based on substrate, unless stated otherwise. [c] ^{1}H NMR yield, based on substrate, see Section 6.4 for details. [d] 0.25 M substrate (0.5 mmol).

1-Ethyl-4-methyl-benzene was found to undergo good conversion (70%) with moderate yield of 4-methyl-acetophenone as the main product, albeit with significant amounts of a white polymeric by-product also (Scheme 7). In general, for cyclic systems full conversion was achieved with moderate to excellent isolated yields of the corresponding

ketone (Table 2, entries 5-9). Surprisingly, in many cases substantial amounts of the intermediate alcohol product was obtained, which would suggest that the rate of C-H oxidation, although slower is nevertheless comparable with the rate of alcohol oxidation. The doubly oxidised product, anthracene-9,10-dione, was obtained from 9,10-dihydroanthracene in excellent yield, (Table 2, entry 7). In contrast, the mono-oxidised alcohol and ketone product was obtained as the primary product in the oxidation of 9,10-dihydrophenanthrene (Table 2, entry 9).

The selective oxidation of 1,2,3,4-tetrahydro-1-naphthol to the corresponding ketone, without further oxidation at the other benzylic position, confirms that benzylic positions are marginally less susceptible to oxidation than secondary aryl alcohols (Table 1, entry 10). Nevertheless, where there is sufficient oxidant available further oxidation to the diketone products is observed.

p-Methoxy- and *o*-nitro-phenylethanes could be converted to the corresponding aryl-methyl-ketones as well (Table 2, entry 10 and 11). The lower yield of 1-(4-methoxy)phenyl-ethanone reflects the lower conversion observed for the corresponding alcohol 1-(4-methoxyphenyl)ethanol also (Table 1, entry 11). Similarly, lower conversion was observed for *o*-nitro-phenylethane (Table 2, entry 11).

Surprisingly, oxidation of 2-benzyl-pyridine to phenyl(pyridin-2-yl)methanone proceeded with good conversion and selectivity without formation of the *N*-oxide product (Table 2, entry 12).

The selectivity towards methylene over methyl C-H groups was investigated using 1-methylpyrrolidin-2-one. Good conversion (83%) to and moderate isolated yield (34%) of 1-methylpyrrolidine-2,5-dione was achieved (Table 2, entry 13), however the selectivity was poor with several side products observed also.

With regard to the mechanism for conversion of aliphatic C-H groups to alcohols and subsequently to ketone, it is likely that a similar active species is responsible as in the oxidation of alkenes reportedly previously.[15,16] The involvement of active oxygen species such as O_2 and hydroxyl radicals should be considered also, however. The direct involvement of atmospheric O_2 can be excluded based on mass balance; at the conversions observed, it would not be possible to obtain the oxygen required from the dissolved oxygen present. The disproportionation of the H_2O_2 present could provide considerably more oxygen; again however this can be discounted due to the relatively low level of catalase type activity observed. Hence, the presence of both alcohol and ketone products can be ascribed to sequential oxidation rather than for example a Russell's mechanism[17] between alkyl radicals and oxygen.

6.3 Conclusions

In this contribution we demonstrate that selective oxidation of secondary alcohols can be achieved at room temperature with an *in situ* prepared manganese catalyst with high turnover numbers (up to 10,000) and with near stoichiometric H_2O_2. The reaction is scalable from 100 mg to 4 g and in many examples highly selective. Although we have demonstrated previously that this catalyst system is tolerant of several common protecting groups,[16] the selectivity of the catalyst towards secondary alcohols over primary alcohols is demonstrated also, which reduces the need for the introduction

prior to oxidation and subsequent removal of protecting groups and is complimentary to catalytic methods for selective primary alcohol oxidation based on copper and Tempo catalysts.[3c,6a] For benzylic alcohol oxidation and in particular for cyclic systems, selective oxidation to the mono-ketone product can be achieved under mild conditions and with good efficiency in terms of the oxidant H_2O_2. The activity of the catalytic system towards alkane oxidation shows an expected preference towards benzylic C-H, but nevertheless the relatively high yield and good selectivity observed in the oxidation of cyclic alkanes such as cyclooctane highlight the absence of other oxidation processes, not least Baeyer-Villiger oxidation.

6.4 Experimental section

6.4.1 General Procedures and methods

Chromatography: Merck silica gel type 9385 230-400 mesh, TLC: Merck silica gel 60, 0.25 mm, with visualisation by UV, cerium/molybdenum or potassium permanganate staining. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian AMX400 (400 and 100.59 MHz, respectively) in CD_3CN or $CDCl_3$. Chemical shift values are reported in ppm with the resonance solvent signal as the internal reference ($CHCl_3$: 7.26 for ^{1}H, 77.0 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q =quartet, br = broad, m = multiplet), coupling constants (Hz), and relative integration. ^{13}C spectra were assigned based on APT ^{13}C-NMR spectroscopy.

General procedure for oxidation of secondary alcohols The alcohol (1 mmol) was added to a stock solution containing $Mn(ClO_4)_2.6H_2O$ (0.01 mol %, 0.0361 mg) and pyridine-2-carboxylic acid (0.5 mol %, 0.123 mg) in acetonitrile to give a final substrate concentration of 0.5 M. NaOAc (aq. 0.6 M, 1 mol %, 16.7 µL) and butanedione (0.5 equiv. 43.5 µL) were added to give a final volume of 2 mL. The solution was stirred with cooling in an ice/water bath before addition of H_2O_2 (50 wt. %, 3.0 equiv., 170 µL). After 12-16 h stirring at room temperature, brine (10 mL) was added and the reaction was extracted with dichloromethane. The combined organic layers were reduced *in vacuo*. The products were isolated by flash column chromatography on silica gel 230-400. Products were characterised by NMR spectroscopy (see the Section 6.4.3).

General procedure for oxidation at alkyl and benzylic moieties C-H The alkane (1 mmol) was added to a stock solution of $Mn(ClO_4)_2{\cdot}6H_2O$ (0.1 mol %, 0.361 mg) and pyridine-2-carboxylic acid (1.0 mol %, 0.246 mg) in acetonitrile to give a final substrate concentration of 0.5 M. NaOAc (aq. 0.6 M, 2 mol %, 33.4 µL) and butanedione (1.5 equiv. 130.5 µL) were added to give a final volume of 2 mL. The solution was stirred with cooling in an ice/water bath before addition of H_2O_2 (50 wt. %, 4.0 equiv., 227 µL). After 12-16 hours, brine (10 mL) was added and the reaction was extracted with dichloromethane (3 by 10 mL). The combined organic layers were concentrated *in vacuo*. The products were isolated by flash column chromatography on silica gel 230-400. Products were characterised by NMR spectroscopy (see the Section 6.4.3). In certain cases a solid material was obtained also, which based on FTIR, Raman and NMR analysis appeared to be a polymer.

Caution. The drying or concentration of solutions that potentially contain H_2O_2 should be avoided. Prior to drying or concentrating, the presence of H_2O_2 should be tested for

using peroxide test strips followed by neutralisation on $NaHSO_3$ or another suitable reducing agent. When working with H_2O_2, suitable protective safeguards should be in place at all times.

Caution. Butanedione has been linked with lung disease upon exposure to vapours. It should be handled in a properly ventilated fumehood and exposure to vapours should be avoided.

Note. All reagents are of commercial grade and used as received unless stated otherwise.

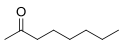
6.4.2 Examples of reactions at > 1g scale

Isoborneol (4 g)  was added to a solution of $Mn^{II}(ClO_4)_2.6H_2O$ (0.01 mol %), pyridine-2-carboxylic acid (0.5 mol %), NaOAc (aq. 0.6 M, 1 mol %) and butanedione (0.5 equiv.) in acetonitrile to give a final substrate concentration of 0.5 M. The solution was cooled in an ice/water bath before addition of H_2O_2 (50 wt. %, 3.0 equiv.) and the temperature was allowed to rise overnight with stirring. Brine was added to the reaction mixture and the product and any unreacted isoborneol extracted with dichloromethane (3 x 10 mL). The combined organic layers were concentrated *in vacuo*, with residual dichloromethane stripped *in vacuo* by addition of acetonitrile. Isoborneol (63%) was converted with full selectivity towards camphor  . The crude mixture was subjected to the same reaction conditions resulting in full conversion of the isoborneol. Camphor was isolated in 87 % yield (3.45 g) after purification by flash column chromatography on silica gel (pentane/ether = 9/1, Rf = 0.3). The product was characterised by ^{1}H NMR spectroscopy (*vide infra*).

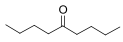
6.4.3 Characterisation of isolated products

 **Cyclooctanone** (Table 1, entry 2) Isolated by flash column chromatography on silica gel (dichloromethane/ether = 9:1, Rf = 0.5).The title compound was obtained as a colourless oil (78% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (m, 4H), 1.94 (m, 4H), 1.62 (m, 4H), 1.43(m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 218.2, 41.9, 27.1, 25.6, 24.7.

 **2-Octanone** (Table 1, entry 3) Isolated by flash column chromatography on silica gel (pentane/ether = 9:1, Rf = 0.5). The title compound was obtained as a colourless oil (88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (t, *J* = 7.4 Hz, 2H), 2.12 (s, 3H), 1.56 (m, 2H), 1.27(br, 6H, CH_2), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.3, 43.8, 31.6, 29.8, 28.8, 23.8, 22.4, 14.0.

 **Nonan-5-one** (Table 1, entry 4) Isolated by flash column chromatography on silica gel (pentane/ether = 95/5, Rf = 0.5).The title compound was obtained as a colourless oil (72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40-2.36 (t, *J* = 7.4 Hz, 4H), 1.58-1.50 (q, *J* = 7.4 Hz, 4H), 1.35-1.25 (sextuplet, *J* = 7.4 Hz, 4H), 0.91-0.88 (t, *J* = 7.3 Hz, 6H); 13C NMR (101 MHz, $CDCl_3$) δ 211.6, 42.5, 26.0, 22.3, 13.8.

 **Camphor** (Table 1, entry 6) Isolated by flash column chromatography on silica gel (pentane/ether = 9/1, Rf = 0.3).The title compound was obtained as a white solid (95% yield).

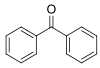
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36-2.30 (m, 1H), 2.08 (t, *J* = 4.5 Hz, 1H), 1.96-1.90 (m, 1H), 1.83 (d, *J* = 18.2 Hz, 1H), 1.70-1.63 (m, 1H), 1.42-1.28 (m, 2H), 0.94(s, 3H), 0.89 (s, 3H), 0.81(s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 219.6, 57.7, 46.8, 43.2, 43.0, 29.9, 27.0, 19.8, 19.1, 9.2.

 **Acetophenone** (Table 1, entry 7) Isolated by flash column chromatography on silica gel (pentane/ether = 9/1, Rf = 0.3).The title compound was obtained as a colourless oil (90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.03 (m, 2H), 7.57-7.53 (m, 1H), 7.46-7.43 (m, 2H), 2.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 137.1, 133.1, 128.5, 128.3, 26.6.

 **Propiophenone** (Table 1, entry 8) Isolated by flash column chromatography on silica gel (pentane/ethyl acetate = 95/5, Rf = 0.5).The title compound was obtained as a colourless oil (77% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ7.98-7.96 (m, 2H), 7.57-7.53 (m, 1H), 7.48-7.44 (m, 2H), 3.04-2.98 (q, *J* = 7.2 Hz , 2H), 1.25-1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 136.9, 132.8, 128.5, 127.9, 31.8, 8.2.

 **Benzophenone** (Table 1, entry 9) Isolated by flash column chromatography on silica gel (pentane/ethyl acetate = 95/5, Rf = 0.5).The title compound was obtained as a colourless oil (80% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.80 (m, 4H), 7.61-7.57 (m, 2H), 7.50-7.47 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 137.6, 132.4, 130.0, 128.3.

 **3,4-dihydronaphthalen-1(2H)-one** (Table 1, entry 10) Isolated by flash column chromatography on silica gel (pentane/ethyl acetate = 95/5, Rf = 0.5).The title compound was obtained as a yellowish oil (75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.02 (m, 1H), 7.49-7.44 (m, 1H), 7.33-7.24 (m, 2H), 2.99-2.95 (t, *J* = 6.1 Hz, 2H), 2.68-2.64 (dd, *J* = 6.2 Hz, *J* = 6.8 Hz, 2H), 2.18-2.10 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 144.4, 133.4, 132.6, 128.7, 127.2, 126.6, 39.2, 29.7, 23.3.

1-(4-Bromophenyl)ethanone (Table 1, entry 12) (missing) Isolated by flash column chromatography on silica gel (pentane/ether = 9/1, Rf = 0.5).The title compound was obtained as white solid (76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.77 (d, *J* = 8.6 Hz, 2H), 7.58-7.56 (d, *J* = 8.6 Hz, 2H), 2.55 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ197.0, 135.8, 131.8, 129.8, 128.2, 26.5.

2,3-dihydro-1H-inden-1-one (Table 2, entry 5) Isolated by flash column chromatography on silica gel (pentane/ether = 80/20), Rf = 0.5).The title compound was obtained as a yellow oil (60% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.14 (m, 1H), 7.60-7.56 (m, 1H), 7.48-7.46 (m, 1H), 7.38-7.34 (m, 1H), 3.13-3.10 (dd, *J* = 5.6 Hz, *J* = 6.1 Hz, 2H)), 2.68-2.65 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.0, 155.1, 137.1, 134.6, 127.2, 126.7, 123.7, 36.2, 25.8.

2,3-dihydronaphthalene-1,4-dione (Table 2, entry 6) Isolated by flash column chromatography on silica gel (pentane/ether = 80/20), Rf = 0.5).The title compound was obtained as a yellow oil (25% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H), 7.76-7.74 (m, 2H), 3.10 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 135.2, 134.3, 126.7, 37.5.

anthracene-9,10-dione (Table 2, entry 7) Isolated directly after workup without purification. The title compound was obtained as an orange solid (99% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34-8.32 (m, 4H), 7.82-7.80 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.1, 134.1, 133.5, 127.2.

9H-fluoren-9-one (Table 2, entry 8) Isolated by flash column chromatography on silica gel (pentane/ether = 80/20), Rf = 0.5).The title compound was obtained as a yellow oil (76% yield).

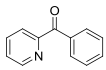
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.66 (m, 2H), 7.54-7.47 (m, 4H), 7.31-7.28 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 144.4, 134.7, 134.1, 129.1, 124.3, 120.3.

1-(4-Methoxyphenyl)ethanone (Table 2, entry 10) Isolated by flash column chromatography on silica gel (pentane/ether = 8/2, Rf = 0.5).The title compound was obtained as a yellowish oil (28% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.92 (m, 2H), 6.94-6.92 (m, 2H), 3.87 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8, 163.5, 130.6, 130.3, 113.7, 55.4, 26.3.

 **1-(2-nitrophenyl)ethanone** (Table 2, entry 11) Isolated by flash column chromatography on silica gel (pentane/ether = 80/20), Rf = 0.5).The title compound was obtained as a colourless oil (17% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.06 (m, 1H), 7.73-7.69 (m, 1H), 7.62-7.57 (m, 1H), 7.44-7.42 (m, 1H), 2.54 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 145.7, 137.8, 134.2, 130.7, 127.3, 124.3, 30.1.

 **phenyl(pyridin-2-yl)methanone** (Table 2, entry 12) Isolated by flash column chromatography on silica gel (pentane/ether = 80/20), Rf = 0.5).The title compound was obtained as a light brown oil (73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.5 Hz, 1H), 8.05 (m, 3H), 7.91 (m, 1H), 7.59 (m, 1H), 7.49 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 155.1, 148.5, 137.0, 136.3, 132.9, 131.0, 128.1, 126.1, 124.6.

 **1-methylpyrrolidine-2,5-dione** (Table 2, entry 13) Isolated by flash column chromatography on silica gel (pentane/ether = 50/50), Rf = 0.5).The title compound was obtained as a white solid (34% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (s, 3H), 2.72 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.3, 28.2, 24.7.

6.5 Bibliography

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