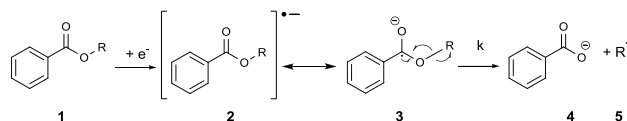# Organic electrosynthesis using toluates as simple and versatile radical precursors.

Kevin Lam[a] and István E. Markó[a]

The electrolysis of toluate esters leads easily to the formation of the radical of the alkyle part. This propriety has been used to develop a new electrochemical deoxygenation reaction.

The transformation of a hydroxyl group into the corresponding alkane represents an important tool for organic chemists. The well-known Barton-McCombie reaction has been considered as a reference to do such transformation.[1] Nevertheless; this last procedure suffers from the fact that sensitive xanthates have to be synthesised and from the use of toxic reagents, as tin derivatives and AIBN. Nowadays, the concern to develop ecological reactions is becoming more and more important, that's why some alternatives have been found like the trialkylborane/water system.[2] Organic electrosynthesis also represents a great alternative in the scope of developing new economical and environmental-friendly reaction. Only few preparative electrochemical deoxygenation reactions have been reported in the literature. They usually require rather negative potential[3], and so, the use of lead or mercury cathode with high overvoltage or they are limited to primary and secondary alcohols.[4] Recently our lab has developed a method for generating radical directly from a simple toluate ester by using samarium(II) iodide[5]. This reaction was successfully transposed to electrosynthesis without the need to use metals or toxic co-solvent anymore.

We, and others,[6] have proposed that the aromatic ester is first reduced into the corresponding radical anion which decompose into the corresponding carboxylate and radical of the alkyle part (See Scheme 1). The kinetic rate of the decomposition is directly correlated to the stability of the produced radical, the more stable will be the produced radical the faster will be the decomposition. This can bee seen from the lost of reversibility in the cyclic voltammetry curve when allyl benzoate cyclic voltammogram is compared to ethyl benzoate cyclic voltammogram (Figure 1).

Scheme 1 Decomposition pathway of the radical anion.

By recording cyclic voltammograms of aromatic esters and by using DigitalSimulation we were able to measure kinetic rates of decomposition (See Table 1). When benzoate is replaced by toluate, the rate of decomposition is dramatically increased. Furthermore, the solvent seems to play an important role in the stabilisation of the radical anion.

Acetonitrile seems to be more stabilizing toward primary and secondary toluates (Entries 1 and 2) whereas DMF is more stabilizing toward tertiary toluate. These results incited us to use toluate moiety for deoxygenation.
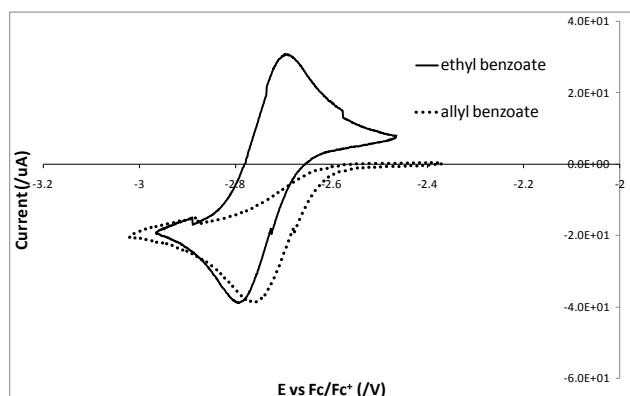
Fig. 1 Cyclic voltammogram of ethyl benzoate (thick line) (10^{-3} M) and allyl benzoate (doted line) (10^{-3} M) in DMF containing 0.1 M NBu_4BF_4. Glassy carbon working electrode/platinum foil counter electrode/reference electrode : Pt wire/sweeping rate 150 mV/s

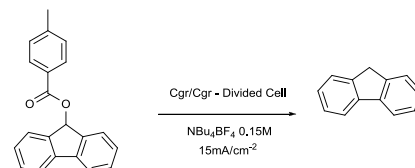**Table 1** Rate of decomposition of aromatic ester radical anion[a].

Entry	Aromatic ester		k /s^{-1} in CH_3CN	Aromatic ester		k /s^{-1} in CH_3CN	k /s^{-1} in DMF
1		**6**	0.012		**10**	0.013	0.091
2		**7**	0.025		**11**	0.048	0.097
3		**8**	0.32		**12**	0.81	0.20
4		**9**	Too fast		**13**		Too fast

[a] All data were measured with 10^{-3} M in analyte.

In a first attempt to deoxygenate, we have tried to electrolyse 9-fluorenyl toluate using an undivided electrolysis cell. All attempts using different sacrificial anodes or different solvents failed. However, to our delight, when the reaction was performed in a divided H-type cell, in NMP, at 130°C, we were able to get the deoxygenated product with a 50% yield.[7]

Surprisingly, when the reaction was carried out in acetonitrile only degradation occurred. Presumably because of side reactions with the solvent. Yields in DMF or NMP are comparable, but NMP is much more convenient for longer electrolysis time since it doesn't not suffer from degradation when heated. Nonetheless NMP suffer from the fact that it is difficult to remove since it has a high boiling point. We have tried to replace NMP by THF. Although the electrochemical window of THF is too short to allow the reduction of the toluate (-2.6V vs Ag/AgCl in EtOH sat. LiCl), it is possible to use a mixture of THF/NMP (9/1 in volume), but the electrochemical cell has to be modified to be enable to work with refluxing THF.
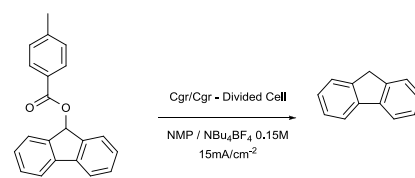
Table 2 Influence of the solvent.[a]

Entry	Solvent	Yield in fluorene
1	CH₃CN	0%
2	NMP	50%
3	THF	0%
4	THF/NMP (90/10)	46%

[a] All reaction were performed under argon in dry and degassed solvent at 130°C or under reflux.

Additionally, the temperature of electrolysis plays a key role. The optimal temperature range lies between 70°C and 130°C. When electrolysis was performed below, only trace of reduced product was found among many other degradation products.

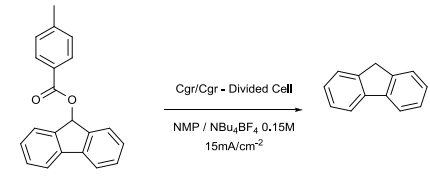**Table 3** Influence of the temperature.[a]

Entry	Temperature	Yield in fluorene
1	25°C	0%
2	70°C	32%
3	100°C	50%
4	130°C	50%

[a] All reaction were performed under argon in dry and degassed NMP.

We have also investigated on the influence of the cathode composition on the final product. As can be seen from Table 4, carbon graphite offers the best yield (entry 1). Surprisingly with copper and lead we obtained, respectively, 10% and 40% of fluorenone instead of fluorene. A plausible explanation could be a reaction between the fluorenyl radical and the oxide layer of the electrode, since copper and lead electrodes are easily recovered by an oxide layer and since we have obtained the same result when using Cgraphite electrode in undegassed NMP.
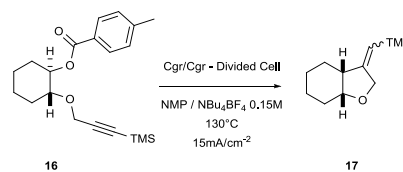
Table 4 Influence of the cathode.[a]

Entry	Cathode	Yield in fluorene
1	Cgraphite	50%
2	Platinum	42%
3	Iron	10%
4	Copper	0%
5	Lead	0%

[a] All reaction were performed under argon in dry and degassed NMP with a 6cm⁻² cathode, except for the platinum cathode which was 9.5cm².
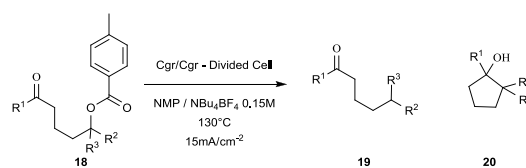
In order to prove the formation of a radical during the reduction process, we have decided to capture this last one by a suitably positioned triple bond in order to form a tetrahydrofuran derivative. When the precursor **16** was subjected to the electrolysis, we were delighted to obtain the excepted tetrahydrofuran **17** with a yield of 60%

Scheme 2. Radicalar cyclization.

We decided to investigate if a radical was formed in each case or if sometimes the radical was further reduced into the corresponding carbanion.

Table 5 Formation of radical or anion.[a]

Entry	R¹	R²	R³		Yield in **19**		Yield in **20**	
1	n-Bu	H	H	**18a**	33%	**19a**	0%	**20a**
2	Me	n-Hex	H	**18b**	64%	**19b**	0%	**20b**
3	Me	Me	Me	**18c**	79%	**19c**	0%	**20c**
4	Me	Ph	H	**18d**	5%	**19d**	62%	**20d**

[a] All reaction were performed under argon in dry and degassed NMP.

As can be seen from Table 5, the substitution of the toluate does not influence the fate of the reduction since reduction of primary, secondary and tertiary toluates give only the reduced non cyclic product (entries 1, 2 and 3). On the other hand, if there is an anion stabilizing group in α of the toluate, the radical is rapidly reduced into the corresponding anion (entry 4). Indeed, benzylic radicals are well-known to be readily reduced into benzylic anion.

Finally, with all these information in hand, we decided to explore the scope and limitations of this method especially regarding to functional group compatibility. Some results are collected in Table 6.

Table 6 Electroreduction of toluates.[a]

Reaction scheme: Toluate **21** (4-methylbenzoate ester, ArCO₂R) converted under Cgr/Cgr – Divided Cell, NBu₄BF₄ 0.15M, 130°C, 15mA/cm⁻² to RH (product **22**).

Entry	Toluate		Product		Yield
1	(adamantyl toluate)	**12**	(adamantane)	**21**	85%
2	(cholesteryl toluate)	**22**	(deoxygenated steroid)	**23**	75%
3	(9-fluorenylmethyl toluate)	**24**	(9-methylfluorene)	**25**	38%
4	(AcO-cyclohexyl toluate)	**26**	(AcO-cyclohexane)	**27**	72%
5	(TBDMSO-cyclohexyl toluate)	**28**	(TBDMSO-cyclohexane)	**29**	83%
6	(HO-cyclohexyl toluate)	**30**	(HO-cyclohexane)	**31**	64%
7	(pyrrolidinone toluate)	**32**	(pyrrolidinyl ketone)	**33**	70%
8	(n-C₂₁H₄₃ alkyl toluate)	**34**	(n-C₂₂H₄₆)	**35**	41%
9	(9-fluorenyl toluate)	**14**	(fluorene)	**15**	50%
10	(phenyl ketone toluate)	**36**	(phenyl ketone)	**37**	67%

[a] All reaction were performed under argon in dry and degassed NMP at 130°C.

As can be seen from Table 6, a wide variety of functional groups are compatible with the deoxygenation reaction. Toluate could be selectively deoxygenated without touching to ester or to silyl ester (entries 4 and 5) and even ketone or unprotected alcohols are compatible (entry 6 and 10). Only primary toluates tend to give lower yields.

In summary, we have developed a new, easy, economical and ecological methodology for deoxygenation of alcohols which tolerates a wide variety of functionalities. In addition, this methodology could also be useful for the electrogeneration of radicals or anions directly from the corresponding toluates.

Notes and references

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7 Standard electrolysis procedure: A H-type cell, with two compartments of 100ml, separated by a sintered glass with a porosity of 40μm, was dried during one night at 200°C. Then two graphite electrodes of 6cm² and magnetical stirred were equipped on the cell and each compartments of the cell were flushed with argon during 10 minutes and then filled with 5g of NBu₄BF₄ and with 100ml of NMP freshly distilled under argon. 600mg of 9-fluorenyl toluate (0,6 mmol), dissolved in few NMP, were added to the cathodic compartment and the solution was stirred and heated up to 130°C. Then the intensity of the current was fixed on 90mA and the mixture was electrolysed until completion of the reaction which was checked by TLC or by GC. Then the cell was cooled down to room temperature and the catholyte was carefully diluted with 100ml of 4N HCl. The resulting solution was extracted 4 times with 30ml of ether, all the organic phases were collected, dried over sodium sulphate and the solvent was removed under reduced pressure. Finally, the crude product was purified by chromatography on silica gel using pentane as eluent (Rf = 0,7) leading to a white powder with a yield of 50%.