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

Preliminary Communication

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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, H₂O, and CO₂. 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 H₂ 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 (\pm) -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

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.



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*).



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	$440^{\circ}4\%$	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

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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 N₂ 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°

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 Mn^{II} catalyst (see also [15]). The anhydride must then form a complex with the amphoteric (acid–base) 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 MnX_2 catalyst and energetically driven by the formation of CO_2^2).



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 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*).

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.



However, the proposed mechanism does not explain the reduction of carboxylic acids (or of our lactone **2**) with H_2 at $300-400^\circ$ 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.

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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. ¹H- and ¹³C-NMR Spectra: Bruker-DPX-400 or - AV-500 spectrometers; δ in ppm downfield from SiMe₄, 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. $Mn^{ll}/Pumice$. Mn(OAc)₂ (Merck; 5 g), pumice stones (Riedel de Haën; 50 g; diameter ca. 1–3 mm), and H₂O (200 ml) were stirred at 50° for 1 h. Then the mixture was filtered and the solid washed with distilled H₂O (100 ml) and finally dried at 450°.

2.2. $Cu^{1/P}$ umice. As described in 2.1, with CuSO₄ (*Reactolab S.A.*; 5 g), pumice stones (50 g), and H₂O (200 ml).

2.3. $Ag^{I}/Pumice$. As described in 2.1, with AgNO₃ (*Acros*; 6 g), pumice stones (50 g), and H₂O (150 ml) (3 h). 2.4. $Cd^{II}/Pumice$. CdSO₄ · 8 H₂O (*Merck*; 3 g), pumice stones (100 g), and H₂O (300 ml) were stirred at 50° for 1 h. Then the mixture was evaporated and the residue dried at 400°.

2.5. $Zn^{ll}/Pumice$. Zn(OAc) \cdot 2 H₂O (*Fluka*; 5 g), pumice stones (50 g), and H₂O (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. $Ru^{II}/Sn^{II}/Pumice$ [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 N₂ stream (300 ml/min) at 370–450°. The pyrolysate was trapped in a flask (cooled with ice) connected to a gas washer (filled with 'BuOMe). The combined org. soln. was washed with brine and then distilled.



Figure. Apparatus used

3.2. (\pm) -3-[4-(tert-Butyl)cyclohex-1-en-1-yl]propanal (1). The pyrolysate was distilled at 120°/0.6 mbar: 1. ¹H-NMR: 0.85 (s, 9 H); 5.41 (br. s, 1 H); 9.75 (t, J = 2, 1 H). ¹³C-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 $115^{\circ}/$ 0.13 mbar and then purified by FC (pentane/Et₂O 8 :2): mixture 6 of C=C bond isomers, not separated by GC. ¹H-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). ¹³C-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 $100^{\circ}/0.15$ 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 $150^{\circ}/$ 0.4 mbar and then purified by FC (toluene/Et₂O 9:1): 7:3 mixture 10 of two C=C bond isomers. ¹H-NMR: 5.03 (t, J = 7, 1 H) and 5.42 (br. s, 1 H); 9.73 (br. s, 1 H). ¹³C-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 $150^{\circ}/30$ mbar and then purified by FC (cyclohexane/Et₂O 9:1): mixture 13 contaminated with some nonanal. ¹H-NMR: 0.88 (t, J = 7, 3 H); 5.31 – 5.52 (m, 2 H); 9.77 (m, 1 H). ¹³C-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/Et₂O 9:1). ¹H-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). ¹³C-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**). ¹H-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). ¹³C-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 NaHCO₃ soln., and ice-cold brine, then dried (Na₂SO₄), and evaporated at 10°: 14.3 g of crude 19. IR: 1762.3, 1787.7. ¹H-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). ¹³C-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. ¹H-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). ¹³C-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 N₂ 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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