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Copper-catalysed aerobic oxidation of alcohols using fluorous biphasic catalysis

Gianna Ragagnin,[a] Bodo Betzemeier,[a] Silvio Quici[b] and Paul Knochel[a,*]

[a]*Department Chemie der Ludwig-Maximilians-Universität, Butenandtstr. 5-13, 81377 Munich, Germany*
[b]*Dipartimento di Chimica Organica e Industriale, Centro CNR Sintesi e Stereochimica di Speciali Sistemi Organici, via Golgi 19, 20133 Milan, Italy*

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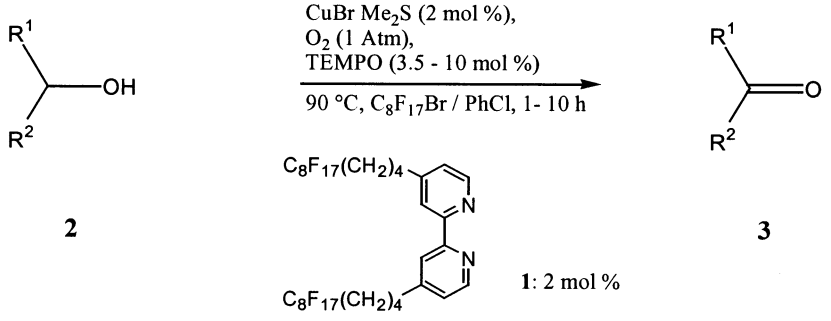
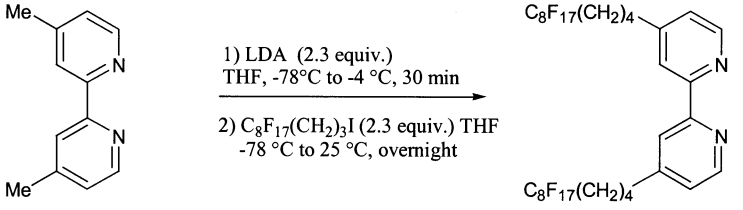
Abstract—A copper(I) catalysed and TEMPO mediated fluorous biphasic oxidation of primary, secondary, allylic and benzylic alcohols with oxygen in the presence of a bipyridine ligand bearing perfluorinated ponytails is described. High chemoselectivities are observed in the oxidation of substituted cyclohexanols (substituted axial cyclohexanols react 6–8 times faster than the corresponding equatorial cyclohexanols). © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The ecologically benign oxidation of alcohols has recently attracted much attention.[1–7] TEMPO and related stable nitroxyl radicals have been extensively used for the oxidation of primary and secondary alcohols.[8–10] Two-phase (organic-aqueous) conditions for the oxidation have been reported.[11–13] Recently, we have shown that primary and benzylic alcohols can be readily oxidised in the presence of catalytic amounts of TEMPO and copper(I) salts using a



Scheme 1.



Scheme 2. Ligand synthesis.

Keywords: alcohols oxidation; TEMPO; fluorinated copper ligands; cyclohexanols; fluorous catalysis.
* Corresponding author. Tel.: +49-89-2180-7681; fax: +49-89-2180-7680; e-mail: paul.knochel@cup.uni-muenchen.de

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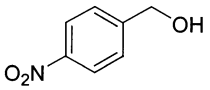
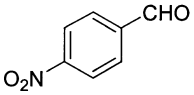
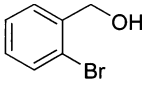
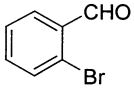
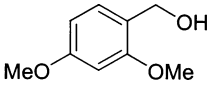
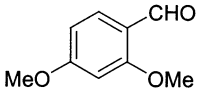
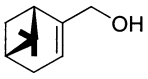
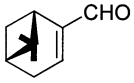
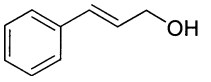
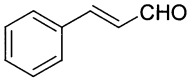
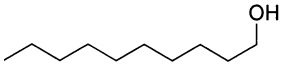
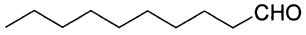
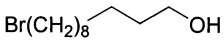
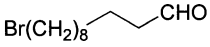
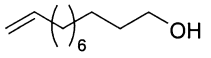
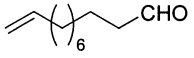
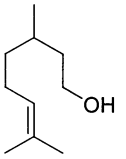
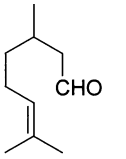
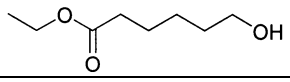
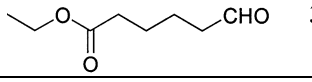
Table 1. Aldehydes of type **3** obtained by the oxidation of alcohols **2** under fluorous biphasic conditions

Entry	Alcohol of type **2**	Aldehyde of type **3**	Yield[a] (%)
1	 **2a**	 **3a**	93 (86)[b,c]
2	 **2b**	 **3b**	96[c]
3	 **2c**	 **3c**	93[c]
4	 **2d**	 **3d**	76[c]
5	 **2e**	 **3e**	79[c]
6	 **2f**	 **3f**	73[c]
7	 **2g**	 **3g**	81[c]
8	 **2h**	 **3h**	78[c]
9	 **2i**	 **3i**	92
10	 **2j**	 **3j**	89

[a] Isolated yield of analytically pure product.
[b] Isolated yield obtained after eight reactions run.
[c] 3.5% TEMPO.

biphasic fluorous reaction media.[14–26] Herein, we wish to report the full details of our study, as well as the scope and the limitations of this oxidation (Scheme 1).

2. Results and discussion

The bipyridine **1** bearing perfluorinated ponytails proves to be an excellent ligand for fluorous biphasic catalysis. It was prepared according to the method of Quici[27] (Scheme 2). The desired bis-alkylated bipyridine **1** is isolated in 35–40% yield together with the monoalkylated product (approx. 20%) which can be separated by recrystallisation from methanol. The ligand **1** and $CuBr{\cdot}Me_2S$ selectively dissolve in perfluorooctyl bromide (PFBO) leading to a brown–green solution. In the presence of 2 mol% of this copper complex and TEMPO (3.5 mol%), the oxidation of benzyl alcohol **2a** to the corresponding aldehyde **3a** proceeds smoothly in a biphasic system of PFBO and chlorobenzene. The reaction is complete within 1.5 h at 90°C and the aldehyde **3a** is isolated in 93% yield (entry 1 of Table 1). At the end of the reaction, the two phases are separated and the perfluorinated phase can be reused for further reaction runs. We have observed no decrease in yield and reaction rate. After eight reaction cycles analytically pure 4-nitrobenzaldehyde **3a** was still isolated in 86% yield.

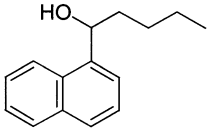
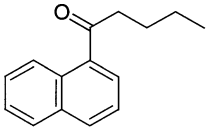
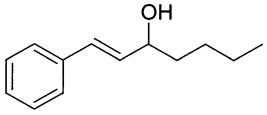
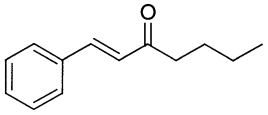
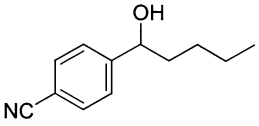
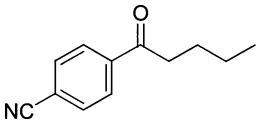
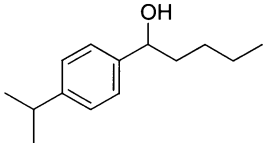
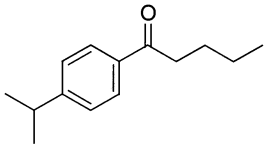
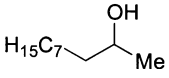
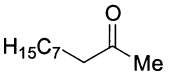
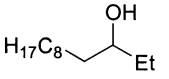
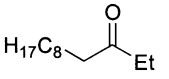
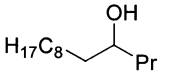
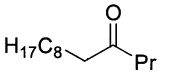
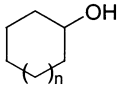
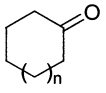
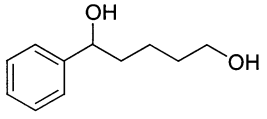
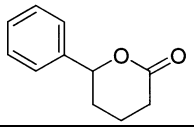
2.1. Oxidation of primary alcohols

In general, benzylic alcohols are smoothly oxidised (approx. 1.5 h at 90°C; entries 1–3 of Table 1). Allylic alcohols, such as **2d** or **2e** are also readily converted to the corresponding aldehydes **3d** and **3e** in 76–79% yield (entries 4 and 5). Primary aliphatic alcohols are oxidised in comparable rates (in strong contrast to aliphatic secondary alcohols; entries 6–10). Thus, the citronellol **2i** (entry 9) is oxidized to citronellal **3i** in 92% yield using 10 mol% of TEMPO within 1 h. Functional groups, such as a bromide (**2g**; entry 7) or an ester (**2j**; entry 10) are well tolerated leading to the expected aldehydes (**3g** and **3j**) in 81–89% yield. In no case, isomerisations of double bonds have been observed.

2.2. Oxidation of secondary alcohols

For the oxidation of secondary alcohols, we have noticed a significantly slower reaction, probably due to steric hindrance (Table 2). We have found that by using

Table 2. Ketones of type **3** obtained by the oxidation of alcohols **2** under fluorous biphasic conditions

Entry	Alcohol of type **2**	Ketone of type **3**	Yield[a] (%)
1	 **2k**	 **3k**	91[b]
2	 **2l**	 **3l**	84[b]
3	 **2m**	 **3m**	97
4	 **2n**	 **3n**	95
5	 **2o**	 **3o**	88 (83)[c]
6	 **2p**	 **3p**	69[b]
7	 **2q**	 **3q**	31[b,d]
8	 *n*=1 **2r**	 **3r**	74 (76)[c]
9	*n*=2 **2s**	**3s**	82
10	*n*=3 **2t**	**3t**	85
11	 **2u**	 **3u**	78[e]

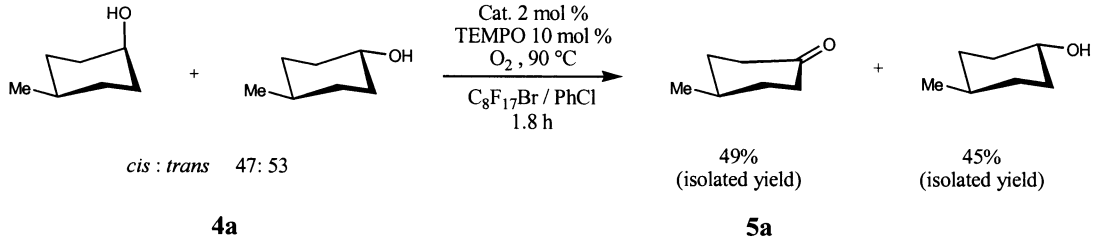
[a] Isolated yield of analytically pure product.
[b] 3.5% TEMPO.
[c] Isolated yield after five reaction runs.
[d] Conversion after 17 h.
[e] A 7% of 5-phenyl, 5-oxo-pentanal was obtained as byproduct.

10 mol% of TEMPO instead of 3.5 mol%, 2-decanol (**2o**, entry 5 of Table 2) could be oxidized to the ketone **3o** within 2 h compared to 7 h with 3.5 mol% of TEMPO. Secondary benzylic and allylic alcohols react usually faster and provide the corresponding ketone in 84–97% (entries 1–4). By enhancing the steric hindrance, the rate of the oxidation dramatically decreases, even in the presence of higher amounts of TEMPO (compare entries 5–7) and in some cases, incomplete conversion was observed. Cyclic secondary alcohols are rapidly oxidized (30 min to 1.5 h, depending on the ring size; entries 8–10).

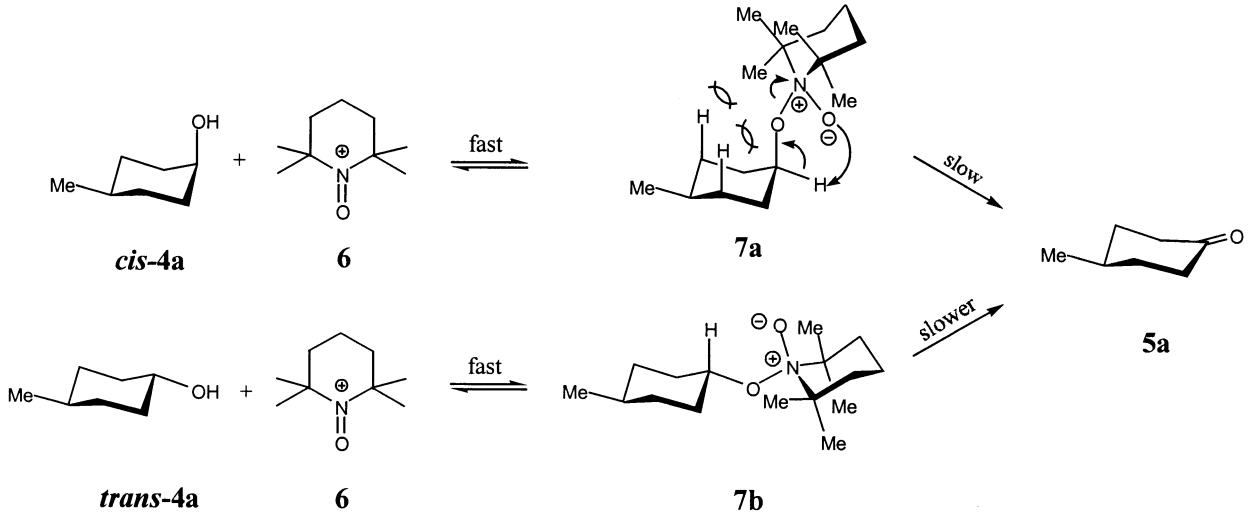
In general, secondary alcohols react slower than primary. This is clearly shown with the diol **2u** (entry 11) in which the primary alcohol is oxidized selectively over the benzylic secondary hydroxyl function. The intermediate aldehyde forms a lactol, which is in situ oxidized to the lactone **3u** in 78% yield. Interesting, a nitrile functionality (see entry 4) and an isopropyl substituent (potentially oxidizable to a cumyl hydroperoxide) are tolerated under our reaction conditions. Various amino-alcohols could not be oxidised due to an inhibition of the catalytic system, probably resulting from a competitive complexation of nitrogen with the copper salts.

2.3. Selectivities in cyclohexanols oxidation

The extreme sensibility of this oxidation to steric hindrance has allowed us to perform selective oxidations of *cis–trans* mixtures of cyclohexanols. Thus, the treatment of a 47:53 *cis*/*trans* mixture of 4-methylcyclohexanols **4a** leads to a selective oxidation of the *cis*-4-methylcyclohexanol



Scheme 3. Selectivity in 4-methylcyclohexanol oxidation.



Scheme 4. Possible explanation for the *cis*- *trans*-selective oxidation.

(*cis*-**4a**) whereas the *trans*-4-methylcyclohexanol (*trans*-**4a**) remains almost unreacted allowing to isolate, after chromatographic purification, pure *trans*-4-methylcyclohexanol (49% yield, the theoretical amount being 53% yield; 92% of selectivity) as well as 45% yield of the ketone **5a** (Scheme 3).

This difference of reactivity can be tentatively explained by assuming that the oxoammonium cation **6** reacts rapidly with both *cis*- and *trans*- **4a** but the axial alcohol **7a** undergoes a faster elimination due to steric hindrance compared to the equatorial intermediate **7b** (Scheme 4). The rate determining step is assumed to be the H abstraction, accordingly with recent studies about TEMPO mediated oxidation of alcohols.[10,28,29]

Several 2-, 3-, and 4-substituted cyclohexanols have been selectively oxidized using this procedure allowing to prepare pure substituted cyclohexanols with hydroxyl group in an equatorial position (Table 3).

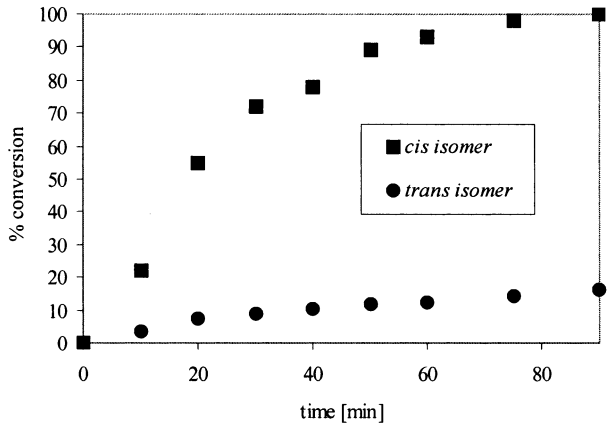
In the case of *cis*- and *trans*- 4-phenylcyclohexanol **4f**, we have also performed oxidation on separate samples, showing that the reaction rate of for the *cis*- isomer is 6–8 times faster than the *trans*- alcohol **4f** (Scheme 5).

In conclusion, the TEMPO mediated copper-catalysed oxidation of alcohols using a fluorous biphasic system, is a convenient method for oxidizing primary, allylic and benzylic alcohols, as well as not too sterically hindered secondary alcohols. Useful chemoselectivities are observed

Table 3. Stereoselective effects in the oxidation of substituted cyclohexanols

Entry	Cyclohexanol derivative	Ratio *cis*/*trans*[a]	Reaction time[b] (h)	Stereochemistry of unreacted alcohol[a]	Yield of unreacted alcohol[c] (%)	Yield of ketone[c] (%)	
4a	4-Methylcyclohexanol	47:53	1.8	*trans*	49	**5a**	45
4b	2-Methylcyclohexanol	33:67	9.5	*trans*	50	**5b**	38
4c	3-Methylcyclohexanol	34:66	1.2	*cis*	29	**5c**	62
4d	4-*i*Pr-cyclohexanol	32:68	1.5	*trans*	65	**5d**	28
4e	4-*t*Bu-cyclohexanol	25:75	1.7	*trans*	70	**5e**	20
4f	4-Phenylcyclohexanol	50:50	1.5	*trans*	46	**5f**	49

[a] Determined by ^{1}H NMR analysis at the C*H*OH proton.
[b] Time to get 100% GC conversion of the more reactive isomer, 10 mol% TEMPO used.
[c] Isolated yield of analytically pure product, calculated on the basis of the initial reaction mixture.



Scheme 5. Kinetics of separate oxidation of *cis*- and *trans*-4-phenylcyclohexanol.

in the case of substituted cyclohexanols, allowing selective oxidation of *cis*- *trans*-mixtures.

3. Experimental

3.1. General remarks

The chemicals were purchased from Aldrich and ABCR Avocado and used without further purification. When not specified, all the analytical data are in agreement with known compounds and literature references have been reported. Reactions were monitored by gas chromatography (GC) analysis of reaction aliquots; chiral gas chromatography has been used for monitoring the oxidation of the *cis*- *trans*-cyclohexanols mixtures. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel. NMR spectra were recorded on a Bruker 300 MHz NMR spectrometer. The ionisation method used was electron impact ionisation (EI, 70 eV). Elemental analyses were performed by the Microanalytical Service Laboratory of Universität München.

3.2. Typical procedure of alcohols oxidation (method A)

A 25 mL Schlenk-flask was charged with the bipyridine **1** (44.0 mg, 40 μmol, 2 mol%) dissolved in perfluorooctyl bromide (2 mL) and $CuBr{\cdot}Me_2S$ (9.2 mg, 40 μmol, 2 mol%) dissolved in a small amount of dimethyl sulfide leading to a green–brown solution. After stirring for 0.5 h a solution of the alcohol **2** (2 mmol) and TEMPO (32.0 mg, 200 μmol, 10 mol%) in chlorobenzene (2 mL) was added. The biphasic reaction mixture was stirred at 90°C while a gentle stream of oxygen was passing. At the end of the reaction, the mixture was cooled to 0°C, the organic layer was decanted and the fluorous phase was washed with chlorobenzene (3×2 mL). The combined organic phases were diluted with ether (30 mL) and washed with brine. After drying ($MgSO_4$), filtration, evaporation of the solvent in vacuo the crude product **3** was purified by flash chromatography (eluent: diethyl ether–pentane, ratio depending on the ketone). The fluorous phase was used directly for further reaction runs.

3.2.1. Modified workup procedure (method B). This procedure is suitable when chromatographic separation between product and TEMPO is difficult (e.g. 2-decanol, cycloheptanone and other aliphatic alcohols).

The reaction mixture is treated with a concentrated aqueous solution of $NaHSO_3$ and 10 mL MeOH. A white, copious precipitate of the bisulphite adduct is obtained, which is filtered, washed with ether and added to a 10% solution of Na_2CO_3 in water, then stirred to a complete dissolution. The product is recovered by extraction from the aqueous phase with ether (3×20 mL). The organic solution is dried ($MgSO_4$), filtered and the solvent evaporated under vacuum, yielding analytically pure product.

3.3. Experimental data

3.3.1. 4-Nitrobenzaldehyde (3a). From 306 mg (2.0 mmol) of **2a**, obtained 281 mg (93%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 10.15 (s, 1H), 8.36 (d, 2H), 8.07 (d, 2H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 189.8, 150.4, 139.4, 129.9, 123.6.

3.3.2. 2-Bromobenzaldehyde (3b). From 380 mg (2.0 mmol) of **2b**, obtained 362 mg (96%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 10.25 (s, 1H), 7.85–7.78 (m, 1H), 7.57–7.52 (m, 1H), 7.34–7.29 (m, 2H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 191.5, 135.3, 133.8, 133.4, 130.1, 127.8, 127.1.

3.3.3. 2,4-Dimethoxybenzaldehyde (3c). From 336 mg (2.0 mmol) of **2c**, obtained 309 mg (93%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 10.28 (s, 1H), 7.77 (d, 1H), 6.50 (dd, 1H), 6.41 (d, 1H), 3.85 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 188.4, 166.4, 163.6, 130.5, 118.8, 105.8, 97.9, 55.7.

3.3.4. (1*R*)-(−)-Myrtenal (3d). From 304 mg (2.0 mmol) of **2d**, obtained 228 mg (76%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.42 (s, 1H), 6.69 (m, 1H), 2.84 (dt, 1H), 2.57–2.52 (m, 2H), 2.45 (dt, 1H), 1.32 (s, 3H), 1.04 (d, 1H), 0.72 (s, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 191.0, 151.3, 147.4, 40.3, 37.9, 37.3, 32.7, 30.8, 25.4, 20.7.

3.3.5. *E*-Cinnamaldehyde (3e). From 268 mg (2.0 mmol) of **2e**, obtained 209 mg (79%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.65 (d, 1H), 7.54–7.50 (m, 2H), 7.43–7.37 (m, 3H), 6.69 (d, 1H), 6.65 (d, 1H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 193.3, 152.4, 133.7, 131.0, 128.9, 128.3, 128.2.

3.3.6. Decanal (3f). From 341 mg (2.1 mmol) of **2f**, obtained 259 mg (73%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.69 (t, 1H), 2.34 (td, 2H), 1.58–1.53 (m, 2H), 1.25–1.20 (m, 12H), 0.81 (t, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 204.6, 43.9, 31.9, 31.7, 29.4, 29.3, 29.2, 22.7, 22.1, 14.0.

3.3.7. 11-Bromoundecanal[30] (3g). From 480 mg (1.9 mmol) of **2g**, obtained 383 mg (81%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.75 (t, 1H), 3.38 (t, 2H), 2.39 (td, 2H), 1.84 (quin, 2H), 1.61 (m, 2H), 1.41 (m, 2H), 1.25 (m, 10H); ^{13}C NMR (δ (ppm), $CDCl_3$,

75 MHz): 202.6, 43.6, 33.8, 32.6, 29.1, 29.0, 28.9, 28.5, 27.9, 21.9.

3.3.8. 10-Undecenal[31] **(3h).** From 224 mg (1.9 mmol) of **2h**, obtained 248 mg (78%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.73 (t, 1H), 5.87–5.83 (m, 1H), 4.94 (d, 1H), 4.90 (d, 1H), 2.38 (td, 2H), 2.01–1.98 (m, 2H), 1.60 (m, 2H), 1.31 (m, 10H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 202.8, 139.1, 114.2, 43.9, 33.8, 29.3, 29.2, 29.1, 29.0, 28.9, 22.1.

3.3.9. Citronellal (3i). From 312 mg (2.0 mmol) of **2i**, obtained 283 mg (92%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.680 (t, 1H), 5.013 (tt, 1H), 2.304 (m, 1H), 2.173 (m, 1H), 1.939 (m, 3H), 1.612 (s, 3H), 1.531 (s, 3H), 1.360–1.118 (m, 2H), 0.902 (d, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 202.0, 130.7, 123.0, 50.0, 35.9, 26.8, 24.7, 24.4, 18.9, 16.6.

3.3.10. 6-Oxohexanoic acid ethyl ester (3j). From 320 mg (2.0 mmol) of **2j**, obtained 281 mg (89%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 9.768 (t, 1H), 4.123 (q, 2H), 2.328 (m, 2H), 2.239 (m, 2H), 1.603 (m, 4H), 1.252 (t, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 202.6, 173.9, 60.7, 44.2, 33.4, 23.8, 22.7, 14.3.

3.3.11. 1-(1-Naphthyl)-pentanone (3k). From 435 mg (2.0 mmol) of **2k**, obtained 393 mg (91%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 8.50 (d, 1H), 7.89 (d, 1H), 7.79–7.70 (m, 2H), 7.55–7.35 (m, 3H), 2.96 (t, 2H), 1.71 (quin, 2H), 1.37 (sext, 2H), 0.87 (t, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 204.9, 136.2, 133.5, 132.4, 130.0, 128.5, 127.9, 127.0, 126.4, 125.6, 124.1, 41.7, 26.7, 22.6, 13.9; IR (ν (cm^{-1}), Film): 3049 (w), 2958 (s), 2931 (s), 2872 (m), 1682 (s), 1593 (w), 1508 (m), 799 (s); MS (EI, 70 eV, *m/e* (rel. int.)): 212 (M^+, 28), 170 (30), 155 (100), 143 (13), 127 (79); Anal. calcd for $C_{15}H_{16}O$ (M= 212.29 g mol^{-1}): C: 84.87, H: 7.60; Found: C: 85.06, H: 7.41.

3.3.12. 1-Phenyl-1-hepten-3-one[32] **(3l).** From 380 mg (2.0 mmol) of **2l**, obtained 316 mg (84%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 7.56–7.50 (m, 2H), 7.54 (d, 1H), 7.33–7.28 (m, 3H), 6.72 (d, 1H), 2.64 (t, 2H), 1.65 (quin, 2H), 1.37 (sext, 2H), 0.90 (t, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 200.7, 142.4, 134.7, 130.4, 129.0, 128.3, 126.4, 40.8, 26.6, 22.5, 14.0.

3.3.13. 1-(4-Cyanophenyl)-1-pentanone[33] **(3m).** From 378 mg (2.0 mmol) of **2m**, obtained 362 mg (97%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 0.885 (t, 3H), 1.328 (p, 2H), 1.656 (p, 2H), 2.908 (t, 2H), 7.695 (d, 2H), 7.968 (d, 2H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 14.3, 22.7, 26.5, 39.0, 116.6, 118.4, 128.8, 132.9, 140.4, 199.4; IR (ν (cm^{-1}), KBr): 3049 (w), 2956 (m), 2233 (m), 1686 (s), 1406 (m), 1206 (m), 854 (m), 574 (w).

3.3.14. 1-(4-Isopropylphenyl)-1-pentanone (3n). From 426 mg (2.1 mmol) of **2n**, obtained 405 mg of colourless liquid (95%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 0.863 (t, 3H), 1.180 (d, 2H), 1.333 (m, 2H), 1.631 (p, 2H), 2.850 (h, 1H), 2.852 (t, 2H), 2.301 (d, 2H), 2.811 (d, 2H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 14.3, 22.9, 24.1, 27.0, 34.6, 38.6, 127.0, 128.7, 135.4, 154.7, 200.6; IR (ν (cm^{-1}), Film): 3031 (w), 2961 (s), 2932 (m), 1683 (s), 1607 (s), 1413 (m), 1184 (m), 111 (m), 844 (w); MS (EI, 70 eV, *m/e* (rel. int.)): 203 (M^+-1), 189 (1), 162 (65), 161 (37), 148 (22), 147 (100), 91 (21); Anal. calcd for $C_{14}H_{20}O$ (M=204.21 g mol^{-1}): C: 82.3, H: 9.87, found: C: 82.0, H: 9.54.

3.3.15. 2-Decanone (3o). From 340 mg (2.0 mmol) of **2o**, obtained 279 mg (88%, method B, 1st run). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 0.808 (t, 3H), 1.203 (m, 10H), 1.497 (p, 2H), 2.061 (s, 3H), 2.343 (t, 2H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 209.8, 44.2, 32.2, 30.2, 29.7, 29.6, 29.5, 24.3, 23.0, 14.5.

3.3.16. 3-Dodecanone[34] **(3p).** From 372 mg (2.0 mmol) of **2p**, obtained 254 mg (69%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 2.33 (t, 2H), 2.31 (q, 2H), 1.60–1.47 (m, 2H), 1.20 (m, 12H), 0.89 (t, 3H), 0.81 (t, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 211.0, 44.9, 42.9, 31.5, 29.6, 29.2, 23.5, 22.5, 17.4, 14.0.

3.3.17. 4-Tridecanone (3q). From 400 mg (2.0 mmol) of **2q**, obtained 122 mg (31%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 2.32 (t, 2H), 2.31 (t, 2H), 1.60–1.47 (m, 4H), 1.20 (m, 12H), 0.85 (t, 3H), 0.81 (t, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 211.2, 44.6, 42.7, 31.8, 29.3, 29.2, 23.8, 22.6, 17.2, 14.0, 13.6.

3.3.18. Cyclohexanone (3r). From 200 mg (2.0 mmol) of **2r**, obtained 145 mg (74%, 1st run, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 1.670–1.729) (m, 2H), 1.795–1.877 (m, 4H), 2.306 (t, 4H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 212.4, 42.3, 27.4, 25.3.

3.3.19. Cycloheptanone (3s). From 232 mg (2.0 mmol) of **2s**, obtained 186 mg (82%, method B). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 2.462–2.219 (m, 4H), 1.565–1.148 (m, 8H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 213.5, 43.2, 27.1, 26.2.

3.3.20. Cyclooctanone (3t). From 258 mg (2.0 mmol) of **2t**, obtained 215 mg (85%, method B). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz) 2.371–2.413 (m, 4H), 1.819–1.901 (m, 4H), 1.492–1.571 (m, 4H), 1.321–1.369 (m, 2H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 218.6, 42.3, 27.5, 26.0, 25.1.

3.3.21. 5-Phenyl, 5-hydroxypentanoic acid lactone[35] **(3u).** From 376 mg (2.1 mmol) of **2u**, obtained 326 mg (89%). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 1.733–1.850 (m, 1H), 1.900 (m, 2H), 2.089 (dq, 1H), 2.448–2.667 (m, 2H), 5.274 (dd, 1H), 7.273 (m, 5H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 18.8, 29.7, 30.7, 81.9, 125.9, 128.5, 128.8, 140.0, 171.6.

3.3.22. 4-Methylcyclohexanone (5a). From 230 mg (2.0 mmol) of **4a** (47:53 *cis*/*trans* mixture), obtained 101 mg (45%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz) 0.775 (d, 3H), 1.169 (p, 2H), 1.571–1.708 (m, 1H), 1.709–1.804 (m, 2H), 2.077–2.122 (m, 4H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 212.6, 41.2, 35.1, 31.5, 21.3; IR (KBr): 2954 (m), 2929 (m), 1716 (s), 1459 (m), 1422 (m), 1121 (s), 616 (m).

3.3.23. 2-Methylcyclohexanone (5b). From 231 mg (2.0 mmol) of **4b** (33:67 *cis*/*trans* mixture), obtained 86 mg (38%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 2.430–2.212 (m, 3H), 1.987–2.112 (m, 2H), 1.885–1.755 (m, 1H), 1.733–1.721 (m, 2H), 1.425–1.281 (m, 1H), 0.997 (d, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 213.9, 45.7, 42.2, 36.5, 28.3, 25.5, 15.1.

3.3.24. 3-Methylcyclohexanone (5c). From 228 mg (2.0 mmol) of **4c** (34:66 *cis*/*trans* mixture), obtained 139 mg (62%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 2.321–2.087 (m, 3H), 2.000–1.723 (m, 4H), 1.646–1.496 (m, 1H), 1.310–1.182 (m, 1H), 0.928 (m, 3H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 212.2, 50.3, 41.5, 34.5, 33.6, 25.6, 22.4.

3.3.25. 4-Isopropyl-cyclohexanone (5d). From 286 mg (2.0 mmol) of **4d** (32:68 *cis*/*trans* mixture), obtained 79 mg (28%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 0.854 (d, 6H), 1.316–1.577 (m, 4H), 1.882–1.992 (m, 2H), 2.172–2.371 (m, 4H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 19.0, 28.6, 30.7, 40.1, 41.5, 211.5.

3.3.26. 4-*t*-Butyl-cyclohexanone (5e). From 320 mg (2.0 mmol) of **4e** (25:75 *cis*/*trans* mixture), obtained 63 mg (20%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 0.922 (s, 9H), 1.375–1.549 (m, 3H), 2.006–2.147 (m, 2H), 2.256–2.438 (m, 4H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 28.0, 32.8, 41.7, 47.1, 212.9.

3.3.27. 4-Phenylcyclohexanone (5f). From 350 mg (2.0 mmol) of **4f** (50:50 *cis*/*trans* mixture), obtained 169 mg (49%, method A). ^{1}H NMR (δ (ppm), $CDCl_3$, 300 MHz): 1.976 (m, 2H), 2.198–2.305 (m, 2H), 2.526 (m, 4H), 3.052 (tt, 1H), 7.282 (m, 5H); ^{13}C NMR (δ (ppm), $CDCl_3$, 75 MHz): 34.4, 41.8, 43.2, 127.0, 127.1, 129.0, 145.2, 211.5.

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