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Chlorotrimethylsilane and Sodium Iodide: A Useful Combination for the Regioselective Deoxygenation of Arylalkyl- α -Diketones

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An efficient regioselective deoxygenation of arylalkyl-1,2-diketones by the couple trimethylsilylchloride/sodium iodide has been reported. In all cases, the deoxygenation takes place on the carbonyl group ($C\alpha=O$) proximal to the aromatic ring in methylene chloride at room temperature in good yields, furnishing a series of variously functionalized alkylbenzylketones. A large range of functional groups were well tolerated on the *ortho*-, *meta*- and *para*-positions by this mild process regardless of their electronic effects,

demonstrating the general character of the present methodology. The trimethylsilylchloride/sodium iodide reducing process was also successfully applied to reduce α -ketoacid and α -ketoester substrates.

Keywords: Deoxygenation, 1,2-diketone, 1,2-ketoester, chlorotrimethylsilane, sodium iodide, selectivity.

Introduction

The combination of chlorotrimethylsilane (TMSCl) with sodium iodide (NaI) has been used as a versatile reagent association in a variety of chemical transformations as the cleavage of ethers, esters, lactones, carbamates, and for the conversion of alcohols into iodide derivatives.^[1] Moreover, the usefulness of the TMSCl/NaI combination was shown acting as a reducing reagent for example, in the deoxygenation of sulfoxides to sulfides.^[2] Very recently, we demonstrated for the first time that this combination was very efficient to regioselectively reduced a large variety of unsymmetrical 1,2-diaryl-diketones **1** (benzils) to provide, at room temperature in CH_2Cl_2 , a series of α -deoxybenzoins **2** (α -DOBs) with good to excellent yields (Scheme 1).^[3] In this work, we have demonstrated that the reducing species in CH_2Cl_2 was unequivocally the equimolar combination of TMSCl with NaI rather than TMSI (which was not generated *in situ*^[4] in CH_2Cl_2) or HI (possibly generated between the couple TMSCl/NaI and traces of water present in CH_2Cl_2). We have also showed that a total α -regioselectivity was observed for a variety of non-symmetrical benzils **1** having necessarily electron-donating groups (*e.g.*, OMe, OH,

SMe, NH_2 , etc) on the *ortho*- and/or on *para*-positions. Here we extend these studies to the deoxygenation of various arylalkyl- α -diketones **3** by the couple TMSCl/NaI in view of preparing rapidly a small library of alkylbenzylketones **4** of biological interest,^[5] or as useful intermediates for chemical transformations.^[6] To our knowledge, the deoxygenation of arylalkyl- α -diketones was only studied with 1-phenylpropane-1,2-dione (**3a**).^[7] Stephenson^[7a] reported the deoxygenation of **3a** through a two-steps sequence using trimethylphosphite (yield not given) followed by a quantitative hydrogenation using H_2 and PtO_2 . Several years later, Kamochi,^[7b] reported the deoxygenation of **3a** using an excess of SmI_2 (8 equiv) which provided only 7% of **4a**.

From a synthetic point of view, the development of a general and simple method for the regioselective deoxygenation of arylalkyl- α -diketones **3** into alkylbenzylketones **4** is still desired. Herein we disclose our success on the development of such a selective and easy to handle mild protocol using the TMSCl/NaI combination in methylene chloride. We found that the total regioselective reduction of substituted arylalkyl- α -diketones of type **3** occurred selectively regardless the electronic nature of the

Scheme 1. TMSCl/NaI promoted the deoxygenation of α -diketones.

substituent on the aromatic ring (electron-withdrawing or electron-donating).

Results and Discussion

At the beginning of the present work, we first studied the deoxygenation of 1-phenylpropanedione **3a** as a model substrate in the presence of TMSCl (5 equiv) and NaI (5 equiv) in CH_2Cl_2 at rt (Table 1, entry 1). We were pleased to observe that after 24 hours of reaction, the α -carbonyl function ($\text{C}\alpha=\text{O}$) of **3a**, closed to the aromatic ring, was totally reduced to furnish 1-phenylpropan-2-one **4a** with a good yield of 80%, and with no trace of its β -regioisomer propiophenone. This result was particularly interesting and could be advantageously compared with those obtained with the deoxygenation of benzil derivatives developed in our group.^[3] (i) the replacement of a phenyl group by a methyl substituent facilitates the reducing process as **3a** was reduced in only 24 h at rt in CH_2Cl_2 , whereas the deoxygenation of PhCOCOPh was incomplete after 72 h of stirring in CH_2Cl_2 at rt;^[8] (ii) on the contrary to benzil derivatives, the reducing process occurred regioselectively on the $\text{C}\alpha$ of **3a** but without the need of an electron-donating group on the *ortho*- or on the *para*-position of the aromatic ring. This result was confirmed with 1-phenyloctane-1,2-dione **3b**, which was also regioselectively reduced into 1-phenyloctan-2-one **4b** in the presence of the TMSCl/NaI combination (90%, entry 2). These two results prompted us to evaluate this reducing process with electron-poor arylalkyl- α -diketones **3c-n** (entries 3-14) and with electron rich arylalkyl- α -diketones **3o-z** (entries 15-26), easily available from the PdI_2/DMSO oxidation of the corresponding arylalkylalkynes.^[9,10] We were very delighted to observe that the deoxygenation process occurred well

with α -diketone **3c** having a *p*- NO_2 substituent on the aromatic ring to yield benzylhexylketone **4c** (65%, entry 3). The general character of this regioselective deoxygenation was confirmed with a series of other substrates **3d-n** having electron-withdrawing substituents on their aromatic rings (entries 4-14). The reactions proceeded in good yields with substrates having a *p*- CF_3 substituent (**3d**, 79%, entry 4) as well as a *p*- CO_2Me (**3e**, 68%, entry 5) a *p*-CN group (**3f**, 70%, entry 6) and a *p*-COMe substituent (**3g**, 70%, entry 7). One can note that using substrate **3h** having a *p*-CHO function, the deoxygenation process did not take place; only 4-(1-hydroxy-2-oxooctyl) benzaldehyde **5** was isolated in a 59% yield after 6 h of stirring.^[11] Halide substituents, possibly useful for further coupling reactions, were well tolerated under these mild conditions affording the corresponding ketones **4i-n** with good yields (entries 9-14). Different electron-donating groups on the aromatic ring of α -diketones **3o-w** were next evaluated (entries 15-23). As expected a OMe-substituent on the aromatic scaffold was well tolerated in this reducing process as observed in examples depicted in entries 15-18 and the corresponding alkylbenzylketones **4o-r** were regioselectively isolated in good to excellent yields. In the case of **3r**, beside the total reduction of the carbonyl function close to the aromatic ring, we also observed the ether cleavage on the more fragile *para*-MeO-substituent of the trimethoxyphenyl ring as it was noticed, for example, with the action of Grignard reagents on trimethylpyrrogallol ether derivatives.^[12] Without surprise, α -diketones **3s-x** bearing various electron-rich aromatic backbone (4- OHC_6H_4 , 4- MeC_6H_4 , 4- SMcC_6H_4 , 4- NHAcC_6H_4 and 2-naphthyl) were successfully transformed into their expected benzylketones with good to excellent yields (entries 19-24).

Table 1: Functional Group Tolerance

<div style="text-align: center;"> <p> $\text{FG}-\text{Het}-\text{C}(=\text{O})-\text{C}(=\text{O})-\text{Alk} \xrightarrow[2/\text{H}_2\text{O}]{1/\text{TMSCl} / \text{NaI} (x \text{ equiv}), \text{CH}_2\text{Cl}_2, \text{rt, time}} \text{FG}-\text{Het}-\text{CH}(\text{Alk})-\text{C}(=\text{O})-\text{Alk}$ </p> <p>3 alkylbenzylketones 4</p> </div>						
Entry	α -Diketone 3	x^a	Time (h)	Ketones 4		Yield of 4 (%) ^b
1		3a	5	7		4a 80
2		3b	10	48		4b 90
3		3c	10	20		4c 65
4		3d	10	20		4d 79
5		3e	7	21		4e 68
6		3f	10	21		4f 70 ^c
7		3g	10	6		4g 70
8		3h	10	6		4h 0 ^d
9		3i	10	48		4i 85
10		3j	10	40		4j 97
11		3k	10	25		4k 75
12		3l	10	48		4l 72
13		3m	10	48		4m 70
14		3n	10	24		4n 65
15		3o	10	4		4o 77
16		3p	10	22		4p 95

17		3q	5	1.5		4q	93
18		3r	10	16		4r	50
19		3s	20	48		4s	60 ^c
20		3t	10	48		4t	97
21		3u	10	48		4u	90
22		3v	10	2		4v	96
23		3w	10	48		4w	98
24		3x	10	48		4x	92
25		3y	10	48		4y	80
26		3z	10	48		4z	78
27		3za	20	72		4za	65
28		3zb	10	3		4zb	52

^a *x* is the number of equivalents of the TMSCl/NaI combination. ^b Yield of isolated **4**. ^c The reaction was achieved in refluxing CHCl₃. ^d A partial reduction occurred on C α of **3h** to give 4-(1-hydroxy-2-oxooctyl)benzaldehyde **5** in a yield of 59%, see ref.^[11]

To our delight, variations on the alkyl chain of compounds **3** were also allowed and primary alcohol **3y** and its methyl ether **3z** were converted into their corresponding reduced products **4y** and **4z** in 80% and 78% yields, respectively (entries 25 and 26). Next, we focused our attention on α -diketone **3za** bearing an alkyl chain and a quinoline-scaffold and showed that the replacement of a phenyl ring by a 6-quinolyl substituent was also possible as ketone **4za** was obtained in an acceptable 65% yield (entry 27). Lastly, the sugar derivative **3zb**, prepared from the Pd-coupling reaction between β -thioglucose and **3l**,^[13] was subjected to the reducing TMSCl/NaI process. We were pleased to observe that the regioselective reduction of the C α =O of **3zb** occurred smoothly to provide **4zb** (52% yield) without anomeric epimerization (entry 28).

The results reported in Table 1 clearly demonstrate that the TMSCl/NaI protocol could be applied on a large variety of arylalkyl- α -diketones **3** bearing on their aromatic rings various substituents whatever their electronic character on the *ortho*-, *meta*-, and *para*-positions. Then, to evaluate whether the presence of an aryl substituent was essential in the deoxygenation of arylalkyl-1,2-diketones **3**, we have also studied the reaction with octan-1,2-dione as a model of dialkyl-1,2-diketone. After 30 minutes of stirring at rt in the presence of 10 equiv of TMSCl/NaI, octan-1,2-dione was rapidly totally degraded to give a mixture of unidentified by-products. Achieving the reaction at lower temperatures (0 °C and -20 °C) with reduced reaction times (10 and 20 minutes) did not give better results. Next, we were interested to evaluate the TMSCl/NaI association as a potent reducing reagent using other

activated groups, such as for example α -ketoesters **6a-d**, α -ketoacids **7a,b** and α -hydrazidoester **8** (Table 2).

Table 2. Deoxygenation of **6-8** by the TMSCl/NaI combination

Under the standard conditions defined in Table 1, the total reduction the keto-group of **6a** and **6b** proceeded smoothly to give the corresponding benzylesters **9a** and **9b** in a nearly quantitative yield after 2 h of reaction with a total α -selectivity. The TMSCl/NaI process was next used in view of reducing the carbonyl function of α -ketoesters **6c** and **6d**. After 2 h of reaction, the desired benzylesters **9c** and **9d** were obtained again with excellent yields (95%). For comparisons, the deoxygenation of **6d** into **9d** was recently reported,^[14] but required a three-step sequence in a 20% overall yield [(i) reduction of the ketogroup of **6d** into alcohol using NaBH_4 (ii) acetylation of the alcohol function, and (iii) reduction of the resulting acetate by SmI_2]. As observed with α -ketoester **6**, we were pleased to observe the carbonyl deoxygenation α -ketoacids **7a,b** by the TMSCl/NaI association to provide 2-phenylacetic acids **10a,b** in similar good yields of 91% and 90%, respectively. A last trial was successfully attempted with arylalkyl-1,2-hydrazido-ester **8** which was chemoselectively reduced after 6 h of reaction by the TMSCl/NaI combination in refluxing CH_2Cl_2 to provide benzylester **9a** in an acceptable 55% yield. The

comparison of the results obtained with derivatives **6a** and **8** indicated that the deoxygenation by TMSCl/NaI of the keto-group of **6a** seems to be easier than the deoxygenation of the hydrazide-function of **8** to provide the same benzylester derivative **9a** (98%, 2 h for **6a** vs 55%, 6 h reflux for **8**). All of the results presented in Table 2 indicated that TMSCl/NaI is a combination of choice for the mild deoxygenation of α -ketoesters and also for other functionalities, such as α -ketoacids or α -hydrazidoesters.

3. Conclusion

In summary, we demonstrated, for the first time, that TMSCl associated to NaI in CH_2Cl_2 is a useful combination to regioselectively reduce a variety of arylalkyl- α -diketones **3**. The keto group of these α -diketones, which is proximal to the aryl ring, was totally reduced into methylene to provide the corresponding alkylbenzylketones **4** in good to excellent yields. The present method can be used for the deoxygenation of a large variety of arylalkyl- α -diketones **3** bearing a wide range of functional groups on the aromatic ring with extreme ease at rt. On the contrary to the deoxygenation of benzil derivatives, which require the presence of an electron-donating substituent on the *ortho*- or *para*-positions of the aromatic ring, the deoxygenation of substituted arylalkyl-1,2-diketones **3** efficiently takes place regardless the electronic nature of the substituent (electron-withdrawing or electron-donating). Moreover, heterocyclic systems as a quinoline and sugar derivatives are also allowed making this elegant reducible method applicable to many compounds of type **3**. This mild process was successfully applied to α -ketoesters, α -ketoacids and α -hydrazidoesters, which were cleanly reduced with high yields. We believe that this soft and easy to handle methodology should find broad applications in synthetic organic chemistry, as well as in the combinatorial and pharmaceutical sciences.

Experimental Section

General experimental methods

All reactions were conducted under an argon atmosphere. Solvents: methylene chloride (CH_2Cl_2) for reaction, cyclohexane, ethyl acetate (EtOAc) for extraction and chromatography were technical grade. These compounds were all identified by the usual physical methods that are ^1H NMR, ^{13}C NMR, IR, HR-MS (ESI or APCI). ^1H NMR, ^{13}C NMR spectra were measured in CDCl_3 with an Advance - 300. ^1H chemical shift are reported in ppm from an internal standard TMS or of residual chloroform (7.26 ppm). The following abbreviations are used: m (multiplet), s (singlet), d (doublet), t (triplet), dd (doublet of doublet), q (quartet). ^{13}C

chemical shift are reported in ppm from central peak of deuteriochloroform (77.14). High-resolution mass spectra (HR-MS) were recorded on a MicroTOF spectrometer, using ESI or APCI with methanol as the carrier solvent. FT-IR spectra were measured on a Vector 22 spectrometer and are reported in wave numbers (cm^{-1}). Analytical TLC was performed on precoated silica gel 60-F254 plates. Silica gel 60 was used for flash chromatography. Melting points were recorded on a B-450 apparatus and are uncorrected. Arylalkyl- α -diketones **3** were prepared according to literature.^[9] Ketones **4a**,^[15] **4b**,^[16] **4p**^[17] and **4t**^[18] are known products and their spectroscopic data are in agreement with literature. **9a**,^[19] **9b**,^[20] **9c**,^[21] **10b**^[22] are known products and their spectroscopic data are in agreement with literature.

General procedure for deoxygenation of arylalkyl- α -diketones **3**

Typical example: under argon, 109 mg (0.5 mmol) of diketone **3b** and 750 mg (5 mmol) of NaI were mixed in 10 mL of CH_2Cl_2 . The resulting mixture was stirred for 5 min. at rt and then 540 mg (5 mmol) of TMSI were added to the solution. After disappearance of **3b** (judged by TLC; 48 h), the dark mixture was washed with 10 mL of a saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution and extracted with CH_2Cl_2 . After drying on Na_2SO_4 and concentration, the crude was purified by silica gel column chromatography to give benzylhexylketone **4b** (92 mg, 90%).

1-Phenylpropan-2-one (**4a**)^[15]

Compound **4a** was prepared according to the general procedure using 1-phenylpropane-1,2-dione **3a** (100 mg, 0.6749 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 80% (72.4 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.65–7.01 (m, 5H), 3.63 (s, 2H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 206.40, 134.24, 129.38, 128.76, 127.07, 51.05, 29.27.

1-Phenyloctan-2-one (**4b**)

Compound **4b** was prepared according to the general procedure using 1-phenyloctane-1,2-dione **3b** (100 mg, 0.4581 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 90% (84.2 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.40–7.12 (m, 5H), 3.69 (s, 2H), 2.45 (t, J = 7.4 Hz, 2H), 1.70–1.50 (m, 2H), 1.35–1.20 (m, 6H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 208.56, 134.41, 129.38, 128.67, 126.92, 50.15, 42.00, 31.54, 28.77, 23.71, 22.46, 13.99.

1-(4-Nitrophenyl)octan-2-one (**4c**)

Compound **4c** was prepared according to the general procedure using 1-(4-nitrophenyl)octan-1,2-dione **3c** (100 mg, 0.38 mmol). The title compound was obtained after flash chromatography as orange liquid; yield 65% (61.5 mg); ^1H NMR (300 MHz, CDCl_3) δ 8.18 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 3.81 (s, 2H), 2.50 (t, J = 7.4 Hz, 2H), 1.60–1.50 (m, 2H), 1.29–1.20 (m, 6H), 0.86 (t, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 206.52, 147.05, 141.67, 130.43, 123.73, 49.21, 42.83, 31.51, 28.75, 23.65, 22.44, 13.98; FT-IR (neat, cm^{-1}): 1714, 1603, 1516, 1494, 1467, 1406, 1344, 1182, 1109, 1064, 1016; HRMS (ESI positive, m/z): found 272.1268 ($[\text{M}+\text{Na}]^+$), calc. for $\text{C}_{14}\text{H}_{19}\text{NNaO}_3$ ($\text{M}+\text{Na}$): 272.1263. Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.46 (Cyclohexane/EtOAc: 9/1).

1-(4-(Trifluoromethyl)phenyl)octan-2-one (**4d**)

Compound **4d** was prepared according to the general procedure using 1-(4-nitrophenyl)octane-1,2-dione **3d** (100 mg, 0.35 mmol). The title compound was obtained after flash chromatography as brown liquid; yield 79% (75.1 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.58 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 3.75 (s, 2H), 2.47 (t, J = 7.4 Hz, 2H), 1.61–1.54 (m, 2H), 1.30–1.20 (m, 6H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 207.38, 138.25, 129.81, 125.51, 49.50, 42.50, 31.53, 28.76, 23.67, 22.46, 14.00; ^{19}F NMR (188 MHz, CDCl_3) δ -62.94; FT-IR (neat, cm^{-1}): 1716, 1419, 1368, 1325, 1164, 1126, 1111, 1067, 1020; HRMS (ESI positive, m/z): found 295.1287 ($[\text{M}+\text{Na}]^+$), calc. for $\text{C}_{15}\text{H}_{19}\text{F}_3\text{NaO}$ ($\text{M}+\text{Na}$): 295.1286. Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.52 (Cyclohexane/EtOAc: 9/1).

Methyl 4-(2-oxooctyl)benzoate (**4e**)

Compound **4e** was prepared according to the general procedure using methyl 4-(2-oxooctanoyl)benzoate **3e** (100 mg, 0.36 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 68% (64.5 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.93 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 3.84 (s, 3H), 3.67 (s, 2H), 2.38 (t, J = 7.4 Hz, 2H), 1.56–1.46 (m, 2H), 1.29–1.12 (m, 6H), 0.79 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 207.52, 166.85, 139.52, 129.91, 129.49, 128.87, 52.08, 49.86, 42.38, 31.52, 28.74, 23.65, 22.44, 13.99; FT-IR (neat, cm^{-1}): 1725, 1712, 1612, 1436, 1280, 1107, 1021, 969, 906; HRMS (ESI positive, m/z): found 285.1467 ($[\text{M}+\text{Na}]^+$), calc. for $\text{C}_{16}\text{H}_{22}\text{NaO}_3$ ($\text{M}+\text{Na}$): 285.1467; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 80/20; R_f = 0.40 (Cyclohexane/EtOAc: 7/3).

4-(2-Oxoethyl)benzonitrile (**4f**)

Compound **4f** was prepared according to the general procedure using 4-(2-oxooctanoyl)benzonitrile **3f** (100 mg, 0.41 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 70% (66.0 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, J = 7.6 Hz, 2H), 7.30 (d, J = 7.7 Hz, 2H), 3.76 (s, 2H), 2.48 (t, J = 7.3 Hz, 2H), 1.59–1.55 (m, 2H), 1.25–1.15 (m, 6H), 0.86 (t, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 206.76, 139.61, 132.33, 130.32, 118.74, 110.96, 49.55, 42.75, 31.52, 28.75, 23.65, 22.45, 14.01; FT-IR (neat, cm^{-1}): 2229, 1716, 1609, 1505, 1468, 1416, 1377, 1306, 1273, 1178, 1127, 1100, 1065, 1021; HRMS (ESI positive, m/z): found 230.1542 ($[\text{M}+\text{H}]^+$), calc. for $\text{C}_{15}\text{H}_{19}\text{NO}$ ($\text{M}+\text{H}$): 230.1545; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 80/20; R_f = 0.35 (Cyclohexane/EtOAc: 7/3).

1-(4-Acetylphenyl)octan-2-one (**4g**)

Compound **4g** was prepared according to the general procedure using 1-(4-acetylphenyl)octane-1,2-dione **3g** (100 mg, 0.38 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 70% (66.2 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.93 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 3.75 (s, 2H), 2.60 (s, 3H), 2.47 (t, J = 7.4 Hz, 2H), 1.45–1.10 (m, 8H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 207.45, 197.69, 139.73, 135.89, 129.70, 128.70, 49.80, 42.48, 31.52, 28.76, 26.61, 23.67, 22.45, 14.00; FT-IR (neat, cm^{-1}): 2958, 2930, 2856, 1760, 1716, 1683, 1607, 1361, 1268, 1228, 1215, 1184, 1080, 1036, 956, 904; HRMS (ESI positive, m/z): found 269.1521 ($[\text{M}+\text{Na}]^+$), calc. for

C₁₆H₂₂NaO₂ (M+Na): 269.1517. Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.45 (Cyclohexane/EtOAc: 9/1).

1-(4-Fluorophenyl)octan-2-one (4i)

Compound **4i** was prepared according to the general procedure using 1-(4-fluorophenyl)octane-1,2-dione **3i** (100 mg, 0.42 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 85% (80.0 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.17-7.14 (m, 2H), 7.03-6.99 (m, 2H), 3.65 (s, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 1.57-1.53 (m, 2H), 1.30-1.24 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 208.39, 162.07 (d, *J* = 245.4 Hz), 131.03 (d, *J* = 7.9 Hz), 130.19, 115.63 (d, *J* = 21.4 Hz), 49.17, 42.25, 31.66, 28.91, 23.84, 22.58, 14.11; ¹⁹F NMR (188 MHz, CDCl₃) δ -115.97; FT-IR (neat, cm⁻¹): 1714, 1602, 1581, 1510, 1466, 1414, 1333, 1223, 1180, 1158, 1129, 1035, 1008; HRMS (ESI positive, *m/z*): found 223.1498 ([M+H]⁺), calc. for C₁₄H₂₀FO (M+H): 223.1498; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.65 (Cyclohexane/EtOAc: 95/5).

1-(4-Chlorophenyl)octan-2-one (4j)

Compound **4j** was prepared according to the general procedure using 1-(4-chlorophenyl)octane-1,2-dione **3j** (100 mg, 0.40 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 97% (91.6 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.29 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 3.65 (s, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 1.57-1.50 (m, 2H), 1.30-1.23 (m, 6H), 0.86 (t, *J* = 6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 208.01, 132.74, 130.76, 128.78, 49.18, 42.22, 31.54, 28.77, 23.68, 22.47, 14.01; FT-IR (neat, cm⁻¹): 1758, 1713, 1610, 1512, 1492, 1467, 1407, 1378, 1269, 1214, 1167, 1128, 1091, 1065, 1016, 908; HRMS (ESI positive, *m/z*): found 239.1197 ([M+H]⁺), calc. for C₁₄H₂₀ClO (M+H): 239.1203; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.60 (Cyclohexane/EtOAc: 95/5).

1-(4-Bromophenyl)octan-2-one (4k)

Compound **4k** was prepared according to the general procedure using 1-(4-bromophenyl)octane-1,2-dione **3i** (100 mg, 0.336 mmol). The title compound was obtained after flash chromatography as brown liquid; yield 75% (71.5 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 8.2 Hz, 2H), 3.63 (s, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 1.60-1.43 (m, 2H), 1.26-1.10 (m, 6H), 0.86 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 207.96, 133.24, 131.75, 131.15, 121.00, 49.26, 42.25, 31.55, 28.78, 23.68, 22.48, 14.04; FT-IR (neat, cm⁻¹): 1713, 1589, 1488, 1466, 1405, 1187, 1128, 1071, 1012, 909; HRMS (ESI positive, *m/z*): found 305.0516 ([M+Na]⁺), calc. for C₁₄H₁₉BrNaO (M+Na): 305.0517; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.55 (Cyclohexane/EtOAc: 95/5).

1-(4-Iodophenyl)octan-2-one (4l)

Compound **4l** was prepared according to the general procedure using 1-(4-iodophenyl)octane-1,2-dione **3l** (100 mg, 0.29 mmol). The title compound was obtained after flash chromatography as brown liquid; yield 72% (69.1 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.65 (d, *J* = 8.3 Hz, 2H), 6.94 (d, *J* = 8.2 Hz, 2H), 3.62 (s, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.55-1.50 (m, 2H), 1.28-1.23 (m, 6H), 0.86 (t, *J*

= 6.6 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 207.82, 137.84, 134.07, 131.53, 92.52, 49.48, 42.37, 31.65, 28.89, 23.82, 22.57, 14.11; FT-IR (neat, cm⁻¹): 1713, 1581, 1485, 1465, 1401, 1377, 1261, 1185, 1126, 1103, 1060, 1007; HRMS (ESI positive, *m/z*): found 331.0556 ([M+H]⁺), calc. for C₁₄H₂₀IO (M+H): 331.0559; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.50 (Cyclohexane/EtOAc: 95/5).

1-(3-Chlorophenyl)octan-2-one (4m)

Compound **4m** was prepared according to the general procedure using 1-(3-chlorophenyl)octane-1,2-dione **3m** (100 mg, 0.396 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 70% (66.1 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.21-7.15 (m, 2H), 7.13 (s, 1H), 7.05 – 6.95 (m, 1H), 3.58 (s, 2H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.51-1.44 (m, 2H), 1.26-1.17 (m, 6H), 0.79 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 207.62, 136.20, 134.42, 129.83, 129.55, 127.61, 127.16, 49.41, 42.29, 31.53, 28.76, 23.67, 22.45, 13.99; FT-IR (neat, cm⁻¹): 1714, 1598, 1574, 1515, 1476, 1433, 1365, 1271, 1208, 1126, 1080; HRMS (ESI positive, *m/z*): found 261.1022 ([M+Na]⁺), calc. for C₁₄H₁₉ClNaO (M+Na): 261.1030; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.65 (Cyclohexane/EtOAc: 95/5).

1-(3-Bromophenyl)octan-2-one (4n)

Compound **4n** was prepared according to the general procedure using 1-(3-bromophenyl)octane-1,2-dione **3n** (100 mg, 0.336 mmol). The title compound was obtained after flash chromatography as brown liquid; yield 65% (61.9 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.51-7.31 (m, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 3.65 (s, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 1.58-1.53 (m, 2H), 1.29-1.24 (m, 6H), 0.86 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 207.57, 136.49, 132.44, 130.09, 128.07, 122.63, 49.35, 42.30, 31.53, 28.76, 23.67, 22.45, 13.99; FT-IR (neat, cm⁻¹): 1714, 1596, 1569, 1473, 1429, 1406, 1376, 1207, 1127, 1072, 997; HRMS (ESI positive, *m/z*): found 305.0514 ([M+Na]⁺), calc. for C₁₄H₁₉BrNaO (M+Na): 305.0517; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.52 (Cyclohexane/EtOAc: 95/5).

1-(4-Methoxyphenyl)octan-2-one (4o)

Compound **4o** was prepared according to the general procedure using 1-(4-methoxyphenyl)octane-1,2-dione **3o** (100 mg, 0.403 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 77% (72.7 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.61 (s, 2H), 2.42 (t, *J* = 7.4 Hz, 2H), 1.59-1.53 (m, 2H), 1.28-1.20 (m, 6H), 0.85 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 209.09, 158.59, 130.38, 126.45, 114.12, 55.26, 49.24, 41.84, 31.55, 28.80, 23.75, 22.47, 14.00; FT-IR (neat, cm⁻¹): 1712, 1612, 1583, 1512, 1466, 1410, 1301, 1248, 1179, 1129, 1036; HRMS (ESI positive, *m/z*): found 235.1700 ([M+H]⁺), calc. for C₁₅H₂₃O₂ (M+H): 235.1698; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 80/20; R_f = 0.60 (Cyclohexane/EtOAc: 70/30).

1-(4-Methoxyphenyl)pentan-2-one (4p) Compound **4p** was prepared according to the general procedure using 1-(4-methoxyphenyl)pentane-1,2-dione **3p** (100 mg, 0.485 mmol). The title compound was obtained after flash

chromatography as yellow liquid; yield 95% (88.6 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.11 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 3.80 (s, 3H), 3.61 (s, 2H), 2.41 (t, *J* = 7.3 Hz, 2H), 1.59-1.56 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 208.84, 158.60, 130.37, 126.43, 114.12, 55.25, 49.25, 43.73, 17.21, 13.65.

1-(2-Methoxyphenyl)pentan-2-one (4q)

Compound **4q** was prepared according to the general procedure using 1-(2-methoxyphenyl)pentane-1,2-dione **3q** (100 mg, 0.485 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 93% (86.7 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.27 (td, *J* = 7.5, 1.7 Hz, 1H), 7.15 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.98-6.86 (m, 2H), 3.82 (s, 3H), 3.68 (s, 2H), 2.43 (t, *J* = 7.3 Hz, 2H), 1.78-1.46 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 209.48, 157.90, 131.71, 128.93, 124.32, 121.16, 110.99, 55.84, 45.25, 44.35, 17.80, 14.24; HRMS (ESI positive, *m/z*): found 193.1224 ([M+H]⁺), calc. for C₁₅H₂₃O₂ (M+H): 193.1229; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 80/20.

1-(4-Hydroxy-3,5-dimethoxyphenyl)octan-2-one (4r)

Compound **4r** was prepared according to the general procedure using 1-(3,4,5-trimethoxyphenyl)octane-1,2-dione **3r** (100 mg, 0.325 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 50% (45.5 mg); ¹H NMR (300 MHz, CDCl₃) δ 6.41 (s, 2H), 5.45 (br, 1H), 3.88 (s, 6H), 3.58 (s, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.59-1.50 (m, 2H), 1.29-1.20 (m, 6H), 0.86 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 208.94, 147.12, 133.75, 125.33, 106.02, 56.31, 50.21, 41.71, 31.56, 28.80, 23.73, 22.47, 14.00; FT-IR (neat, cm⁻¹): 1706, 1614, 1518, 1462, 1429, 1367, 1331, 1245, 1217, 1115, 903; HRMS (ESI positive, *m/z*): found 303.1566 ([M+Na]⁺), calc. for C₁₆H₂₄NaO₄ (M+Na): 303.1572; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 70/30; R_f = 0.30 (Cyclohexane/EtOAc: 70/30).

1-(4-Hydroxyphenyl)octan-2-one (4s)

Compound **4s** was prepared according to the general procedure using 1-(4-hydroxyphenyl)octane-1,2-dione **3s** (100 mg, 0.427 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 60% (56.4 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.05 (d, *J* = 8.3 Hz, 2H), 6.78 (d, *J* = 8.3 Hz, 2H), 5.06 (br, 1H), 3.60 (s, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.73-1.45 (m, 2H), 1.30-1.20 (m, 6H), 0.86 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 209.40, 154.65, 130.56, 126.44, 115.59, 49.20, 41.89, 31.53, 28.79, 23.75, 22.45, 13.99; FT-IR (neat, cm⁻¹): 1711, 1696, 1615, 1595, 1514, 1486, 1443, 1364, 1270, 1223, 1107, 1065, 1014; HRMS (ESI positive, *m/z*): found 243.1358 ([M+Na]⁺), calc. for C₁₄H₂₀NaO₂ (M+Na): 243.1361; Flash chromatography conditions: Cyclohexane/EtOAc 70/30 to 50/50; R_f = 0.50 (Cyclohexane/EtOAc: 50/50).

1-(*p*-Tolyl)octan-2-one (4t)

Compound **4t** was prepared according to the general procedure using 1-(*p*-tolyl)octane-1,2-dione **3t** (100 mg, 0.43 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 97% (91.2 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.20-7.05 (m, 4H), 3.63 (s, 2H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.33 (s, 3H), 1.69-1.44 (m, 2H), 1.24-1.20 (m, 4H), 0.85 (t, *J* = 6.6 Hz, 3H); ¹³C NMR

(75 MHz, CDCl₃) δ 208.93, 136.53, 131.32, 129.38, 129.25, 49.76, 41.88, 31.56, 28.79, 23.74, 22.48, 21.06, 14.01.

1-(*p*-Tolyl)pentan-2-one (4u) Compound **4u** was prepared according to the general procedure using 1-(*p*-tolyl)pentane-1,2-dione **3u** (100 mg, 0.5256 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 90% (83.4 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.20-7.04 (m, 4H), 3.63 (s, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 1.62-1.50 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 208.74, 136.53, 131.31, 129.38, 129.24, 49.78, 43.77, 21.05, 17.20, 13.64; FT-IR (neat, cm⁻¹): 1711, 1608, 1513, 1486, 1464, 1409, 1379, 1363, 1277, 1181, 1123, 1054, 1039, 1015; HRMS (ESI positive, *m/z*): found 199.1100 ([M+Na]⁺), calc. for C₁₂H₁₆NaO (M+Na): 199.1099; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.85 (Cyclohexane/EtOAc: 98/2).

1-(4-(Methylthio)phenyl)octan-2-one (4v)

Compound **4v** was prepared according to the general procedure using 1-(4-(methylthio)phenyl)octane-1,2-dione **3v** (100 mg, 0.38 mmol). The title compound was obtained after flash chromatography as pink liquid; yield 96% (90.9 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.22 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 3.63 (s, 2H), 2.47 (s, 3H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.65-1.41 (m, 2H), 1.29-1.20 (m, 6H), 0.85 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 208.51, 137.02, 131.19, 129.86, 126.99, 49.49, 42.04, 31.55, 28.79, 23.71, 22.47, 15.96, 14.02; FT-IR (neat, cm⁻¹): 1712, 1589, 1555, 1493, 1466, 1437, 1403, 1377, 1321, 1261, 1184, 1127, 1093, 1064, 1016, 968; HRMS (ESI positive, *m/z*): found 273.1281 ([M+Na]⁺), calc. for C₁₅H₂₂NaOS (M+Na): 273.1289; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 80/20; R_f = 0.45 (Cyclohexane/EtOAc: 70/30).

***N*-(4-(2-Oxoocetyl)phenyl)acetamide (4w)**

Compound **4w** was prepared according to the general procedure using *N*-(4-(2-oxooctanoyl)phenyl)acetamide **3w** (100 mg, 0.3632 mmol). The title compound was obtained after flash chromatography as brown liquid; yield 98% (93.0 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 3.63 (s, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.17 (s, 3H), 1.61-1.46 (m, 2H), 1.35-1.02 (m, 6H), 0.85 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 209.05, 168.64, 136.94, 130.06, 129.87, 120.21, 49.41, 42.11, 31.53, 28.77, 24.44, 23.72, 22.45, 14.00; FT-IR (neat, cm⁻¹): 1712, 1668, 1603, 1538, 1514, 1467, 1412, 1371, 1319, 1264, 1178, 1128, 1066; HRMS (ESI positive, *m/z*): found 262.1802 ([M+H]⁺), calc. for C₁₆H₂₃NO₂ (M+H): 262.1807; Flash chromatography conditions: Cyclohexane/EtOAc 70/0 to 50/50; R_f = 0.55 (Cyclohexane/EtOAc: 50/50).

1-(Naphthalen-2-yl)octan-2-one (4x)

Compound **4x** was prepared according to the general procedure using 1-(naphthalen-2-yl)octane-1,2-dione **3x** (100 mg, 0.37 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 92% (87.2 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.75-7.61 (m, 3H), 7.54 (s, 1H), 7.40-7.30 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 1H), 3.69 (s, 2H), 2.34 (t, *J* = 7.4 Hz, 2H), 1.50-1.40 (m, 2H), 1.17-1.03 (m, 6H), 0.73 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 208.49, 133.62, 132.46, 132.01,

128.35, 128.10, 127.69, 127.62, 127.52, 126.19, 125.77, 50.29, 42.09, 31.58, 28.81, 23.75, 22.48, 14.01; FT-IR (neat, cm^{-1}): 1713, 1632, 1600, 1509, 1466, 1406, 1260, 1126, 1069, 1017, 959, 908; HRMS (ESI positive, m/z): found 255.1749 ($[\text{M}+\text{H}]^+$), calc. for $\text{C}_{18}\text{H}_{23}\text{O}$ ($\text{M}+\text{H}$): 255.1749; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 98/2; R_f = 0.70 (Cyclohexane/EtOAc: 95/5).

6-Hydroxy-1-(4-methoxyphenyl)hexan-2-one (4y)

Compound **4y** was prepared according to the general procedure using 6-hydroxy-1-(4-methoxyphenyl)hexane-1,2-dione **3y** (100 mg, 0.42 mmol). The title compound was obtained after flash chromatography as colorless liquid; yield 80% (75.3 mg); ^1H NMR (300 MHz, CDCl_3) δ 7.11 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 3.79 (s, 3H), 3.61 (s, 2H), 3.11 (t, J = 6.7 Hz, 2H), 2.45 (t, J = 7.0 Hz, 2H), 1.99-1.49 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 208.06, 158.70, 130.36, 126.16, 114.22, 55.28, 49.30, 40.30, 32.72, 24.55, 6.08; FT-IR (neat, cm^{-1}): 1710, 1611, 1583, 1511, 1462, 1406, 1301, 1245, 1177, 1112, 1032; HRMS (ESI positive, m/z): found 223.1340 ($[\text{M}+\text{H}]^+$), calc. for $\text{C}_{13}\text{H}_{19}\text{O}_3$ ($\text{M}+\text{H}$): 223.1334; Flash chromatography conditions: Cyclohexane/EtOAc 70/30 to 50/50; R_f = 0.45 (Cyclohexane/EtOAc: 70/30).

6-Methoxy-1-(4-methoxyphenyl)hexan-2-one (4z)

Compound **4z** was prepared according to the general procedure using 6-methoxy-1-(4-methoxyphenyl)hexane-1,2-dione **3z** (100 mg, 0.40 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 78% (73.6 mg); ^1H NMR (400 MHz, CDCl_3) δ 7.03 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 3.70 (s, 3H), 3.53 (s, 2H), 3.33-2.86 (m, 5H), 2.38 (t, J = 7.2 Hz, 2H), 1.55-1.48 (m, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 208.58, 158.69, 130.42, 126.44, 114.19, 72.43, 58.52, 55.28, 49.25, 41.47, 29.01, 20.50; FT-IR (neat, cm^{-1}): 1713, 1613, 1598, 1573, 1513, 1464, 1408, 1363, 1301, 1248, 1178, 1119, 1080, 1036; HRMS (ESI positive, m/z): found 259.1310 ($[\text{M}+\text{Na}]^+$), calc. for $\text{C}_{13}\text{H}_{20}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}$): 259.1310; Flash chromatography conditions: Cyclohexane/EtOAc 90/10 to 70/30; R_f = 0.60 (Cyclohexane/EtOAc: 70/30).

1-(Quinolin-6-yl)octan-2-one (4za)

Compound **4za** was prepared according to the general procedure using 1-(quinolin-6-yl)octane-1,2-dione **3za** (100 mg, 0.37 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 65% (61.6 mg); ^1H NMR (300 MHz, CDCl_3) δ 8.89 (d, J = 4.2 Hz, 1H), 8.29-7.92 (m, 2H), 7.64 (s, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.50-7.40 (m, 1H), 3.87 (s, 2H), 2.49 (t, J = 7.4 Hz, 2H), 1.95-1.42 (m, 2H), 1.28-1.22 (m, 6H), 0.83 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 208.01, 150.28, 147.41, 135.73, 132.80, 131.22, 129.78, 128.30, 127.90, 121.33, 49.79, 42.39, 31.52, 28.77, 23.70, 22.43, 13.96; FT-IR (neat, cm^{-1}): 1712, 1622, 1595, 1572, 1501, 1466, 1406, 1379, 1366, 1325, 1119, 1065, 1032, 957; HRMS (ESI positive, m/z): found 256.1707 ($[\text{M}+\text{H}]^+$), calc. for $\text{C}_{17}\text{H}_{22}\text{NO}$ ($\text{M}+\text{H}$): 256.1701; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 70/30; R_f = 0.65 (Cyclohexane/EtOAc: 50/50).

(2R,3R,4S,5R,6S)-2-(acetoxymethyl)-6-((4-(2-oxooctyl)phenyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (4zb)

Compound **4zb** was prepared according to the general procedure using (2R,3R,4S,5R,6S)-2-(acetoxymethyl)-6-((4-(2-oxooctanoyl)phenyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate **3zb** (100 mg, 0.1722 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 50% (48.8 mg); $[\alpha]_{\text{D}}^{25}$ -11 (c, 0.55 in CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 7.45 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 5.22 (t, J = 9.3 Hz, 1H), 5.04 (t, J = 9.8 Hz, 1H), 4.97 (t, J = 9.7 Hz, 1H), 4.69 (d, J = 10.1 Hz, 1H), 4.29-4.12 (m, 2H), 3.75-3.70 (m, 1H), 3.68 (s, 1H), 2.46 (t, J = 7.4 Hz, 2H), 2.08 (s, 6H), 2.02 (s, 3H), 1.99 (s, 3H), 1.58-1.54 (m, 2H), 1.28-1.24 (m, 6H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 207.99, 170.67, 170.27, 169.50, 169.36, 134.95, 133.51, 130.42, 130.17, 86.01, 75.98, 74.12, 70.12, 68.38, 62.29, 49.57, 42.53, 31.69, 28.93, 23.85, 22.60, 20.87, 20.71, 14.14; FT-IR (neat, cm^{-1}): 2930, 1756, 1713, 1603, 1367, 1248, 1214, 1037, 915; HRMS (ESI positive, m/z): found 589.2083 ($[\text{M}+\text{Na}]^+$), calc. for $\text{C}_{28}\text{H}_{38}\text{O}_{10}\text{SNa}$ ($\text{M}+\text{Na}$): 589.2078; Flash chromatography conditions: Cyclohexane/EtOAc 70/30 to 50/50; R_f = 0.30 (Cyclohexane/EtOAc: 50/50).

4-(1-Hydroxy-2-oxooctyl)benzaldehyde (5)

Compound **5** was prepared according to the general procedure using 4-(2-oxooctanoyl)benzaldehyde **3h** (100 mg, 0.41 mmol). The title compound was obtained after flash chromatography as yellow liquid; yield 59%; ^1H NMR (300 MHz, CDCl_3) δ 10.03 (s, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 5.16 (s, 1H), 2.49-2.18 (m, 2H), 1.48-0.99 (m, 8H), 0.82 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 208.46, 191.61, 144.62, 136.53, 130.27, 128.00, 79.37, 37.91, 31.31, 28.58, 23.55, 22.35, 13.93; FT-IR (neat, cm^{-1}): 2958, 2929, 2855, 1703, 1607, 1579, 1467, 1363, 1306, 1209, 1167, 904; HRMS (ESI positive, m/z): found 271.1315 ($[\text{M}+\text{Na}]^+$), calc. for $\text{C}_{15}\text{H}_{20}\text{NaO}_3$ ($\text{M}+\text{Na}$): 271.1310; Flash chromatography conditions: Cyclohexane/EtOAc 100/0 to 90/10; R_f = 0.50 (Cyclohexane/EtOAc: 9/1).

Ethyl 2-(4-methoxyphenyl)acetate (9a)

Compound **9a** was prepared according to the general procedure using ethyl 2-(4-methoxyphenyl)-2-oxoacetate **6a** (100 mg, 0.48 mmol). ^1H NMR (300 MHz, CDCl_3) δ 7.20 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.55 (s, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.92, 158.66, 130.23, 126.24, 113.97, 60.75, 55.23, 40.52, 14.18.

Ethyl 2-(2-methoxyphenyl)acetate (9b)

Compound **9b** was prepared according to the general procedure using ethyl 2-(2-methoxyphenyl)-2-oxoacetate **6b** (100 mg, 0.48 mmol). ^1H NMR (300 MHz, CDCl_3) δ 7.33-7.02 (m, 2H), 6.89-6.75 (m, 2H), 4.08 (q, J = 7.1 Hz, 2H), 3.73 (s, 3H), 3.54 (s, 2H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.86, 157.54, 130.82, 128.46, 123.23, 120.49, 110.48, 60.56, 55.41, 36.01, 14.23.

Ethyl 2-(4-(methylthio)phenyl)acetate (9c) Compound **9c** was prepared according to the general procedure using ethyl 2-(4-(methylthio)phenyl)-2-oxoacetate **6c** (100 mg, 0.45 mmol). ^1H NMR (300 MHz, CDCl_3) δ 7.25-7.20 (m, 4H), 4.14 (q, J = 7.1 Hz, 2H), 3.56 (s, 2H), 2.47 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.49, 137.12, 131.01, 129.70, 126.92, 60.88, 40.85,

15.99, 14.18.

Ethyl 2-(3-chloro-4-(methylthio)phenyl)acetate (9d)

Compound **9d** was prepared according to the general procedure using ethyl 2-(3-chloro-4-(methylthio)phenyl)-2-oxoacetate **6d** (100 mg, 0.386 mmol). ¹H NMR (300 MHz, CDCl₃) δ 7.28 (s, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.54 (s, 2H), 2.46 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.00, 136.40, 131.81, 130.14, 128.16, 125.81, 61.08, 40.39, 15.27, 14.17; FT-IR (neat, cm⁻¹): 1733, 1551, 1470, 1435, 1397, 1367, 1335, 1263, 1175, 1156, 1125, 1095, 1033, 903; HRMS (ESI positive, *m/z*): found 267.0214 ([M+Na]⁺), calc. for C₁₁H₁₃O₂NaS (M+Na): 267.0222.

2-(4-(methylthio)phenyl)acetic acid (10a) Compound **10a** was prepared according to the general procedure using 2-(4-(methylthio)phenyl)-2-oxoacetic acid **7a** (100 mg, 0.386 mmol). The title compound was obtained after flash chromatography as white solid; yield 91% (67.6 mg); mp: 98.5-99.4 °C; ¹H NMR (300 MHz, CDCl₃) δ 10.81 (broad, 1H), 7.68-6.37 (m, 4H), 3.52 (s, 2H), 2.38 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.95, 137.64, 130.00, 129.83, 126.90, 40.49, 15.90; FT-IR (neat, cm⁻¹): 2920, 2742, 1712, 1680, 1605, 1495, 1425, 1406, 1348, 1257, 1202, 1115, 1089, 1016, 971, 907; found 205.0307 ([M+Na]⁺), calc. For C₉H₁₀NaO₂S (M+Na) 205.0299. Flash chromatography conditions: Cyclohexane/EtOAc 70/30 to 50/50; R_f = 0.45 (Cyclohexane/EtOAc: 70/30).

2-(4-methoxyphenyl)acetic acid (10b) Compound **10b** was prepared according to the general procedure using 2-(4-(methoxyphenyl)phenyl)-2-oxoacetic acid **7a** (100 mg, 0.5551 mmol). The title compound was obtained after flash chromatography as white solid; yield 90% (83.0 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.20 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.60 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.66, 158.86, 130.40, 125.39, 114.08, 55.26, 40.12.

Ethyl-2-(4-methoxyphenyl)-2-(2-tosylhydrazono)acetate (8)

A solution of compound **6a** (1 mmol) in EtOH (3 mL) was added to a stirred mixture of *p*-toluenesulfonyl hydrazide (1.1 mmol) in ethanol (3 mL) containing H₂SO₄ (0.015 mmol). The reaction was refluxed at 85 °C overnight then cooled to room temperature. The white precipitated solid was filtered, washed with cold MeOH and cold hexane, and then dried under reduced pressure to give crude. The pure compound was obtained after flash chromatography as colorless liquid. Yield 70% (263.5 mg). ¹H NMR (300 MHz, CDCl₃) δ 11.29 (br, 1H), 7.87 (d, *J* = 7.5 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 2.41 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 162.21, 160.63, 144.28, 138.50, 135.57, 129.90, 129.68, 127.94, 126.45, 113.51, 62.34, 55.31, 21.60, 14.01; FT-IR (neat, cm⁻¹): 1731, 1690, 1608, 1513, 1465, 1369, 1347, 1303, 1292, 1255, 1228, 1167, 1123, 1084, 1035, 1016, 989, 920; HRMS (ESI positive, *m/z*): found 399.0984 ([M+Na]⁺), calc. for C₁₈H₂₀O₅N₂NaS (M+Na): 399.0991. Flash chromatography conditions: Cyclohexane/EtOAc 90/10 to 70/30; R_f = 0.45 (Cyclohexane/EtOAc: 80/20).

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References

- [1] G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra, *J. Org. Chem.*, **1979**, *44*, 1247-1251.
- [2] G. A. Olah, B. G. B. Gupta, S. C. Narang, *Synthesis*, **1977**, 583-584.
- [3] L. Z. Yuan, D. Renko, I. Khelifi, O. Provot, J. D. Brion, A. Hamze, M. Alami, *Org. Lett.*, **2016**, *18*, 3238-3241.
- [4] A similar observation was reported in CH₃CN, see: G. A. Olah, S. C. Narang, *Tetrahedron*, **1982**, *38*, 2225-2277.
- [5] G. Xu, L. Feng, P. Song, F. Xu, A. Li, Y. Wang, Y. Shen, X. Wu, Q. Luo, X. Wu, Y. Sun, X. Wu, Q. Xu, *Int. Immunopharmacol.*, **2016**, *38*, 175-185.
- [6] See for examples: a) M. Zhao, B. Lu, G. Ding, K. Ren, X. Xiea, Z. Zhang, *Org. Biomol. Chem.*, **2016**, *14*, 2723-2730. b) B. Rao, J. Tang, X. Zeng, *Org. Lett.*, **2016**, *18*, 1678-1681. c) M. Islam, H. Tomiyasu, T. Matsumoto, J. Tanaka, S. Rahman, P. E. Georgiou, C. Redshawd, T. Yamato, *Org. Biomol. Chem.*, **2015**, *13*, 9055-9064.
- [7] L. M. Stephenson, L. C. Falk, *J. Org. Chem.*, **1976**, *41*, 2928. b) Y. Kamochi, T. Kudo, T. Masuda, A. Takadate, *Chem. Pharm. Bull.*, **2005**, *53*, 1017-1020.
- [8] When the deoxygenation of benzil (1,2-diphenylethanedione) was achieved in CH₂Cl₂, after 3 days of reaction, a complex mixture containing benzil (6%), benzoin (2-hydroxy-1,2-diphenylethan-1-one) (13%), deoxybenzoin (11%) and 2,2'-oxybis(1,2-diphenylethan-1-one) (43%) and other unidentified by-products was obtained.
- [9] a) C. Mousset, O. Provot, A. Hamze, J. Bignon, J. D. Brion, M. Alami, *Tetrahedron*, **2008**, *64*, 4287-4294. b) C. Mousset, A. Giraud, O. Provot, A. Hamze, J. Bignon, J.M. Liu, S. Thoret, J. Dubois, J. D. Brion, M. Alami, *Bioorg. Med. Chem. Lett.*, **2008**, *18*, 3266-3271. c) A. Giraud, O. Provot, J.F. Peyrat, M. Alami, J. D. Brion, *Tetrahedron* **2006**, *62*, 7667-7673.
- [10] For a review concerning the oxidation of diarylalkynes into benzils, see: L.Z. Yuan, A. Hamze, M. Alami, O. Provot, *Synthesis*, **2017**, *49*, 504-525.

- [11] In the presence of 10 equivalents of TMSCl/NaI and after 6 h of stirring at rt in CH₂Cl₂, **3h** was partially reduced and transformed into 4-(1-hydroxy-2-oxooctyl)benzaldehyde **5** (59%). Increasing the reaction time or the number of equivalents of TMSCl/NaI was unsuccessful and led to a mixture of non-identified by-products.

- [12] C. D. Hurd, H. E. Winberg, *J. Am. Chem. Soc.*, **1942**, *64*, 2085-2086.
- [13] A. Bruneau, M. Roche, A. Hamze, J. D. Brion, M. Alami, S. Messaoudi, *Chem. Eur. J.*, **2015**, *21*, 8375-8379.
- [14] R. Sarabu, F. T. Bizzarro, W. L. Corbett, M. T. Dvorozniak, W. Geng, J. F. Grippo, N.-E; Haynes, S. Hutchings, L. Garofalo, K. R. Guertin, D. W. Hiliard, M. Kabat, R. F. Kester, W. Ka, Z. Liang, P. E. Mahaney, L. Marcus, F. M. Matschinsky, D. Moore, J. Racha, R. Radinov, Y. Ren, L. Qi, M. Pignatello, C. L. Spence, T. Steele, J. Teng, J. Grimsby, *J. Med. Chem.*, **2012**, *55*, 7021-7036.
- [15] J. M. Zimbron, M. Seeger-Weibel, H. Hirt, F. Gallou, *Synthesis*, **2008**, *8*, 1221-1226.
- [16] L. Ackermann, L. T. Kaspar, *J. Org. Chem.*, **2007**, *72*, 6149-6153.
- [17] A. Schäfer, A. Wellner, R. Gust, *ChemMedChem*, **2011**, *6*, 794-803.
- [18] D. F. Taber, W. Tian, *J. Org. Chem.*, **2007**, *72*, 3207-3210.
- [19] H. Sadeghiana, N. Attaranb, Z. Jafarib, M. Saberib, M. Pordela, M. Riazib, *Bioorg. Med. Chem.*, **2009**, *17*, 2327-2335.
- [20] N. Ríos-Lombardía, E. Busto, E. García-Urdiales, V. Gotor-Fernández, V. Gotor, *J. Org. Chem.*, **2009**, *74*, 2571-2574.
- [21] B. Song, F. Rudolphi, T. Himmler, L. Gooßen, *Adv. Synth. Catal.*, **2011**, *353*, 1565-1574.
- [22] L. Shen, X. Yang, B. Yang, Q. He, Y. Hu, *Eur. J. Med. Chem.*, **2010**, *45*, 11-18.

Chlorotrimethylsilane and Sodium Iodide: A Useful Combination for the Regioselective Deoxygenation of Arylalkyl- α -Diketones

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Alk = Me, C₃H₇, C₆H₁₃, (CH₂)₄OH, (CH₂)₄OMe
R = NO₂, COMe, Br, Cl, I, CF₃, CN, CO₂Me, OMe
Me, SMe, NHAc, OH, S-sugar,...