γ,δ- and δ,ε-Unsaturated Aldehydes from γ- and δ-Lactones in One Step

Preliminary Communication

by **Wolfgang Giersch** and **Ferdinand Naef***

Firmenich SA, Corporate R&D Division, CH-1211 Geneva 8
(phone: +41227803034; fax: +41227803334; e-mail: ferdinand.naef@firmenich.com)

Dedicated to *Günther Ohloff* on the occasion of his 80th birthday

A one-step transformation of γ- and δ-(spiro)lactones into γ,δ- and δ,ε-unsaturated aldehydes with an excess of formic acid in the vapor phase over a supported manganese catalyst is described for the first time. The scope and limitations of this new reaction are shown with different lactones as substrate, and a mechanistic rationale is proposed.

1. Introduction. – One of the most efficient syntheses of aldehydes consists of the one-step reduction of carboxylic acids by means of the so called *Piria–Limpricht* reaction first published in 1856 and more or less forgotten in the meantime [1][2]. In the original procedure, a mixture of the calcium salts of the acid to be reduced and formic acid as reducing agent were pyrolyzed in a retort by heating with a *Bunsen* burner. The resulting reaction products were the aldehyde, H_2O, and CO_2. After further refinement of the method and the use of barium instead of calcium salts [3][4], the reaction could be rendered catalytic by *Sabatier* and *Mailhe* [5][6] in 1912–14 by using titanium or manganese oxides as catalysts at temperatures between 300° and 360°, with yields of 50–70%. More surprisingly, and already in 1907, a patent of the *Badische Anilin und Sodafabrik* (*BASF*) [7] disclosed the catalytic reduction in the gas phase of carboxylic acids to aldehydes with H_2 at *ca.* 300°. In the 1980s, this reaction was rediscovered and refined as can be seen from the patent literature (for some leading but not exhaustive references see [8–12]).

As we were seeking an efficient process for the synthesis of the fragrance aldehyde (±)-3-[4-(*tert*-butyl)cyclohex-1-en-1-yl]propanal (**1**) [13], we asked ourselves whether it might be possible to transform the known lactone **2** (64:36 mixture of *cis*- and *trans*-8-(*tert*-butyl)-1-oxaspiro[4.5]decan-2-one (**2a** and **2b**, resp.)) [14] in one step into the unsaturated aldehyde **1** (*Scheme 1*) by making use of a *Piria–Limpricht*-type reduction with simultaneous lactone opening.

2. Results. – When a solution of lactone **2** (64:36 mixture **2a**/**2b** throughout this report, not further specified) in 5 volumes of formic acid was allowed to pass through a quartz tube filled with a catalyst of manganese oxide on pumice¹) (for apparatus, see

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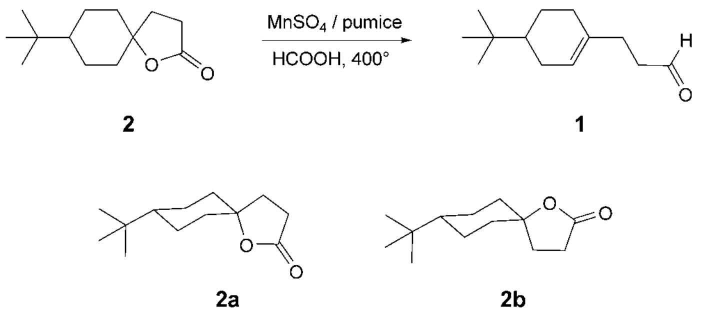
¹) Pumice is a light kind of lava, usually consisting of obsidian made spongy or porous by the escape of steam or gas during the process of cooling.

Scheme 1



Exper. Part) at *ca.* 400°, we obtained the unsaturated aldehyde **1** in 47% yield. To optimize the reaction conditions, we varied the metal salts (Fe, Cu, Ag, Pd, Ni, Co, Zn, Mn, Zn/Mn, Ru/Sn salts), the support (coarse and fine pumice, Al_2O_3), catalyst quantity, column dimensions, and temperature. Interestingly, some catalysts furnished structures other than the desired aldehyde **1** (see *Scheme 2* and *Table 1*).

Scheme 2

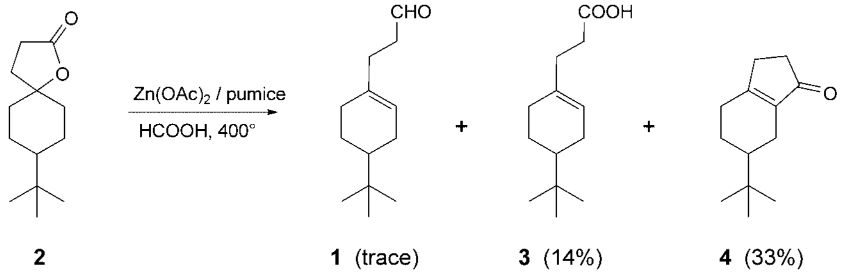


Table 1. *Reduction of Spirolactone* **2** *with Formic Acid and Different Catalysts*

Entry	Catalyst[a])	Temp.	Product mixture **1**	**2**	**3**	**4**
1	$MnSO_4$/pumice	400°	51%	49%	–	–
2	$CuSO_4$/pumice	440°	1%	20%	30%	42%
3	$AgNO_3$/pumice	440°	–	17%	32%	40%
4	$CdSO_4$/pumice	440°4%	20%	30%	42%	
5	$Zn(OAc)_2$/pumice	440°	13%	–	14%	33%
6	$Zn(OAc)/Mn(OAc)_2$/pumice	440°	60%	7%	3%	–

[a]) For catalyst preparation, see *Exper. Part.* However, the nature of the actual catalytic species remains unknown.

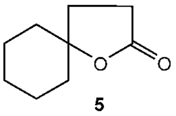
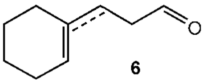
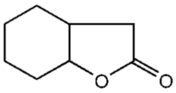
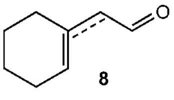
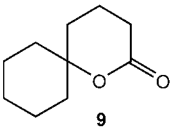
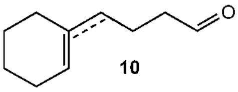
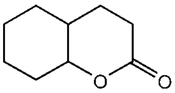
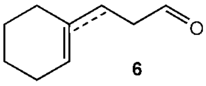
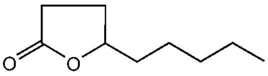
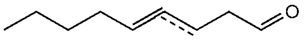
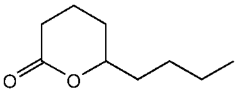
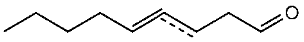
In our preliminary experiments Mn^{II} salts showed the best selectivity and yield of all the salts tested. With a Zn^{II} catalyst and formic acid, we obtained mostly acid **3** and only traces of the desired aldehyde **1**. A result that suggests that the first step in our new reaction is a *Lewis* acid catalyzed opening of the lactone to the unsaturated acid **3**, which then undergoes a *Piria–Limpricht* reduction. Under stronger reaction conditions, however, and with the same catalyst, in addition to **3**, major amounts of ketone **4** were formed. This product can be accounted for as an intra-molecular *Friedel–Crafts*-type acylation of unsaturated acid **3**.

Therefore, we decided to test a mixed catalyst containing Zn^{II} in addition to Mn^{II} on pumice, which turned out to be a much better system in our hands. With formic acid as reducing agent and solvent (twelve-fold excess) at 400° in an N_2 stream, **1** (60%) besides **2** (7%) and **3** (3%) were obtained (*Table 1*, *Entry 6*).

Preliminary experiments with H_2 as reducing agent instead of formic acid (see [7–12]) gave low yields of aldehyde **1** and were, therefore, not further pursued.

To explore the structural scope and limitations of the reaction, we tested a variety of five- and six-membered lactones. Thus, lactones **5**–**14** were transformed to aldehydes **6**–**13** in the presence of different catalysts (see *Table 2*).

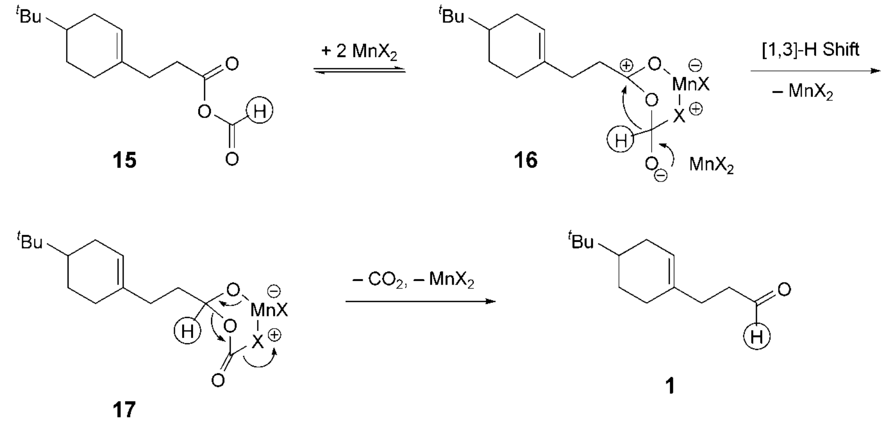
Table 2. *Reduction of Various Lactones with Formic Acid and Different Catalysts at 450°*

Entry	Starting materials	Catalyst	Products	Yield
1	 **5**	$MnSO_4$/pumice	 **6**	27.9%
2	 **7**	$MnSO_4$/pumice	 **8**	6%
3	 **9**	$MnSO_4$/pumice	 **10**	35.7%
4	 **11**	$MnSO_4$/pumice	 **6**	31.4%
5	 **12**	$RuCl_3/SnCl_2$/pumice	 **13**	8%
		$Mn(OAc)_2/Zn(OAc)_2$/pumice		0%
6	 **14**	$Mn(OAc)_2/Zn(OAc)_2$/pumice	 **13**	15.3%

3. Discussion. – As exemplified in *Table 2*, this new reaction converts in one step five- and six-membered lactones to the corresponding γ,δ- and δ,ε-unsaturated aldehydes, however, not always in satisfactory yields for preparative purposes. The best yields resulted from the five- and six-membered spirolactones **5** and **9** and the octahydro-2*H*-1-benzopyranone **11** (28–36%; *Table 2*, *Entries 1*, *3*, and *4*). In the case of the monosubstituted five- and six-membered lactones **12** and **14**, low yields of the same linear, unsaturated aldehyde **13** with (*E*)-configuration were obtained (*Entries 5* and *6*).

For a mechanistic rationale of this surprising reaction, we would like to discuss the following possibility (see *Scheme 3*). We postulate as a first intermediate the mixed anhydride **15**, which is assumed to be formed with formic acid under concomitant ring opening of the lactone directly or *via* the unsaturated acid **3**. The reaction is probably assisted by our $\mathrm{Mn^{II}}$ catalyst (see also [15]). The anhydride must then form a complex with the amphoteric (acid–base) $\mathrm{MnX_2}$ catalyst of the polar structure type **16** which, in close similarity to the *Meerwein–Ponndorf–Verley* reduction [16][17], favors a 1,3-H shift to **17**, helped by the $\mathrm{MnX_2}$ catalyst and energetically driven by the formation of $\mathrm{CO_2}$[2]).

Scheme 3



To establish that mixed formic carboxylic anhydrides may be intermediates in the *Piria–Limpricht* reaction, we pyrolyzed the readily accessible formic octanoic anhydride (**19**; prepared from **18** as shown in *Scheme 4*). The mixed anhydride **19** proved extremely unstable and was transformed at room temperature into the symmetrical octanoic anhydride (**20**) and formic acid. Excess of formic acid should then drive the equilibrium towards the mixed anhydride (see also the preparation of acetic formic anhydride from acetic anhydride and formic acid [18]). At 300° over a $\mathrm{Mn^{II}/Zn^{II}}$ catalyst, **19** decomposed to octanal (**21**; 3%), octanoic acid (**22**; 34%), and pentadecan-8-one (**23**; 62%) (originating from the symmetrical anhydride **20** being formed under the reaction conditions). However, **19** in the presence of a two-fold excess of formic acid gave octanal (**21**; 19%), octanoic acid (**22**; 63%), and ketone **23** (only 11%) (*Scheme 4*).

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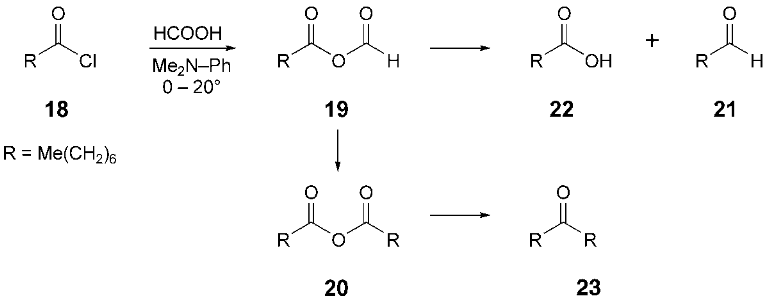
[2] The involvement of a possible metal hydride as a reducing agent was discounted mainly due to the absence of any alcohol by-products as well as the absence of C=C bond reduction in the unsaturated aldehydes obtained.

Scheme 4



However, the proposed mechanism does not explain the reduction of carboxylic acids (or of our lactone **2**) with H_2 at 300–400° in the presence of the same type of heterogeneous catalysts [7–12], an interesting question beyond the scope of the present study, but which should be addressed in future investigations.

4. Conclusions. – In spite of many open mechanistic questions, this new one-step transformation of (spiro)lactones into unsaturated aldehydes is attractive from a preparative point of view. Further examples and yet better catalysts will be needed to show the real value of this surprising reaction.

The authors are indebted to Mrs. *V. Revillet* and *C. Bise* for careful experimental work, to Prof. *P. Vogel*, EPF-Lausanne, for helpful mechanistic discussions, to Mr. *W. Thommen* for having recorded the spectral data, to Dr. *O. Haefliger* for LC/MS measurements, and to Dr. *E. Walther* for reference samples.

Experimental Part

1. *General.* Flash chromatography (FC): Silica gel *60*, 30–70 μm. GC: *Varian STAR 3400*; He as carrier gas; fushed-silica capillary columns *SPB-1* and *Supelcowax®*, each 30 m × 0.25 mm i.d. with 0.25 μm film. IR Spectra: *Perkin-Elmer-1600*-FT-IR spectrometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker-DPX-400* or *-AV-500* spectrometers; δ in ppm downfield from $SiMe_4$, J in Hz. GC/MS: *Hewlett-Packard-5890* or *-6890* system equipped with a capillary column, 30 m × 0.25 μm i.d. coupled with a *Hewlett-Packard-MSD-5972* or *-5973* quadrupole mass spectrometer; electron energy *ca.* 70 eV; in *m/z* (rel. int. in % of the base peak).

2. *Catalyst Preparation.* 2.1. *Mn^{II}/Pumice.* $Mn(OAc)_2$ (*Merck*; 5 g), pumice stones (*Riedel de Haën*; 50 g; diameter *ca.* 1–3 mm), and H_2O (200 ml) were stirred at 50° for 1 h. Then the mixture was filtered and the solid washed with distilled H_2O (100 ml) and finally dried at 450°.

2.2. *Cu^{II}/Pumice.* As described in *2.1*, with $CuSO_4$ (*Reactolab S.A.*; 5 g), pumice stones (50 g), and H_2O (200 ml).

2.3. *Ag^{I}/Pumice.* As described in *2.1*, with $AgNO_3$ (*Acros*; 6 g), pumice stones (50 g), and H_2O (150 ml) (3 h).

2.4. *Cd^{II}/Pumice.* $CdSO_4 \cdot 8\,H_2O$ (*Merck*; 3 g), pumice stones (100 g), and H_2O (300 ml) were stirred at 50° for 1 h. Then the mixture was evaporated and the residue dried at 400°.

2.5. *Zn^{II}/Pumice.* $Zn(OAc) \cdot 2\,H_2O$ (*Fluka*; 5 g), pumice stones (50 g), and H_2O (100 ml) were stirred at 50° for 1 h and stored overnight at r.t. Then the mixture was evaporated and the residue dried at 430°.

2.6. *Zn^{II}/Mn^{II}/Pumice.* As described in *2.5*, with $Zn(OAc)_2 \cdot 2\,H_2O$ (*Fluka*; 2.5 g), $Mn(OAc)_2$ (*Merck*; 2.5 g), pumice stones (50 g), and H_2O (100 ml).

2.7. *Ru^{III}/Sn^{II}/Pumice* [12]. $RuCl_3$ hydrate (*Fluka*; 2 g), $SnCl_2$ (*Fluka*; 10 g), and 3N HCl (15 ml) were stirred at 90° (water bath) for 1 h. Then pumice stones (*Riedel de Haën*; 50 g; diameter 1.4 mm) were added at r.t. The mixture was stored overnight, then dried at 450° in a steam of N_2 in a column, and finally reduced with H_2 during 4 h at 450°.

3. *Thermal Reaction*. 3.1. *Thermolysis: General Procedure*. The apparatus consisted of an oven (*Carbolite*) and a quartz column (1 m × 30 mm i.d.) filled with catalyst (length 10 cm) in its upper part (see *Fig.*). A 10% soln. of lactone in formic acid (*Acros*; 99%) was introduced at the top of the column (10 ml/h) with an automatic syringe pump (*Bioblock Scientific-Razel Scientific Instruments, Inc.*) in an N_2 stream (300 ml/min) at 370–450°. The pyrolysate was trapped in a flask (cooled with ice) connected to a gas washer (filled with ^{t}BuOMe). The combined org. soln. was washed with brine and then distilled.

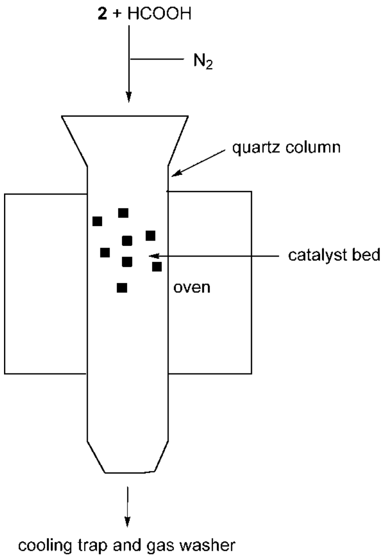


Figure. *Apparatus used*

3.2. *(±)-3-[4-(*tert*-Butyl)cyclohex-1-en-1-yl]propanal* (**1**). The pyrolysate was distilled at 120°/0.6 mbar: **1**. ^{1}H-NMR: 0.85 (*s*, 9 H); 5.41 (br. *s*, 1 H); 9.75 (*t*, *J* = 2, 1 H). ^{13}C-NMR: 24.1 (*t*); 26.8 (*t*); 27.2 (*q*); 29.7 (*t*); 29.9 (*t*); 32.2 (*s*); 41.9 (*t*); 44.0 (*d*); 122.1 (*d*); 135.5 (*s*); 202.8 (*d*). MS: 194 (7, M^+), 150 (10), 137 (9), 120 (23), 94 (43), 79 (30), 57 (100), 41 (49).

3.3. *3-(Cyclohex-1-en-1-yl)propanal/3-Cyclohexylidenepropanal* (**6**). The pyrolysate was distilled at 115°/0.13 mbar and then purified by FC (pentane/Et_2O 8:2): mixture **6** of C=C bond isomers, not separated by GC. ^{1}H-NMR: 5.41 (br. *s*); 5.52–5.71 (*m*); 9.77 (*ca.* 70%) and 9.79 (*ca.* 30%) (2*t*, *J* = 2, 1 H). ^{13}C-NMR: major isomer: 22.4 (*t*); 22.8 (*t*); 25.2 (*t*); 28.4 (*t*); 30.2 (*t*); 41.9 (*t*); 121.9 (*d*); 135.7 (*s*); 202.8 (*d*); minor isomer: 21.3 (*t*); 25.3 (*t*); 28.2 (*t*); 28.7 (*t*); 34.6 (*t*); 41.4 (*t*); 128.0 (*d*); 130.8 (*d*). MS: 138 (9, M^+), 120 (12), 109 (13), 94 (88), 79 (100), 67 (41), 41 (27).

3.4. *(Cyclohex-1-en-1-yl)acetaldehyde/Cyclohexylideneacetaldehyde* (**8**). The pyrolysate was distilled at 100°/0.15 mbar: complex mixture containing **8**. MS (less polar peak): 124 (16, M^+), 109 (6), 95 (31), 80 (100), 67 (37), 53 (19), 39 (28).

3.5. *4-(Cyclohex-1-en-1-yl)butanal/4-Cyclohexylidenebutanal* (**10**). The pyrolysate was distilled at 150°/0.4 mbar and then purified by FC (toluene/Et_2O 9:1): 7:3 mixture **10** of two C=C bond isomers. ^{1}H-NMR: 5.03 (*t*, *J* = 7, 1 H) and 5.42 (br. *s*, 1 H); 9.73 (br. *s*, 1 H). ^{13}C-NMR: major isomer: 20.1 (*t*); 22.5 (*t*); 22.9 (*t*); 25.2 (*t*); 28.1 (*t*); 37.3 (*t*); 43.4 (*t*); 122.1 (*d*); 136.5 (*s*); minor isomer: 26.8 (*t*); 27.7 (*t*); 28.6 (*t*); 28.7 (*t*); 37.1 (*t*); 44.3 (*t*); 118.7 (*d*); 140.5 (*s*); 202.7 (*d*). MS: major isomer: 152 (1, M^+), 134 (57), 108 (62), 93 (68), 93 (68), 79 (100), 67 (50), 41 (38); minor isomer: 152 (2, M^+), 134 (69), 108 (65), 93 (56), 81 (93), 67 (100), 41 (56).

3.6. *Non-3-enal/Non-4-enal* (**13**). The pyrolysate was distilled at 150°/30 mbar and then purified by FC (cyclohexane/Et_2O 9:1): mixture **13** contaminated with some nonanal. ^{1}H-NMR: 0.88 (*t*, *J* = 7, 3 H); 5.31–5.52 (*m*, 2 H); 9.77 (*m*, 1 H). ^{13}C-NMR: major isomer: 13.7 (*q*); 22.0 (*t*); 29.1 (*t*); 31.8 (*t*); 31.9 (*t*); 43.6 (*t*); 127.6 (*d*); 132.1 (*d*); 202.5 (*d*); minor isomer: 14.0 (*q*); 22.1 (*t*); 29.2 (*t*); 31.6 (*t*); 32.1 (*t*); 44.0 (*t*); 127.0 (*d*); 131.7 (*d*); 203.0

(*d*). MS: major isomer: 140 (1, M^+), 122 (14), 96 (42), 84 (100), 67 (49), 55 (77), 41 (81); minor isomer: 140 (1, M^+), 122 (17), 96 (72), 81 (90), 67 (78), 55 (96), 41 (100).

3.7. *3-[4-(*tert*-Butyl)cyclohex-1-en-1-yl]propanoic Acid* (**3**). The pyrolysate from **2** was purified by FC (toluene/Et_2O 9:1). ^{1}H-NMR: 0.86 (*s*, 9 H); 1.12–1.31 (*m*, 2 H); 1.72–1.85 (*m*, 2 H); 1.93–2.05 (*m*, 3 H); 2.21–2.31 (*m*, 2 H); 2.42–2.53 (*m*, 2 H); 5.41 (br. *s*, 1 H). ^{13}C-NMR: 24.2 (*t*); 26.8 (*t*); 27.2 (*q*); 29.8 (*t*); 32.1 (*t*); 32.2 (*s*); 32.7 (*t*); 44.0 (*d*); 121.9 (*d*); 135.6 (*s*); 180.3 (*s*). MS: 210 (12, M^+), 195 (4), 154 (40), 136 (54), 93 (59), 57 (100).

3.8. *6-(*tert*-Butyl)-2,3,4,5,6,7-hexahydro-1*H*-inden-1-one* (**4**). ^{1}H-NMR: 0.91 (*s*, 9 H); 1.25–1.32 (*m*, 2 H); 1.73–1.81 (*m*, 1 H); 1.92–1.99 (*m*, 1 H); 2.31–2.55 (*m*, 7 H). ^{13}C-NMR: 21.7 (*t*); 23.7 (*t*); 27.3 (*q*); 29.6 (*t*); 32.4 (*s*); 35.1 (*t*); 44.1 (*d*); 139.3 (*s*); 173.7 (*s*); 209.3 (*s*). MS: 192 (28, M^+), 177 (8), 136 (100), 121 (21), 91 (14), 79 (15), 57 (42), 41 (27).

3.9. *Formic Octanoic Anhydride* (**19**). To a soln. of formic acid (6.5 g, 140 mmol) in *N,N*-dimethylaniline (*Fluka*; 17.8 ml, 140 mmol) was added dropwise octanoyl chloride (**18**) (*Fluka*; 20 g, 123 mmol) at $-5°$ (ice/salt bath) with stirring. After 1 h, the mixture was poured onto ice and extracted with pentane. This soln. was washed with ice-cold 10% HCl soln., ice-cold $NaHCO_3$ soln., and ice-cold brine, then dried (Na_2SO_4), and evaporated at 10°: 14.3 g of crude **19**. IR: 1762.3, 1787.7. ^{1}H-NMR: 0.88 (*t*, $J = 7$, 3 H); 1.28–1.35 (*m*, 8 H); 1.69 (*quint.*, $J = 7$, 2 H); 2.5 (*t*, $J = 7$, 2 H); 9.1 (*s*, 1 H). ^{13}C-NMR: 14.1 (*q*); 22.6 (*t*); 23.9 (*t*); 28.80 (*t*); 28.81 (*t*); 31.6 (*t*); 34.3 (*t*); 156.4 (*d*); 170.8 (*s*).

3.10. *Octanoic Anhydride* (**20**). As described in *3.9*, but washing at r.t. resulted in rearrangement to **20**. IR: 1749.4, 1817.3. ^{1}H-NMR: 0.88 (*t*, $J = 7$, 6 H); 1.21–1.38 (*m*, 16 H); 1.67 (*quint.*, $J = 7$, 4 H); 2.45 (*t*, $J = 7$, 4 H). ^{13}C-NMR: 14.05 (*q*); 14.13 (*q*); 22.6 (*t*); 22.7 (*t*); 24.3 (*t*); 28.9 (*t*); 29.7 (*t*); 31.6 (*t*); 35.3 (*t*); 169.7 (*s*).

3.11. *Octanal* (**21**). Crude **19** (14 g) was subjected to thermolysis at 400° in an N_2 stream (catalyst: $Zn(OAc)_2/Mn(OAc)_2$ on pumice, 15-cm catalyst bed), and the product was cooled in two traps (ice cooling). Distillation of the pyrolysate at 95–175°/0.28 mbar gave 9.7 g of **21** (2.7%), octanoic acid (**22**; 33.2%), and pentadecan-8-one (**23**; 62.2%) (by GC/MS).

The same thermolysis (14 g of **19**) but in the presence of formic acid (7.7 g, 2 mol-equiv.) furnished a crude mixture (8.8 g) of **21** (18.6%), **22** (62.7%), and **23** (11.3%).

Data of **21**: MS: 128 (2, M^+), 110 (18), 100 (27), 95 (19), 84 (100), 69 (58), 57 (96), 43 (94).

Data of **22**: MS: 144 (2, M^+), 115 (15), 101 (34), 85 (28), 73 (80), 60 (100), 43 (31).

Data of **23**: MS: 226 (3, M^+), 155 (18), 142 (25), 127 (100), 109 (10), 99 (13), 82 (23), 71 (37), 57 (87), 43 (25).

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