$SmCl_3$-catalysed Electrosynthesis of γ-Butyrolactones from 3-Chloroesters and Carbonyl Compounds

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Electrosynthesis of γ-butyrolactones has been achieved by the direct reductive coupling of ethyl 3-chloropropionate and a series of carbonyl compounds in the presence of a catalytic amount of $SmCl_3$.

The direct activation and functionalization of the C–X bond of 3-halocarbonyl compounds, avoiding hydride elimination, is of interest in organic synthesis,[1] the homoenolate anions being versatile synthons of reversed polarity (umpolung[2]). The preparation of metal homoenolates by direct reaction of β-halogenoesters is not common. A lithium homoenolate has been reported in the reaction of 3-bromopropionic acid with lithium naphthalenide.[3] The reaction of β-lithiopropionate with carbonyl compounds at −70 °C leads to γ-lactones in moderate yields.[3] Zinc homoenalotes have also been prepared from ethyl 3-iodopropionate.[1a,4]

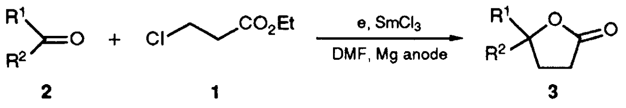
Lanthanoid metals (Ce, Sm) have been reported to mediate the reaction of β-bromo- or β-iodo-esters with ketones to yield γ-lactones and pinacols.[5] SmI_2 has been used to effect the coupling of 3-bromoesters with carbonyl compounds in the presence of hexamethylphosphoric triamide (HMPA) or zirconocene dichloride,[6,7] hence enlarging the applicability of SmI_2-mediated reactions.[8]

We have recently been interested in samarium-catalysed electrosynthesis coupling reactions,[9] and we report here the one-step preparation of γ-lactones *via* the electroreductive cross-coupling of 3-chloroesters with carbonyl compounds (Scheme 1).

The reaction proceeds by the constant-current electrolysis, at room temperature, of a dimethylformamide (DMF) solution of ethyl 3-chloropropionate **1**, the carbonyl compound **2** and a catalytic amount of commercial $SmCl_3$ (Scheme 1). The electrosyntheses were carried out in an undivided cell,[10] fitted with a consumable magnesium rod as the anode and a stainless steel cathode. The $SmCl_3$ is reduced to Sm^{II} species at the cathode [$E^0 = -1.88$ V *vs.* standard calomel electrode (SCE) in DMF] and the magnesium rod is oxidized to Mg^{2+} at the anode.

The results of the reductive coupling of **1** with carbonyl compounds are in Table 1. Spiro-γ-lactones **3a** and **b** were isolated in 60 and 76% yield respectively from cyclic ketones such as cyclohexanone or cyclopentanone (entries 1, 2). The $SmCl_3$-catalysed reaction with **1** afforded better yields and selectivity than the SmI_2-promoted spirolactonization[7] using methyl 3-bromopropionate (27 and 29% reported yields for the same lactones), in which aldol and pinacol type derivatives were the main products.

Other aliphatic ketones such as octan-2-one **2c** or 4-phenylbutan-2-one **2d** led to the corresponding chiral γ-lactones in 63



a; $R^1R^2 = -[CH_2]_5-$
b; $R^1R^2 = -[CH_2]_4-$
c; $R^1 = n\text{-}C_6H_{13}$, $R^2 = Me$
d; $R^1 = PhCH_2CH_2$, $R^2 = Me$
e; $R^1 = Me_2C{=}CHCH_2CH_2$, $R^2 = Me$
f; $R^1 = Ph$, $R^2 = Me$
g; $R^1 = n\text{-}C_6H_{13}$, $R^2 = H$

Scheme 1

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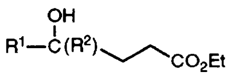

4e; $R^1 = Me_2C{=}CHCH_2CH_2$, $R^2 = Me$
4f ; $R^1 = Ph$, $R^2 = Me$

Table 1 Electrosynthesis of γ-lactones catalysed by $SmCl_3$[a]

Entry	Carbonyl compound	Products (isolated yield)
1	**2a**	**3a** (60%)
2	**2b**	**3b** (76%)
3	**2c**	**3c** (63%)
4	**2d**	**3d** (50%)
5	**2e**	**3e** (25%), **4e** (30%)
6	**2f**	**3f** (35%), **4f** (11%)
7	**2g**	**3g** (25%)

[a] Electrochemical procedure: in a single compartment cell[10] with an Mg rod as the anode (diameter 1 cm) and a stainless steel cathode (apparent surface 20 cm^2) were introduced: freshly distilled DMF (40 ml), $Bu^n{}_4NBF_4$ (10^{-2} mol l^{-1}), $SmCl_3$ (1 mmol), the ketone (10 mmol) and **1** (10 mmol). The solution was electrolysed at 20 °C, at constant current of 100 mA (apparent current density 0.5 A dm^{-2}), under argon, until disappearance of the starting ketone (4–6 h). When **1** was consumed (according to GC analysis of aliquots), further portions of **1** (5–10 mmol) were added during the electrolysis, the final ratio of **1** to carbonyl compound being 3–4 : 1. After acidic hydrolysis and diethyl ether extraction, the products were purified by column chromatography on silica gel with pentane–diethyl ether mixtures as eluent.

and 50% isolated yields, respectively. In the case of a γ,δ-unsaturated ketone **2e** (entry 5), the coupling products were formed in 55% yield without the double bond being affected. The unsaturated lactone **3e** was isolated together with the non-cyclized γ-hydroxyester **4e**, in a lactone to alcohol ratio of 45 : 55. The steric hindrance of the intermediate alcoholate-ester might explain this partial cyclization.

With an aromatic ketone **2f** (entry 6) yields of lactone **3f** were moderate (35%) and 11% of non-cyclized hydroxyester **4f** was also formed. Heptanal **2g** afforded the γ-lactone **3g** in moderate yield, accompanied by pinacol condensation products. In the absence of the chloroester, aldehydes undergo pinacol coupling under the $SmCl_3$-catalysed electrosynthesis conditions.[11] The lack of reactivity of aldehydes for lactone formation has been reported in the case of lanthanoid-mediated lactonization with 3-iodo- or 3-bromo-esters.[5] With SmI_2 in tetrahydrofuran (THF)–HMPA, a single example of efficient aldehyde ($C_6H_{11}CHO$) lactonization with methyl 3-bromopropionate has been described.[6]

The presence of $SmCl_3$ in the electrosynthesis of γ-lactones was essential; in its absence, electrode passivation, polymerisation, lack of selectivity and lower yields were obtained. Thus, for the reaction of cyclohexanone **2a** with **1** (entry 1) in the absence of $SmCl_3$, the lactone **3a** was formed in 37% yield with a ketone conversion of 70%.

In conclusion, a new samarium-catalysed γ-lactone synthesis by direct reductive coupling of 3-haloesters with carbonyl compounds was carried out by electrosynthesis, in a simple electrochemical set-up. $SmCl_3$ was the catalyst precursor; the active Sm^{II} species is formed *in situ* and recycled by electrochemical reduction. Moreover, for the first time, 3-chloroesters have been utilized as the starting materials in these cyclizations, instead of the more reactive bromo or iodo derivatives generally needed.

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