Barbier-Type Reactions of Cyclic Acid Anhydrides and Keto Acids Mediated by an SmI_2/(NiI_2-Catalytic) System – Preparation of Disubstituted Lactones

Fouzia Machrouhi, Elena Pârlea, and Jean-Louis Namy*

Laboratoire des Réactions Organiques Sélectives, associé au CNRS, Institut de Chimie Moléculaire d'Orsay, Université Paris-Sud,
F-91405 Orsay, France
Fax: (internat.) + 33-1/69154680
E-mail: jelonamy@icmo.u-psud.fr

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Cyclic acid anhydrides (succinic and glutaric anhydrides and some of their derivatives) undergo fast Barbier-type reactions mediated by samarium diiodide in the presence of catalytic amounts of nickel diiodide (1 mol-% with respect to SmI_2), to give disubstituted lactones in high yields. Without NiI_2 no reaction occurs. Various alkyl and allyl iodides can be used. In these reactions the formation of a samarium keto carboxylate intermediate is likely; as a matter of fact, keto carboxylic acids react under similar conditions to also yield disubstituted lactones. It is demonstrated that lactonisation occurs during hydrolysis of the reaction.

Introduction

Samarium diiodide is known to be a powerful electron donor able to promote a wide range of reductions and coupling reactions.[1][2] The reactions of ketones and aldehydes mediated by samarium(II) compounds have been widely studied (reductions, pinacol couplings, Barbier-Grignard-type reactions etc.).[3][4][5]

The reactions of acid chlorides with these reagents have also been investigated during the last fifteen years.[6][7] Recently, intramolecular and intermolecular Barbier-type reactions on esters mediated by SmI_2 have been reported.[7][8][9]

The lack of studies concerning the reactivity of samarium(II) compounds towards acid anhydrides is surprising. However, reactions between organomagnesium or organolithium compounds and acid anhydrides are not very well documented either.[10] According to the experimental conditions, keto acids, hydroxy acids, or lactones are formed in reactions with succinic and glutaric anhydrides.[11] In a recent work it has been reported that organodimagnesium compounds react with these substrates leading to spirolactones.[12]

Results and Discussion

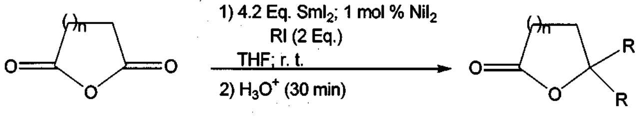
We wish to report some results concerning Barbier-type reactions on cyclic acid anhydrides mediated by SmI_2 in THF in the presence of a catalytic amounts of NiI_2.

Attempts to perform reactions under standard conditions (namely SmI_2/THF without any additives) failed (halides are recovered, whereas acid anhydrides are hydrolysed during the work-up).

On the contrary, use of catalytic amounts of NiI_2 (1 mol-% with respect to SmI_2) gives fast reaction. The precise part of NiI_2 in this reaction has not been cleared up; however, the beneficial effect of catalytic amounts of NiI_2 (and some others transition-metal salts) on reactions mediated by SmI_2 has been previously reported and is again established here.[9]

Disubstituted lactones are obtained in high yield (Table 1).

Table 1. Barbier-type reactions of succinic and glutaric anhydrides



Entry	*n*	R	Reaction time [min]	Isolated yield [%]
1	1	C_2H_5	5	92
2	1	n-C_7H_{15}	15	95
3	1	n-$C_{12}H_{25}$	15	78
4	1	allyl	15	80
5	1	cyclohexyl	5	75
6	1	$Cl(CH_2)_3$	5	95
7	1	$Cl(CH_2)_4$	15	95
8	2	n-C_4H_9	1	95
9	2	allyl	5	75[a]
10	2	n-$C_{12}H_{25}$	5	72

[a] 5-Allyl-5-hydroxy-7-octenoic acid is the product of the reaction.

Trace amounts of hydroxy acids are sometimes detected. Only in the case of allyl iodide and glutaric anhydride is the hydroxy acid the major product (entry 9); 3-chloro-1-iodopropane and 4-chloro-1-iodobutane undergo a regioselective reaction, 5,5-disubstituted 2-tetrahydrofuranones are obtained with chlorine in the terminal position of the alkyl group (entries 6, 7). Use of 1,4-diiodobutane or 1,5-diiodopentane did not allow the preparation of the expected spiro-

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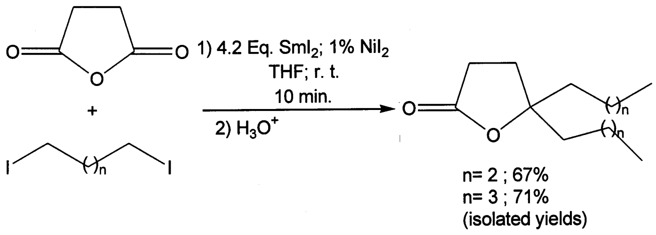
Scheme 1. Reactions of diiodoalkanes with succinic anhydride

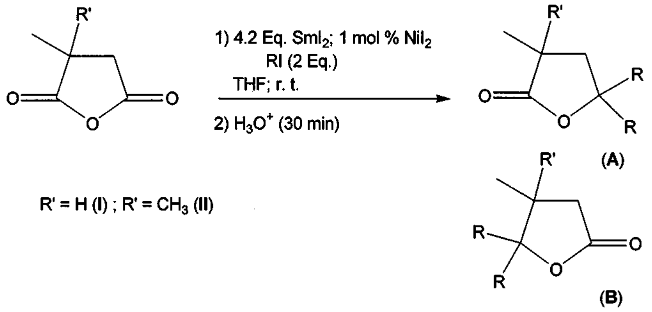


lactones. In these cases, dialkyl lactones were formed (Scheme 1).

Equimolar mixture of 1-iodobutane and succinic anhydride did not lead to keto acid but to 5,5-dibutyl-2-tetrahydrofuranone in yields close to 50%. This result indicates that the species which is formed after the first reaction with 1-iodobutane is more reactive than the starting acid anhydride.

Mono- and disubstituted succinic anhydrides were also studied. The results are gathered in Table 2.

Table 2. Barbier-type reactions of substituted succinic anhydrides



Entry	Acid anhydride	R	Reaction time [min]	Isolated yield [%]	A/B
1	I	n-C_7H_{15}	10	95	60:40
2	I	n-$C_{12}H_{25}$	1	89	50:50
3	II	C_2H_5	2	95	80:20
4	II	n-C_7H_{15}	10	95	60:40
5	II	n-$C_{12}H_{25}$	2	85	> 99:1
6	II	allyl	1	95	70:30

In all experiments, the lactones are produced in high yields with short reaction times. The reactions are not very sensitive to steric hindrance as two regioisomers are obtained. However, with predominance of the lactone arising from attack on the less hindered carbonyl group is predominant. In one case (entry 5) a single regioisomer was isolated.

It was also possible to perform this reaction on *trans*-hexahydrophthalic anhydride and on *cis*-1,2,3,6-tetrahydrophthalic anhydride (Scheme 2).

In all of these reactions, the formation of a samarium keto carboxylate is likely. In order to gain some insights into mechanistic pathways, we have tested reactions of 4-oxopentanoic acid (levulinic acid) and 5-oxohexanoic acid with iodoalkanes, mediated by SmI_2 in the presence of a catalytic amount of NiI_2 (Table 3).

Scheme 2. Reactions of *trans*-hexahydrophtalic and *cis*-tetrahydrophtalic anhydrides

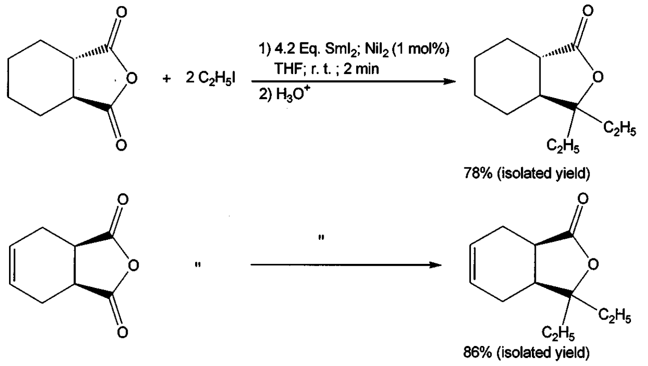
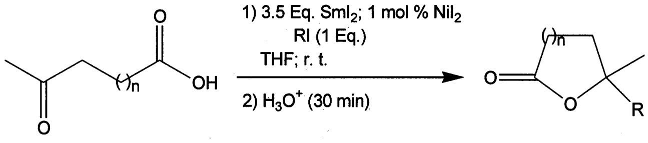


Table 3. Barbier-type reactions of keto carboxylic acids



Entry	n	RI	Isolated yield [%]
1	1	none	95[a]
2	1	n-C_4H_9I	95
3	1	n-$C_7H_{15}I$	85
4	2	none	95[b]
5	2	n-C_4H_9I	95
6	2	n-$C_7H_{15}I$	86

[a] 5-Methyl-2-tetrahydrofuranone. – [b] 6-Methyl-2-tetrahydropyranone.

In each case, lactones were obtained in high yields. These reactions allowed the preparation of various methyl alkyl lactones. Treatment of the keto acids with SmI_2/(NiI_2 catalytic) in the absence of an alkyl halide resulted in the formation of monosubstituted methyl lactones (entries 1, 4).

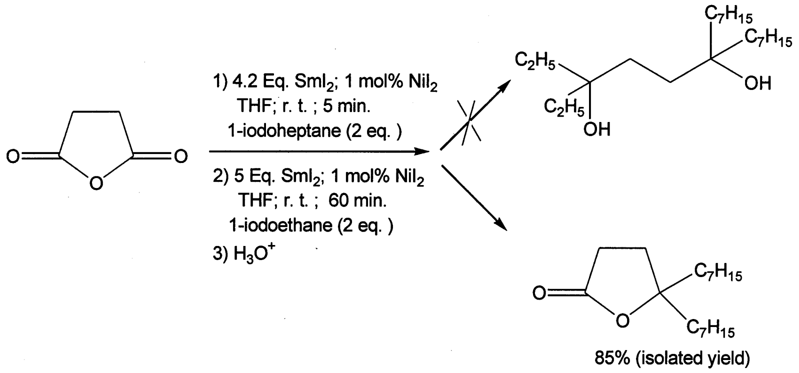
The results reported in Table 2 support the hypothesis of the formation of a samarium keto carboxylate as an intermediate in the reactions of acid anhydrides.

In order to decide whether the lactones are formed before or after hydrolysis of the reaction, the experiment outlined in Scheme 3 has been carried out.

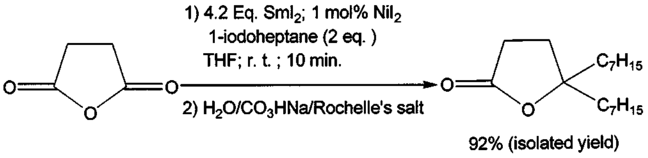
The formation of the lactone prior to hydrolysis should result in the formation of the diol, as we have demonstrated that a lactone is reactive in Barbier-type reactions with alkyl iodides.[9] However, the product of the reaction is the 5,5-diheptyl-2-furanone, thus the formation of the lactone before hydrolysis can be ruled out.

Very recently work-up of reactions mediated by SmI_2 under basic conditions (H_2O/$NaHCO_3$/Rochelle's salt) has been proposed.[13] Results after hydrolysis under basic conditions have been compared to results obtained after hydrolysis under acidic conditions. No effect has been observed. Clearly, the hydroxy acid precursor of the lactone

Scheme 3. Attempt at performing consecutive reactions with succinic anhydride



Scheme 4. Hydrolysis under basic conditions

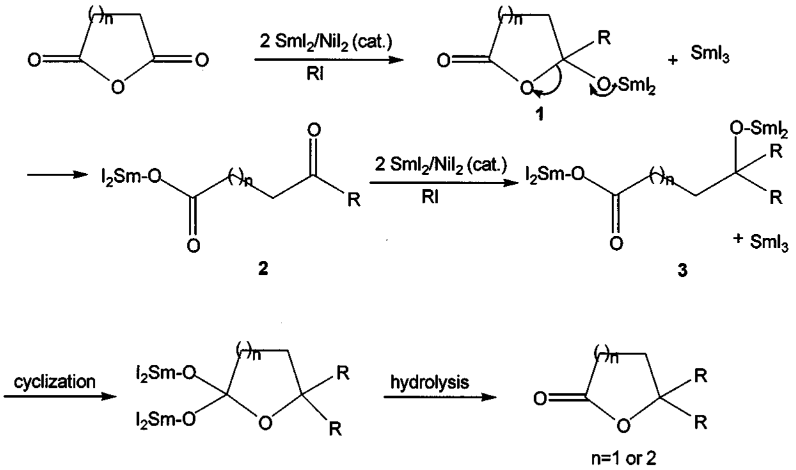


is never obtained whichever the hydrolysis conditions used (Scheme 4).

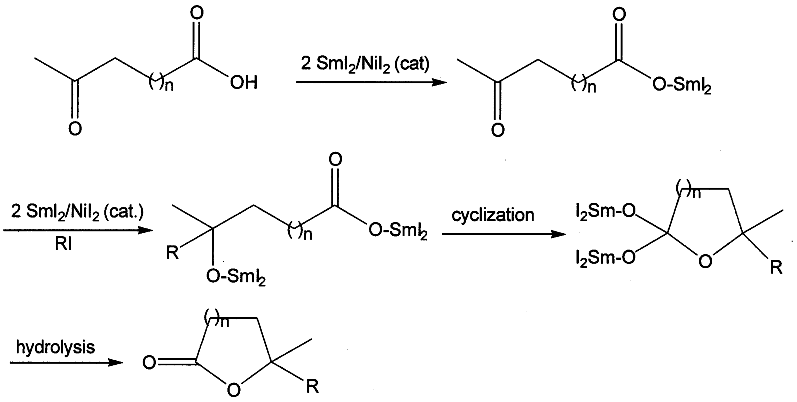
It might be assumed that cyclisation takes place before hydrolysis, without leading to lactone. The following mechanism shown in Scheme 5 can be proposed.

The second Barbier-type reaction of keto carboxylate **2** leading to **3** must be faster than that which gives **1**. A simi-

Scheme 5. Mechanistic scheme for reactions of cyclic acid anhydrides



Scheme 6. Mechanistic scheme for reactions of keto carboxylic acids



lar mechanistic scheme (Scheme 6) accounts for the formation of lactones from keto acids.

The first step of the reaction is probably the formation of a samarium keto carboxylate. We have checked that hexanoic acid reacts instantaneously with SmI_2/NiI_2 (cat.) to give the samarium carboxylate, whereas in the absence of NiI_2, the reaction is very slow.

Conclusion

To conclude, acid anhydrides react in Barbier-type reactions with SmI_2 and alkyl (or allyl) iodides like many other carbonyl compounds. However, reactions must be performed in the presence of a catalytic amount of NiI_2 (esters behave in a similar fashion). Cyclic acid anhydrides and keto acids undergo fast reactions to give disubstituted lactones in high yields.

The preparation of functionalized lactones and reactions with acyclic acid anhydrides are currently under investigation.

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Experimental Section

General Remarks: ^1H- and ^{13}C-NMR spectra were recorded at 250 MHz and 63 MHz respectively with a Bruker AM 250 instrument (unless otherwise stated). Chemical shifts are reported in part per million (δ) downfield from TMS. Coupling constants are reported in Hz. − Infrared (IR) spectra were recorded neat with an FT-IR IFS 66 Bruker and are reported in cm^{-1}. − Mass spectra (MS) were determined with a GC/MS Ribermag R10-10 instrument. Chemical ionisation (CI) was carried out using NH_3 as the reactant gas and electronic impact was performed at 70 eV. High Resolution Mass Spectra were performed with a GC/MS Finningan-MAT-95-S. − Flash chromotography was performed on silica gel (Merck 230−240 mesh; 0.0040−0.0630 mm). − All commercially available organic compounds were distilled before use. Samarium powder (40 mesh) was purchased from the Labelcomat Company. Tetrahydrofuran was distilled under argon from sodium benzophenone ketyl. Samarium diiodide was prepared as previously described.[3] All the reactions were carried out under argon in Schlenk tubes using standard vacuum-line techniques.

General Procedure for Reactions of Acid Anhydrides (and Keto Acids): To a solution of SmI_2 ($4.2\cdot10^{-3}$ mol) in THF (42 ml) was added a solution of NiI_2 ($4.2\cdot10^{-5}$ mol) in THF (4.2 ml). Acid anhydride (10^{-3} mol) and organic halide ($2.0\cdot10^{-3}$ mol) were mixed in THF (4 ml) and added dropwise to SmI_2 within 5 min. The initially deep blue solution turned brown, the mixture was quenched with HCl (0.1 M) and stirred during 30 min to obtain a clear solution and then extracted with ether. The combined extracts were washed with sodium thiosulfate and brine. The organic layer was dried with $MgSO_4$ and the solvents were removed under reduced pressure; the crude material was purified by flash chromatography on silica gel. A similar procedure was used for the reactions with keto acids.

5,5-Diethyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 92%. − ^1H NMR: δ = 0.96 (t, *J* = 7.8 Hz, 6 H), 1.51 (q, *J* = 7.8 Hz, 4 H), 1.77 (t, *J* = 8.7 Hz, 2 H), 1.84 (t, *J* = 8.7 Hz, 2 H). − ^{13}C NMR: δ = 13.8, 22.6, 34.4, 40.8, 89.7, 177.9. − IR ($CHCl_3$): $\tilde{\nu}$ = 2933, 2840, 1740, 1663, 1210, 940. − MS (70 eV, EI): *m/z* (%) = 143 (6) [MH^+], 113 (100) [$C_6H_9O_2{}^+$], 84 (25) [$C_4H_4O_2{}^+$]; CI/NH_3: *m/z* (%) = 142 (27) [M^+], 143 (100) [MH^+], 160 (100) [$MNH_4{}^+$]. − $C_8H_{14}O_2$ (142.01): C 67.56, H 9.93, found C 67.78, H 10.01.

5,5-Diheptyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: > 95%. − ^1H NMR: δ = 0.80 (t, *J* = 7.6 Hz, 6 H), 1.21−1.54 (m , 24 H), 1.95 (t, *J* = 8.7 Hz, 2 H), 2.48 (t, *J* = 8.7 Hz, 2 H). − ^{13}C NMR: δ = 14.7, 23.9, 24.7, 30.1, 30.5, 31.1, 31.9, 33.1, 39.7, 90.9, 179.5. − IR (film): $\tilde{\nu}$ = 2960, 1755, 1163, 1143. − MS (70 eV, EI): *m/z* (%) = 282 (19) [M^+], 183 (100) [$C_{11}H_{17}O_2{}^+$], 99 (4) [$C_7H_{15}{}^+$], 85 (10) [$C_6H_{13}{}^+$], 71 (7) [$C_5H_{11}{}^+$], 57 (26) [$C_4H_9{}^+$], 43 (25) [$C_3H_7{}^+$]; CI/NH_3: *m/z* (%) = 281 (100) [MH^+], 300 (100) [$MNH_4{}^+$]; HRMS: calcd. for $C_{18}H_{34}O_2$ [M^+] 282.2550, found 282.2553.

5,5-Didodecyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 78%. − ^1H NMR: δ = 0.85 (t, *J* = 7.8 Hz, 2 H), 1.23 (m, 42 H), 1.59 (m, 4 H), 1.98 (t, *J* = 7.9 Hz, 2 H), 2.55 (t, *J* = 7.8 Hz, 2 H). − ^{13}C NMR: δ = 14.4, 23.0, 23.8, 29.4, 29.5, 29.7, 29.8, 29.9, 30.0, 30.2, 31.2, 32.2, 39.1, 89.6, 177.4. − IR (film): $\tilde{\nu}$ = 2929, 2857, 2828, 1777, 1663, 1592, 1160, 973, 810. − MS (70 eV, EI): *m/z* (%) = 422 (13) [M^+], 253 (100) [$C_{16}H_{29}O_2{}^+$], 169 (34) [$C_{12}H_{25}{}^+$], 155 (9) [$C_{11}H_{23}{}^+$]; 127 (7) [$C_9H_{19}{}^+$], 113 (11) [$C_8H_{17}{}^+$], 99 (43) [$C_7H_{15}{}^+$], 85 (23) [$C_6H_{13}{}^+$], 71 (10) [$C_5H_{11}{}^+$]; IC/NH_3: *m/z* (%) = 251 (99) [MH^+], 268 (100) [$MNH_4{}^+$]; HRMS: calcd. for $C_{28}H_{54}O_2$ [M^+] 422.4133, found 422.4138.

5,5-Dicyclohexyl-2-tetrahydrofuranone: Purification: pentane/ether (80/20), yellow oil, yield: 72%. − ^1H NMR: δ = 1.21−1.38 (m, 22 H), 1.87 (t, *J* = 7.8 Hz, 2 H), 1.92 (t, *J* = 7.8 Hz, 2 H). − ^{13}C NMR: δ = 22.2, 24.9, 27.2, 27.7, 28.4, 42.1, 91.6, 189.7. − IR (film): $\tilde{\nu}$ = 2956, 2716, 1750, 1240. − MS (70 eV, EI): *m/z* (%) = 250 (15) [M^+], 167 (100) [$C_{10}H_{15}O^+$], 83 (27) [$C_6H_{11}{}^+$]; IC/NH_3: *m/z* (%) = 251(99) [MH^+], 268 (100) [$MNH_4{}^+$]; HRMS: calcd. for C16H26$^+$O2 [M^+] 250.1926, found 250.1927.

5,5-(-3-Chloropropyl)-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^1H NMR: δ = 1.15−1.01 (m, 8 H), 1.73 (t, *J* = 7.8 Hz, 4 H), 1.84 (t, *J* = 7.8 Hz, 2 H), 1.91(t, *J* = 7.9 Hz, 2 H). − ^{13}C NMR: δ = 22.6, 24.2, 25.4, 27.3, 41.9, 88.9, 174.9. − IR ($CHCl_3$): $\tilde{\nu}$ = 2942, 2837, 1742, 1666, 1194, 901. − MS (70 eV, EI): *m/z* (%) = 242 (9) [M^+], 163 (33), 161 (100), 105 (21), 71(12), 56(15), 41 (20); CI/NH_3: *m/z* (%) = 243 (23) [MH^+], 260 (100) [$MNH_4{}^+$]; HRMS: calcd. for $C_{10}H_{16}Cl_2$ [M^+] 242.1146, found 242.1149

5,5-(4-Chlorobutyl)-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^1H NMR: δ = 1.09−0.96 (m, 12 H), 1.68 (t, *J* = 7.8 Hz, 4 H), 1.82 (t, *J* = 7.8 Hz, 2 H),1.95 (t, *J* = 7.9 Hz, 2 H). − ^{13}C NMR: δ = 22.4, 23.8, 24.1, 25.8, 27.6, 42.0, 89.4, 178.4. − IR ($CHCl_3$): $\tilde{\nu}$ = 2950, 2863, 1758, 1605, 1203, 980. − MS (70 eV, EI): *m/z* (%) = 270 (12) [M^+], 191 (23), 189 (100), 105 (17), 70 (13), 56 (9), 41 (23); CI/NH_3: *m/z* (%) = 271 (9) [MH^+], 288 [$MNH_4{}^+$]; HRMS: calcd. for $C_{12}H_{20}Cl_2O_2$ [M^+] 270.1458, found 270.1561.

6,6-Dibutyl-2-tetrahydropyranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^1H NMR: δ = 0.98 (t, *J* = 7.8 Hz, 6 H), 1.13 (m, 8 H), 1.24 (t, *J* = 7.8 Hz, 4 H), 1.62 (t, *J* = 7.8 Hz, 4 H), 2.27 (t, *J* = 7.8 Hz, 2 H). − ^{13}C NMR: δ = 13.9, 23.1, 24.2, 27, 31.0, 32.3, 41.5, 87.7, 185.7. − IR (film): $\tilde{\nu}$ = 2930, 2874, 1760, 1232, 1148; MS (70 eV, EI): *m/z* (%) = 212 (12) [M^+], 197 (20) [$C_{12}H_{21}O_2{}^+$], 183 (15) [$C_{11}H_{19}O_2{}^+$]; 155 (100) [$C_9H_{15}O_2{}^+$], 98

(9) $[C_5H_6O_2^+]$, 57 (53) $[C_4H_9^+]$, 43 (32) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 213 (48) $[MH^+]$, 230 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{13}H_{24}O_2$ $[M^+]$ 212.1770, found 212.1770.

6,6-Didodecyl-2-tetrahydropyranone: Purification: pentane/ether (80:20), yellow oil, yield: 72%. − ^{1}H NMR: $\delta = 0.91$ (t, $J = 7.8$ Hz, 6 H), 0.96−1.18 (m, 46 H), 2.03 (t, $J = 7.9$ Hz, 2 H), 2.14 (t, $J = 7.8$ Hz, 2 H). − ^{13}C NMR: $\delta = 14.5$, 23.1, 23.9, 28.2, 29.7, 29.8, 29.9, 30.0, 30.2, 32.3, 40.3, 40.8, 46.1, 85.7, 182.8. − IR (film): $\tilde{\nu} = 2928$, 2860, 1741, 1658, 1189, 940. − MS (70 eV, EI): *m/z* (%) = 436 (14) $[M^+]$, 366 (20) $[C_{25}H_{50}O^+]$, 267 (100) $[C_{17}H_{31}O_2^+]$, 169 (70) $[C_{12}H_{25}^+]$, 85 (13) $[C_3H_{13}^+]$, 71 (43) $[C_5H_{11}^+]$, 70 (22) $[C_4H_6O^+]$, 57 (12) $[C_4H_9^+]$, 56 (23) $[CH_4O^+]$, 43 (31) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 436 (21) $[M^+]$, 437 (100) $[MH^+]$, 454 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{29}H_{56}O_2$ $[M^+]$ 436.4266, found 436.4266.

5-Allyl-5-hydroxy-7-octenoic Acid: Purification: pentane/ether (70:30), yellow oil, yield: 75%. − ^{1}H NMR: $\delta = 1.18$−1.23 (m, 5 H), 1.43 (t, $J = 7.9$ Hz, 2 H), 2.10 (dd, $J = 7.8$ Hz, $J = 5$ Hz, 4 H), 4.31 (dd, $J = 2$ Hz, $J = 16$ Hz, 4 H), 6.13 (ddt, $J = 16$ Hz, $J = 12$ Hz, $J = 4.8$ Hz, 2 H), 12 (s, 1 H). − ^{13}C NMR: $\delta = 18.7$, 20.6, 22.8, 24.9, 35.8, 113.3, 140.2, 178.1. − IR ($CHCl_3$): $\tilde{\nu} = 3156$, 3049, 2932, 1711, 1642, 1413, 909. − MS (70 eV, EI): *m/z* (%) = 182 (18) $[M^+]$, 164 (51) $[C_1H_{16}O^+]$, 141 (78) $[C_8H_{13}O_2^+]$, 136 (10) $[C_{10}H_{17}^+]$, 100 (12) $[C_5H_8O_2^+]$, 73 (8) $[C_3H_5O_2^+]$, 59 (13) $[C_2H_{36}O_2^+]$, 45 (21) $[CHO_2^+]$; CI/NH_3: *m/z* (%) = 183 (100) $[MH^+]$, 200 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{11}H_{18}O_2$ $[M^+]$ 182.1302, found 182.1307.

5,5-Dibutyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 67%. − ^{1}H NMR: $\delta = 0.93$ (t, $J = 7.8$ Hz, 6 H), 1.23−1.14 (m, 12 H), 1.68 (t, $J = 8.4$ Hz, 2 H), 1.71 (t, $J = 8.4$ Hz, 2 H). − ^{13}C NMR: $\delta = 13.8$, 16.5, 21.3, 25.2, 34.9, 41.6, 91.3, 179,7. − IR ($CHCl_3$): $\tilde{\nu} = 2940$, 2847, 1748, 1660, 1215, 922. − MS (70 eV, EI): *m/z* (%) = 198 (18) $[M^+]$, 183 (31) $[C_{11}H_{19}O_2^+]$, 169 (15) $[C_{10}H_{17}O_2^+]$, 141 (100) $[C_8H_{13}O_2^+]$, 84 (18) $[C_4H_4O_2^+]$, 57 (67) $[C_4H_9^+]$, 43 (13) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 199 (100) $[MH^+]$, 216 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{12}H_{22}O_2$ $[M^+]$ 198.1614, found 198.1619.

5,5-Dipentyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 71%. − ^{1}H NMR: $\delta = 1.01$ (t, $J = 7.8$ Hz, 6 H), 1.30−1.14 (m, 16 H), 1.64 (t, $J = 7.8$ Hz, 2 H), 1.69 (t, $J = 7.8$ Hz, 2 H). − ^{13}C NMR: $\delta = 13.5$, 17.3, 22.4, 24.9, 28.4, 35.2, 42.0, 91.4, 179.9. − IR ($CHCl_3$): $\tilde{\nu} = 2940$, 2851, 1750, 1660, 1225, 908. − MS (70 eV, EI): *m/z* (%) = 226 (13) $[M^+]$, 211 (13) $[C_{13}H_{23}O_2^+]$, 196 (8) $[C_{12}H_{20}O_2^+]$, 183 (10) $[C_{11}H_{19}O_2^+]$, 155 (13) $[C_9H_{15}O_2^+]$, 84 (10) $[C_4H_4O_2^+]$, 71 (12) $[C_5H_{11}^+]$, 57 (21) $[C_4H_9^+]$, 43 (15) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 227 (98) $[MH^+]$, 224 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{14}H_{26}O_2$ $[M^+]$ 226.1924, found 226.1925.

5,5-Diheptyl-3-methyl-2-tetrahydrofuranone and 5,5-Diheptyl-4-methyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^{1}H NMR: $\delta = 0.91$ (t, $J = 7.8$ Hz, 6 H), 1.12−1.4 (m, 27 H), 2.18 (dd, $J = 7.8$ Hz, $J = 2$ Hz, 2 H), 2.39 (m, 1 H), 2.41 (m, 1 H). − ^{13}C NMR: $\delta = 14.3$, 15.2, 23.7, 24.9, 30.4, 30.5, 31.3, 32.1, 33.5, 40.7, 89.4, 180.2. − IR (film): $\tilde{\nu} = 2960$, 2853, 1755, 1140, 1163. − MS (70 eV, EI): *m/z* (%) = 296 (13) $[M^+]$, 253 (12) $[C_{16}H_{29}O_2^+]$, 197 (100) $[C_{12}H_{21}O_2^+]$, 139 (20) $[C_{15}H_{25}O_2^+]$, 99 (87) $[C_7H_{15}^+]$, 85 (13) $[C_6H_{13}^+]$, 71 (8) $[C_5H_{11}^+]$, 57 (23) $[C_4H_9^+]$, 43 (33) $[C_3H_7^+]$, 41 (43); CI/NH_3: *m/z* (%) = 297 (99) $[MH^+]$, 314 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{19}H_{36}O_2$ $[M^+]$ 296.2706, found 296.2709.

5,5-Didodecyl-3-methyl-2-tetrahydrofuranone and 5,5-Didodecyl-4-methyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 89%. − ^{1}H NMR: $\delta = 0.89$ (t, $J = 7.8$ Hz, 6 H), 1.12−1.51 (m, 47 H), 2.20 (dd, $J = 7.8$ Hz, $J = 1.8$ Hz, 2 H), 2.27 (m, 1 H), 2.49 (m, 1 H). − ^{13}C NMR: $\delta = 14.8$, 15.2, 23.1, 23.8, 25.5, 27.7, 29.5, 29.6, 29.8, 30.0, 31.2, 31.3, 31.5, 31.8, 32.1, 76.7, 178.3. − IR ($CHCl_3$): $\tilde{\nu} = 2929$, 2857, 28,30, 1774, 1662, 1592, 1163, 967, 905. − MS (70 eV, EI): *m/z* (%) = 436 (15) $[M^+]$, 267 (100) $[C_{17}H_{31}O_2^+]$, 169 (76) $[C_{12}H_{25}^+]$, 97 (1) $[C_7H_{15}^+]$, 85 (9) $[C_6H_{13}^+]$, 71 (13) $[C_5H_{11}^+]$, 57 (12) $[C_4H_9^+]$, 43 (18) $[C_3H_5^+]$; CI/NH_3: *m/z* (%) = 437 (22) $[M^+]$, 454 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{29}H_{56}O_2$ $[M^+]$ 436.4266, found 436.4269.

5,5-Diethyl-3,3-dimethyl-2-tetrahydrofuranone and 5,5-Diethyl-4,4-dimethyl-2-tetrahydrofuranone: Purification: pentane/ether (90:10), yellow oil, yield: 95%. − ^{1}H NMR: $\delta = 0.87$ (t, $J = 7.9$ Hz, 6 H), 1.14 (q, $J = 7.9$ Hz, 4 H), 1.19 (s, 6 H), 1.86 (s, 2 H), 2.07 (s, 2 H). − ^{13}C NMR: $\delta = 13.7$, 14.3, 14.5, 22.8, 41.3, 92.5, 179.4. − IR ($CHCl_3$): $\tilde{\nu} = 2933$, 2841, 1752, 1630, 1170, 938. − MS (70 eV, EI): *m/z* (%) = 170 (13) $[M^+]$, 141 (13) $[C_8H_{13}O_2^+]$, 126 (8) $[C_9H_{18}^+]$, 114 (21) $[C_6H_{10}^+]$, 57 (100), 56 (10) $[C_4H_8^+]$, 42 (31) $[C_3H_6^+]$; CI/NH_3: *m/z* (%) = 171 (100) $[MH^+]$, 188 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{10}H_{18}O_2$ $[M^+]$ 170.1302, found 170.1302.

5,5-Diheptyl-3,3-dimethyl-2-tetrahydrofuranone and 5,5-Diheptyl-4,4-dimethyl-2-tetrahydrofuranone: Purification: pentane/ether (90:10), yellow oil, yield: 95%. − ^{1}H NMR: $\delta = 0.89$ (t, $J = 7.8$ Hz, 6 H), 1.20−1.56 (m, 30 H), 1.89 (s, 2 H), 2.28 (s, 2 H). − ^{13}C NMR: $\delta = 12.9$, 21.7, 22.7, 26.5, 28.3, 30.9, 38.9, 39.8, 44.6, 62.2, 85.4, 182.7. − IR ($CHCl_3$): $\tilde{\nu} = 2840$, 1758, 1150, 1162, 903. − MS (70 eV, EI): *m/z* (%) = 310 (12) $[M^+]$, 211 (100) $[C_{13}H_{23}O_2^+]$, 167 (21) $[C_{17}H_{31}O_2^+]$; 99 (50) $[C_7H_{15}^+]$, 85 (12) $[C_6H_{13}^+]$, 71 (8) $[C_5H_{11}^+]$, 57 (40) $[C_4H_9^+]$, 43 (20) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 311 (100) $[MH^+]$, 328 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{20}H_{38}O_2$ $[M^+]$ 310.2862, found 310.2865.

5,5-Didodecyl-3,3-dimethyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 85%. − ^{1}H NMR: $\delta = 0.94$ (t, $J = 7.9$ Hz, 6 H), 1.14−1.29 (m, 50 H), 1.91 (s, 2 H). − ^{13}C NMR: $\delta = 14.8$, 15.6, 22.3, 23.0, 23.9, 29.5, 29.8, 30.0, 30.2, 30.5, 30.9, 31.5, 31.8, 35.4, 69.8, 187.3. − IR ($CHCl_3$): $\tilde{\nu} = 2920$, 2847, 2831, 1750, 1640, 1162, 810, 802. − MS (70 eV, EI): *m/z* (%) = 450 (12) $[M^+]$, 407 (15) $[C_{23}H_{53}O_2^+]$, 127 (17) $[C_9H_{19}^+]$, 113 (10) $[C_8H_{17}^+]$, 112 (23) $[C_6H_8O_2^+]$, 99 (6) $[C_7H_{15}^+]$, 85 (10) $[C_6H_{13}^+]$, 84 (18) $[C_5H_8O^+]$, 70 (6) $[C_5H_{11}^+]$, 70 (22) $[C_4H_6O^+]$, 57 (13) $[C_4H_9O^+]$, 43 (30) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 451 (100) $[MH^+]$, 468 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{30}H_{58}O_2$ $[M^+]$ 450.4422, found 450.4424.

5,5-Diallyl-3,3-dimethyl-2-tetrahydrofuranone and 5,5-Diallyl-4,4-dimethyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^{1}H NMR: $\delta = 1.09$ (s, 6 H) , 1.81 (s, 2 H), 1.93 (s, 2 H), 2.10 (d, $J = 5$ Hz, 4 H), 4.56 (dd, $J = 16$ Hz, $J = 12$ Hz, 4 H), 6.04 (ddt, $J = 16$ Hz, $J = 12$ Hz, $J = 4.8$ Hz, 2 H). − IR ($CHCl_3$): $\tilde{\nu} = 3060$, 2910, 2851, 1748, 1631, 994, 809. − MS (70 eV, EI): *m/z* (%) = 194 (12) $[M^+]$, 153 (45) $[C_9H_{13}O_2^+]$, 125 (20) $[C_8H_{13}O^+]$, 69 (100) $[C_3H_3O^+]$, 41 (89) $[C_3H_5^+]$; CI/NH_3: *m/z* (%) = 195 (79) $[MH^+]$, 212 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{12}H_{18}O_2$ $[M^+]$ 194.1302, found 194.1302.

trans-3,3-Diethyl-hexahydro-isobenzofuran-1-one: Purification: pentane/ether (80:20), yellow oil, yield: 78%. − ^{1}H NMR: $\delta = 0.97$ (t, $J = 7.8$ Hz, 6 H), 1.18−1.44 (m, 12 H), 2.10 (d, $J = 9.5$ Hz, 1 H), 2.41 (d, $J = 9.5$ Hz, 1 H). − ^{13}C NMR: $\delta = 13.5$, 22.3, 24.6, 26.6, 30.4, 31.6, 89.7, 178.7. − IR ($CHCl_3$): $\tilde{\nu} = 2930$, 2870, 1778, 1680, 1310. − MS (70 eV, EI): *m/z* (%) = 196 (12) $[M^+]$, 181 (41) $[C_{11}H_{17}O_2^+]$, 167 (100) $[C_{10}H_{15}O_2^+]$, 81 (25) $[C_6H_9^+]$; CI/NH_3: *m/z*

(%) = 197 (84) $[MH^+]$, 214 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{12}H_{20}O_2$ $[M^+]$ 196.1458, found 196.1459.

cis-3,3-Diethyl-3a,4,7,7a-tetrahydro-3H-isobenzofuran-1-one: Purification: pentane/ether (80:20), yellow oil, yield: 86%. − ^{1}H NMR: δ = 1.11 (t, *J* = 7.8 Hz, 6 H), 1.18 (q, *J* = 7.8 Hz, 4 H), 1.96 (m, 4 H), 2.14 (d, *J* = 10 Hz, 1 H), 2.38 (d, *J* = 10 Hz, 1 H), 5.61 (dt, *J* = 12 Hz, *J* = 2 Hz, 2 H). − ^{13}C NMR: δ = 13.5, 13.9, 32.6, 42.5, 79.9, 117.3, 126.2, 140.4, 184.2. − IR (film): $\tilde{\nu}$ = 3061, 2940, 2813, 1778, 1720, 1650, 1332, 917. − MS (70 eV, EI): *m/z* (%) = 194 (18) $[M^+]$, 165 100) $[C_{10}H_{13}O_2^+]$, 136 (15) $[C_8H_8O_2^+]$, 80 (57) $[C_6H_8^+]$; CI/NH_3: *m/z* (%) = 195 (100) $[MH^+]$, 212 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{12}H_{18}O_2$ $[M^+]$ 194.1302, found 194.1304.

5-Butyl-5-methyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^{1}H NMR: δ = 0.98 (t, *J* = 7.8 Hz, 3 H), 1.16−1.40 (m, 9 H), 1.68 (t, *J* = 7.8 Hz, 2 H), 1.79 (t, *J* = 7.8 Hz, 2 H). − ^{13}C NMR: δ = 13.5, 14.2, 22.8, 25.2, 25.8, 26.4, 28.3, 69.2, 178.1. − IR ($CHCl_3$): $\tilde{\nu}$ = 2940, 2871, 1742, 1658, 1215, 940. − MS (70 eV, EI): *m/z* (%) = 156 (13) $[M^+]$, 141 (18) $[C_8H_{13}O_2^+]$, 99 (100) $[C_5H_7O_2^+]$, 57 (63) $[C_4H_9^+]$, 43 (15) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 157 (91) $[MH^+]$, 178 (100) $[MNH_4^+]$; HRMS: calcd. for $C_9H_{16}O_2$ $[M^+]$ 156.1146, found 156.1146.

5-Heptyl-5-methyl-2-tetrahydrofuranone: Purification: pentane/ether (80:20), yellow oil, yield: 85%. − ^{1}H NMR: δ = 1.10 (t, *J* = 7.8 Hz, 3 H), 1.16−1.51 (m, 15 H), 1.71 (t, *J* = 7.8 Hz, 2 H), 1.93 (t, *J* = 7.8 Hz, 2 H). − ^{13}C NMR: δ = 14.1, 15.2, 23.4, 25.6, 31.4, 32.1, 32.4, 34.2, 40.7, 91.2, 180.2. − IR ($CHCl_3$): $\tilde{\nu}$ = 2958, 1761, 1143, 1101, 950. − MS(70 eV, EI): *m/z* (%) = 198 (16) $[M^+]$, 183 (23) $[C_{11}H_{19}O_2^+]$, 99 (100) $[C_5H_7O_2^+]$, 71 (8) $[C_5H_{11}^+]$, 57 (43) $[C_4H_9^+]$, 43 (33) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 199 (77) $[MH^+]$, 206 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{12}H_{22}O_2$ $[M^+]$ 198.1614, found 198.1614.

6-Butyl-6-methyl-2-tetrahydropyranone: Purification: pentane/ether (80:20), yellow oil, yield: 95%. − ^{1}H NMR: δ = 0.98 (t, *J* = 7.8 Hz, 3 H), 1.14−1.42 (m, 9 H), 2.27 (t, *J* = 7.8 Hz, 2 H), 1.67 (t, *J* = 7.8 Hz, 4 H). − ^{13}C NMR: δ = 13.9, 14.2, 24.2, 25.3, 28.2, 31.9, 32.4, 42.2, 86.9, 184.9. − IR ($CHCl_3$): $\tilde{\nu}$ = 2941, 2863, 1762, 1250, 1138, 904. − MS (70 eV, EI): *m/z* (%) = 170 (13) $[M^+]$, 155 (41) $[C_9H_{15}O_2^+]$, 140 (8) $[C_8H_{12}O_2^+]$, 113 (100) $[C_6H_9O_2^+]$, 57 (60) $[C_4H_9^+]$, 43 (18) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 170(57) $[MH^+]$, 188 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{10}H_{18}O_2$ $[M^+]$ 170.1302, found 170.1302.

6-Heptyl-6-methyl-2-tetrahydropyranone: Purification: pentane/ether (80:20), yellow oil, yield: 86%. − ^{1}H NMR: δ = 1.09 (t, *J* = 7.8 Hz, 3 H), 1.16−1.52 (m, 15 H), 1.73 (t, *J* = 7.8 Hz, 4 H), 2.34 (t, *J* = 7.8 Hz, 2 H). − ^{13}C NMR: δ = 14.1, 15.6, 22.4, 23.2, 25.3, 27.7, 29.7, 32.6, 33.4, 35.5, 68.6, 180.9. − IR ($CHCl_3$): $\tilde{\nu}$ = 2936, 2915, 2867, 1758, 1258, 1160, 980. − MS (70 eV, EI): *m/z* (%) = 212 (20) $[M^+]$, 197 (40) $[C_{12}H_{21}O_2^+]$, 183 (28) $[C_{11}H_{19}O_2^+]$, 169 (17) $[C_{10}H_{17}O_2^+]$, 155 (13) $[C_9H_{17}O_2^+]$, 141 (10) $[C_8H_{15}O_2^+]$, 99 (52) $[C_7H_{15}^+]$, 57 (8) $[C_4H_9^+]$, 43 (8) $[C_3H_7^+]$; CI/NH_3: *m/z* (%) = 212 (82) $[MH^+]$, 230 (100) $[MNH_4^+]$; HRMS: calcd. for $C_{13}H_{24}O_2$ $[M^+]$ 212.1770, found 212.1770.

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