Iron-Mediated Electrochemical Reaction of α -Chloroesters with Carbonyl Compounds

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Experimental

General Information. GC analysis was carried out using a 25-m DB-1 capillary column. Mass spectra were recorded with an ITD spectrometer coupled to a gas chromatograph (DB1, 30 m). Elemental analysis were performed by the Service Central de Microanalyses (C.N.R.S., Lyon). Column chromatography was performed on silica gel 60, 70-230 mesh. ^1H , ^{13}C NMR spectra were recorded in CDCl_3 at 200 MHz with TMS as an internal standard.

All solvents and reagents were purchased and used without further purification. DMF and acetonitrile were stored under argon.

2,2'-Bipyridine was used as obtained commercially. NBu_4BF_4 was dried by heating overnight at 70°C in vacuum.

General Procedure for the Fe(II)-Catalyzed Electrosynthesis. In an undivided cell equipped with a nickel sponge (area 20 cm^2) as the cathode and an iron rod as the anode, under argon tetrabutylammonium tetrafluoroborate (0.6 mmol) was dissolved as supporting electrolytes in DMF (40 mL). 1,2-dibromoethane (1.25 mmol) was introduced. A short electrolysis was run at constant current (0.3 A) and at room temperature within 15 minutes to generate a small amount of iron ions. Then the current was turned off. 2,2'-Bipyridine (5 mmol), carbonyl compounds (10 mmol), and a part of α -chloroester (ca. 0.3 mmol) were added. The excess of α -chloroester was introduced *via* a syringe pump at a rate of ca. 4 mmol/h. The electrosynthesis was run at constant current (0.25 A). The reaction was monitored by GC and stopped after carbonyl compounds was consumed (ca. 4.5 h). A charge of 4 F.mole^{-1} was used in most reactions described in this paper. The mixture was then hydrolyzed with hydrochloric acid (1 N, 40 mL) and diluted with diethyl ether (40 mL). The aqueous layer was extracted with diethyl ether (2x40 mL), the combined organic layers were washed with water to ensure complete removal of DMF and saturated NaCl solution, dried

over MgSO₄ and the solvent was evaporated. The product was isolated by silica-gel column chromatography eluted with 85/15 pentane/diethylether to give desired compounds.

Methyle 3-ethyl-3-hydroxy-2-methyl-pentanoate

NMR ¹H : 3,71 (s, 3H) ; 3,20 (s, 1H) ; 2,61 (q, J=7,2Hz, 1H) ; 1,50 (m, 4H) ; 1,17 (d, J=7,2Hz, 3H) ; 0,88 (t, J=7,4Hz, 3H) ; 0,82 (t, J=7,6Hz, 3H).

MS : 175 (M+1), 157 (M-OH), 145 (M-Et), 113, 97, 88, 57 (base)

Methyle 1-hydroxy- α -methylcyclohexane acetate

NMR ¹H : 3,70 (s, 3H) ; 3,04 (s, 1H) ; 2,52 (q, J=7,1Hz, 1H) ; 1,48 (m, 10H) ; 1,19 (d, J=7,1Hz, 3H).

MS : 187 (M+1), 169 (M-OH), 155 (M-OMe), 143, 130, 113, 99, 81 (base), 55.

Methyle 3-hydroxy-2-methyl-3-phenyl-butanoate

NMR ¹H : *erythro* : 7,41 (m, 2H) ; 7,20 (m, 3H) ; 4,15 (s, 1H) ; 3,33 (s, 3H) ; 2,98 (q, J=7,07Hz, 1H) ; 1,42 (s, 3H) ; 1,23 (d, J=7,07Hz, 3H).

threo : 7,40 (m, 2H) ; 7,25 (m, 3H) ; 3,91 (s, 1H) ; 3,70 (s, 3H) ; 2,86 (q, J=7,12Hz, 1H) ; 1,55 (s, 3H) ; 0,95 (d, J=7,12Hz, 3H).

MS : 209 (M+1), 191 (M-OH), 121 (base), 105, 77.

Methyle 3,3-diphenyl-3-hydroxy-2-methyl-propanoate

NMR ¹H : 7,50 (m, 4H) ; 7,20 (m, 6H) ; 4,68 (s, 1H) ; 3,66 (q, J=7,1Hz, 1H) ; 3,00 (s, 3H) ; 1,16 (d, J=7,1Hz, 3H).

MS : 270 (M); 253 (M-OH), 183 (base), 105, 77.

Methyle 3-hydroxy-2,3-dimethyl heptanoate

NMR ¹H : *erythro* : 3,71 (s, 3H) ; 3,12 (s, 1H) ; 2,57 (q, J=7Hz, 1H) ; 1,42 (m, 4H) ; 1,19 (d, J=7Hz, 3H) ; 1,18 (s, 3H) ; 0,91 (m, 3H).

threo : 3,7 (s, 3H) ; 3,1 (s, 1H) ; 2,54 (q, J=7Hz, 1H) ; 1,4 (m, 4H) ; 1,2 (d, J=7Hz, 3H) ; 1,1 (s, 3H) ; 0,9 (m, 3H).

MS : 175 (M+1), 157 (M-OH, base), 131 (M-C₃H₇), 99, 71, 57

Methyle 3-hydroxy-2,3,7-trimethyl-6-octenoate

NMR ¹H : *erythro* : 5,13-5,05 (m, 1H) ; 3,70 (s, 3H) ; 3,24 (s, 1H) ; 2,59 (q, J=7,1Hz, 1H) ; 2,08-2,01 (m, 2H) ; 1,67 (s, 3H) ; 1,61 (s, 3H) ; 1,53-1,43 (m, 2H) ; 1,21 (s, 3H) ; 1,20 (d, J=7,1Hz, 3H).

threo : 5,13-5,05 (m, 1H) ; 3,70 (s, 3H) ; 3,24 (s, 1H) ; 2,57 (q, J=7,09Hz, 1H) ; 2,08-2,01 (m, 2H) ; 1,67 (s, 3H) ; 1,61 (s, 3H) ; 1,53-1,43 (m, 2H) ; 1,15 (s, 3H) ; 1,20 (d, J=7,09Hz, 3H).

MS : 215 (M+1), 196 (M-OH), 136, 121, 109 (base), 99, 93, 81, 67, 57

Methyle 1-hydroxy- α -methyl-2-cyclohexeneacetate

NMR 1H : *erythro* : 5,50-5,92 (m, 2H) ; 3,70 (s, 3H) ; 2,98 (s, 1H) ; 2,63 (q, J=7,2Hz, 1H), 2,10-1,50 (m, 6H) ; 1,22 (d, J=7,2Hz, 3H).

threo : 5,9-5,5 (m, 2H); 3,7 (s, 3H); 3 (s, 1H); 2,60 (q, J=7,4Hz, 1H), 2,10-1,50 (m, 6H); 1,18 (d, J=7,4Hz, 3H).

MS: 184 (M), 156 (M-CO), 124 (M-CO₂Me), 97 (base), 79, 55.

Methyle 3-hydroxy-2,3-dimethyl-3-thienyl-propanoate

NMR 1H : *erythro* : 7,17-7,14 (m, 1H); 6,92-6,85 (m, 2H); 4,4 (s, 1H); 3,57 (s, 3H); 2,99 (q, J=7,13 Hz, 1H); 1,54 (s, 3H); 1,28 (d, J=7,13Hz, 3H).

threo : 7,7-7,6 (m, 1H) ; 7,2-7,1 (m, 2H) ; 4,09 (s, 1H) ; 3,7 (s, 3H) ; 2,87 (q, J=6,7Hz, 1H) ; 1,62 (s, 3H) ; 1,11 (d, J=6,7Hz, 3H).

MS: 214 (M), 197 (M-OH), 127 (M-C₂H₇O₂, base), 111, 97, 85, 57.

Anal. Calcd for C₁₀H₁₄O₃S: C, 56.05; H, 6.58, S 14.96. Found: C, 56.17; H, 6.53, S 15.04.

Methyle 3-hydroxy-2-methyl-3-phenyl-propanoate

NMR 1H : *erythro* : 7,23 (m, 5H) ; 4,97 (d, J=5,1Hz, 1H) ; 3,76 (s,1H) ; 3,53 (s, 3H) ; 2,73 (qd, J₁=7,0Hz, J₂=5,1Hz, 1H) ; 1,10 (d, J=7,0Hz, 3H).

threo : 7,28 (m, 5H) ; 4,68 (d, J=8,7Hz, 1H); 3,65 (s, 3H); 3,51 (s, 1H); 2,76 (qd, J₁=8,7Hz; J₂=7,2Hz, 1H); 0,91 (d, J=7,2Hz, 3H).

MS: 195, 177 (base), 121, 107, 88, 79, 57.

Methyle 3-hydroxy-2-methyl-undecanoate

NMR 1H : *erythro* : 3,88 (m, 1H) ; 3,69 (s, 3H) ; 2,54 (dq, J₁=7,1Hz, J₂=4,5Hz, 1H); 1,45-1,28 (m, 15H); 1,18 (d, J=7,1Hz, 3H); 0,88 (t, J=6,4Hz, 3H).

threo : 3,7 (m,1H) ; 3,69 (s, 3H); 2,3 (m, 1H); 1,45-1,28 (m, 15H); 1,18 (d, J=7,1Hz, 3H); 0,88 (t, J=6,4Hz, 3H).

MS: 231 (M+1), 215 (M-CH₃), 197, 181, 163, 117, 88 (base), 57.

Methyle 3-ethyl-3-hydroxy-pentanoate

NMR 1H : 3,69 (s, 3H) ; 3,46 (s, 1H) ; 2,46 (s, 2H) ; 1,54 (q, J=7,2Hz, 4H) ; 0,88 (t, J= 7,2Hz, 6H).

MS: 161 (M+1, base), 143 (M-OH), 131 (M-C₂H₅), 111, 99, 83, 69, 57.

Methyle (1-hydroxy-cyclohexyl)-acetate

NMR 1H : 3,7 (s, 3H) ; 3,38 (s, 1H) ; 2,48 (s, 2H) ; 1,68-1,36 (m, 10H).

MS: 173 (M+1), 155 (M-OH), 130, 123, 116, 97, 79 (base), 69, 55.

Methyle 3-hydroxy-3-phenyl butanoate

NMR ^1H : 7,45-7,40 (m, 2H) ; 7,39-7,15 (m, 3H) ; 4,35 (s, 1H), 3,53 (s, 3H) ; 2,96 (d, J=15,9Hz, 1H); 2,77 (d, J=15,9Hz, 1H); 1,52 (s, 3H).

MS: 195 (M+1), 179 (M-CH₃, base), 177 (M-OH), 121 (M-CH₂CO₂CH₃), 105, 91, 77, 51.

Methyle 3-hydroxy-3,3-diphenyl propanoate

NMR ^1H : 7,4-7,2 (m, 10H) ; 5,04 (s, 1H) ; 3,63 (s, 3H); 3,28 (s, 2H).

MS: 256 (M), 239 (M-OH), 183 (M-CH₂CO₂CH₃), 105 (base), 77, 51.

Methyle 3-hydroxy-3-methyl hexanoate

NMR ^1H : 3,72 (s, 3H) ; 3,70 (s, 1H) ; 2,58 (s, 2H) ; 1,53-1,32 (m, 4H) ; 1,23 (s, 3H) ; 0,92 (t, J=6Hz, 3H).

 α -Propane(1-ethyl-1-hydroxy)- γ -valerolactone

NMR ^1H : *trans* : 4,75-4,60 (m, 1H) ; 3,32 (s, 1H) ; 2,98-2,84 (m, 1H) ; 2,47-2,28 (m, 1H) ; 2,02-1,88 (m, 1H) ; 1,64-1,46 (m, 4H); 1,36 (d, J=6,4Hz, 3H); 0,92 (t, J=7,45Hz, 6H).

cis : 4,58-4,47 (m, 1H) ; 3,32 (s, 1H) ; 2,59-2,51 (m, 1H) ; 2,47-2,28 (m, 1H) ; 2,02-1,88 (m, 1H) ; 1,84-1,66 (m, 4H) ; 1,42 (d, J=6,1Hz, 3H), 0,90 (t, J=7,4Hz, 6H).

NMR ^{13}C : *trans* : 178,9 (1C) ; 75 (1C) ; 74,1 (1C) ; 45,9 (1C) ; 30,9 (1C) ; 28,6 (1C) ; 21,3 (2C) ; 7,3 (2C).

cis : 178,8 (1C) ; 75,2 (1C) ; 75 (1C) ; 48,1 (1C) ; 32,6 (1C) ; 28,4 (1C) ; 20,7 (2C) ; 7,6 (2C).

MS: 187 (M+1), 169 (M-OH), 157 (M-C₂H₅, base), 139, 124, 111, 100, 95, 83, 67, 57.

Anal. Calcd for C₁₀H₁₈O₃: C 64,49; H 9,74. Found: C 63,75; H 9,73.

 α -Cyclohexane-(1-hydroxy)- γ -valerolactone

NMR ^1H : *trans* : 4,75-4,61 (m, 1H) ; 2,97 (s, 1H) ; 2,85-2,73 (m, 1H) ; 2,45-2,30 (m, 1H) ; 2,01-1,88 (m, 1H) ; 1,84-1,04 (m, 10H) ; 1,37 (d, J=6,4Hz, 3H).

cis : 4,55-4,43 (m, 1H) ; 2,97 (s, 1H) ; 2,6-2,52 (m, 1H) ; 2,45-2,30 (m, 1H) ; 2,01-1,88 (m, 1H) ; 1,84-1,04 (m, 10H) ; 1,43 (d, J=6,1Hz, 3H).

NMR ^{13}C : *trans* : 178 (1C) ; 72 (1C) ; 71 (1C) ; 49 (1C) ; 35,3 (1C) ; 33,2 (2C) ; 30,7 (1C) ; 25,2 (2C) ; 21 (1C).

cis : 178 (1C) ; 75 (1C) ; 71,8 (1C) ; 51,2 (1C) ; 35,3 (1C) ; 33,2 (2C) ; 32,6 (1C) ; 25,2 (2C) ; 21,1 (1C).

MS: 199 (M+1), 181 (M-OH), 156, 142, 124, 116 (M-C₆H₁₀), 107, 100, 93, 79 (base), 67, 55.

Anal. Calcd for C₁₁H₁₈O₃: C 66,64; H 9,1. Found: C 66,61; H 9,14.

α -Ethane(1-phenyl-1-hydroxy)- γ -valerolactone

NMR^1H : 7,51-7,44 (m, 2H) ; 7,38-7,21 (m, 3H) ; 4,63-4,12 (m, 1H) ; 3,68 (s, 1H) ; 3,11-3,0; 2,54-2,46 (2 m, 1H total); 2,35-2,21 (m, 1H); 1,78; 1,70; 1,66 (3 s, 3H total); 1,69-1,26 (m, 1H); 1,38; 1,33; 1,22 (3 d, J=6,4Hz, 3H total).

$NMR^{13}C$: 177,8 (1C); 144,8-144,4 (1C total); 128,3 (2C); 127,4 (1C); 125,3 (2C); 75,4-75,2-73,7-73,2 (1C total); 74,1 (1C); 53,1-51,4 (1C total); 31,8 (1C); 25,3-25,2 (1C total); 21,3-21,2 (1C total).

MS : 221 (M+1), 203 (M-OH), 143 (M-C₆H₅), 121 (M-C₅H₇O₂), 105, 100 (base), 77, 51.

α -Ethane(1-hydroxy-1-thienyl)- γ -valerolactone

NMR^1H : 7,24-7,17 (m, 1H); 6,97-6,92 (m, 2H); 4,67-4,22 (m, 1H); 4,11 (s, 1H); 3,2-2,99; 2,55-2,45 (2 m, 1H total); 2,41-2,16 (m, 1H); 1,93-1,65 (m, 1H); 1,79 (s, 3H); 1,38; 1,33 (2d, J=6,4Hz, 3H total).

$NMR^{13}C$: 177,4 (1C); 150,3-149,6-149,2 (1C tot.); 126,9 (1C); 124,7 (1C); 123,3 (1C); 75,3-74,5-73,6 (1C tot.); 73,4-73,3-65,7 (1C tot.); 53,5-52,5-52 (1C tot.); 33,8-33-32,5 (1C tot.); 31,9-29,6 (1C tot.); 21,3-20,7 (1C tot.).

MS : 226 (M), 209 (M-OH), 127 (M-C₅H₇O₂, base), 111, 100, 82, 65, 55.

Anal. Calcd for C₁₁H₁₄O₃S: C 58,38; H 6,24; S 14,17. Found: C 58,11; H 6,49; S 12,89.

α -Benzyl-(1-hydroxy)- γ -valerolactone

NMR^1H : 7,37-7,27 (m, 5H); 7,36 (d, 1H); 4,76-4,65; 4,48-4,44 (2 m, 1H total); 3,15 (s, 1H); 3,05-2,95; 2,57-2,42 (2 m, 1H total); 2,07-1,96 (m, 1H); 1,67-1,45 (m, 1H); 1,40; 1,29 (2 d, J=6,4Hz, 3H total).

$NMR^{13}C$: 178,2 (1C); 141,8 (1C); 128,5 (2C); 127,6 (1C); 125,4 (2C); 76 (1C); 71,6 (1C); 49,9-48 (1C total); 29,4-28,7 (1C total); 21,5 (1C).

MS : 206 (M), 164, 146, 128, 115, 100 (base), 91, 79, 65, 54.

Anal. Calcd for C₁₂H₁₄O₃: C 69,89; H 6,84. Found: C 69,93; H 7,01.

3-Ethyl-3-hydroxy-2-methyl pentanenitrile

NMR^1H : 2,9 (s, 1H) ; 2,79 (q, J=7,2Hz, 1H) ; 1,66 (q, J=7,1Hz, 2H) ; 1,61 (q, J=7,7Hz, 2H) ; 1,29 (d, J=7,2Hz, 3H) ; 0,92 (t, J=7,1Hz, 3H) ; 0,89 (t, J=7,7Hz, 3H).

MS : 142 (M+1), 124 (M-OH), 112, 87, 69, 56 (base).

2-(1-Hydroxy-cyclohexyl)-propionitrile

NMR^1H : 2,67 (q, J=7,2Hz, 1H) ; 2,5 (s, 1H) ; 1,79-1,34 (m, 10H) ; 1,33 (d, J=7,2Hz, 3H).

MS : 154 (M+1), 136 (M-OH), 99 (M-C₃H₄N), 81 (base), 71 (M-C₆H₁₀), 55.

3-Hydroxy-2-methyl-3-phenyl-butyronitrile

NMR 1H : *erythro* : 7,41-7,20 (m, 5H); 2,96 (q, J=7,2Hz, 1H); 2,88 (s, 1H); 1,73 (s, 3H); 1,16 (d, J=7,2Hz, 3H).

threo: 7,5-7,3 (m, 5H); 2,96 (q, J=7,2Hz, 1H); 2,81 (s, 1H); 1,70 (s, 1H); 1,14 (d, J=7,2Hz, 3H).

MS: 175 (M); 158 (M-OH), 121 (M-C₃H₄N, base), 115, 105, 91, 77, 51.

Methyle 3,3-diethyl-2-oxiranecarboxylate

NMR 1H : 3,78 (s, 3H) ; 3,37 (s, 1H) ; 1,71 (q, J=7,5Hz, 2H) ; 1,67 (q, J=7,7Hz, 2H) ; 0,94 (t, J= 7,7Hz, 3H) ; 0,95 (t, J=7,5Hz, 3H).

MS: 159, 141 (M-OH), 129, 101 (base), 67, 59.

1-(3,3-Dimethyl-2-oxobutyl)cyclohexanol

NMR 1H : 1,14 (s, 9H) ; 1,20-1,55 (m, 6H) ; 1,60-1,73 (m, 4H) ; 2,62 (s, 2H) ; 4,30 (s, 1H).

MS: 199 (M, base), 181, 123, 95, 81, 57.

1-Cyclohexylidene-3,3-dimethyl-butan-2-one

NMR 1H : 1,14 (s, 9H); 1,22-1,66 (m, 6H) ; 2,17-2,22 (m, 2H); 2,70-2,73 (m, 2H); 6,21 (s, 1H).

MS: 180, 123 (base), 95, 67.

Analytical experiments Cyclic voltammetry studies were carried out in DMF at room temperature under argon in a three-electrode cell using an EG&G 273A potentiostat. The reference electrode was a SCE one separated from the solution by a bridge compartment filled with the same solvent-supporting electrolyte solution as that used in the cell. The working electrode was a gold disk (0.25 mm diameter), and the counter electrode was a gold wire.

Fig. 1. Cyclic Voltammograms in DMF + 0.1 M NBu₄BF₄, at a gold disc microelectrode (0.25 mm diameter) at $\nu = 0.2 \text{ V.s}^{-1}$ and at r.t of 10⁻² M FeBr₂ in the presence of 3.10⁻² M 2,2'-bipyridine.