Intramolecular reductive cyclisations using electrochemistry: development of environmentally friendly synthetic methodologies

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This review summarises electrochemical reductive intramolecular cyclisations, including transition-metal catalysed reactions. It presents some selected examples of organic halide electroreductions with further intramolecular coupling reactions, carbonyl group reductions with further coupling and intramolecular cyclisations involving electrogenerated bases.

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1. Introduction

The development of alternative methods for selective carbon–carbon bond formation constitutes an important goal in synthetic organic chemistry. In recent years there has been a growing search for clean, catalytic and environmentally friendly methodologies in organic synthesis. Organic electrochemistry may offer an interesting alternative to several synthetic transformations, the electron being a clean, cheap and energetically efficient reagent. The uptake or input of electrons, avoiding the use of stoichiometric reagents, is of particular interest in the area of redox chemistry.

In spite of some important achievements including industrial applications, electrosynthesis remains an under-utilised tool in organic synthesis. However, electrosynthesis does not always need sophisticated equipment or complicated set-up. A simple battery as a power supply and common glassware can be used for preparative synthetic purposes. The possibility of controlling the electrode potential allows a large functional group compatibility. The use of various electroanalytical techniques (in particular cyclic voltammetry) enables the detailed study of mechanistic aspects.

In the field of synthetic organic chemistry, intramolecular C–C bond-forming reactions able to assemble rings for the construction of complex molecules are of particular interest. Intramolecular C–C bond forming reactions by electro-

oxidation have been recently reviewed.[1,2] This review will focus on electroreductive strategies involving cyclisation reactions. Whether effected directly (by direct reduction of the organic substrate at the cathode) or indirectly (in the presence of a mediator or catalyst) these transformations allow ring construction under mild conditions.

From a preparative point of view, one- or two-compartment cells can be used. Single-compartment cells, avoiding membranes and compartment separators allow for much simplicity and for an easier scale-up of the reactions. In the field of electroreduction processes, this methodology is generally associated with the use of sacrificial metal anodes.[3,4]

Electrochemical reduction reactions can be carried out at constant current or at controlled potential. In a constant-current mode, the cathode potential is set on the most easily reducible species, on the first reductive functional group presenting the lowest reduction potential. At the anode, the equivalent anodic process takes place. The advantage of a constant-current transformation lies in the extremely easy set-up; the disadvantage may concern the selectivity decrease once the first reducible species is consumed and the cathodic potential shifts to the next reducible species. In controlled-potential electrolysis, the potential of the working electrode (the cathode in a reduction process) is fixed with respect to a reference electrode. Indeed, only the functional groups with an equal or lower reduction potential than the one set for the cathode will be reduced. The selectivity is maintained all along the processes but the current diminishes with substrate consumption and reactions may take a long time to reach completion.

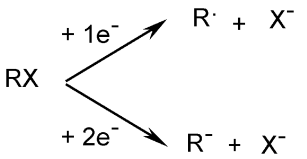
Electroanalytical studies constitute a highly valuable tool that has been successfully employed to determine reaction mechanisms and to study redox reactions and mechanistic aspects of electron-transfer processes.[5]

The aim of this review is to focus on the utilisation of electrolysis as an alternative methodology in organic synthesis, and we concentrated on particular cyclisation strategies for the construction of carbocyclic and heterocyclic compounds, which are common structural components of naturally occurring and biologically active molecules.[6] We will present here some selected recent developments and some traditional examples as well. Reported examples mainly include organic halide electroreductions with further intramolecular coupling reactions, carbonyl group reductions with further coupling and intramolecular cyclisations involving electrogenerated bases.

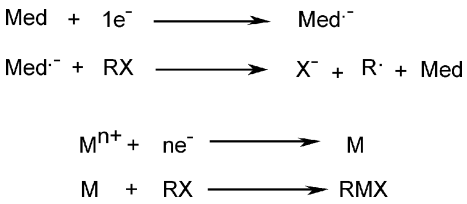
2. Cyclisations involving electroreduction of organic halides

The electroreduction of organic halides is a well studied process in electrosynthesis. The reactions can proceed either through the direct electrochemical reduction of the substrate at the electrode surface (Scheme 1) or through an indirect process, *via* the electrode reduction of a catalyst or mediator and a further electron-transfer or organometallic reaction with the organic halide (Scheme 2).

Direct electrolytic cathodic cleavage of the carbon–halogen bond is an intrinsically irreversible process involving generally a two-electron process to the corresponding carbanion R^- and



Scheme 1 Direct electroreduction of an organic halide R–X.

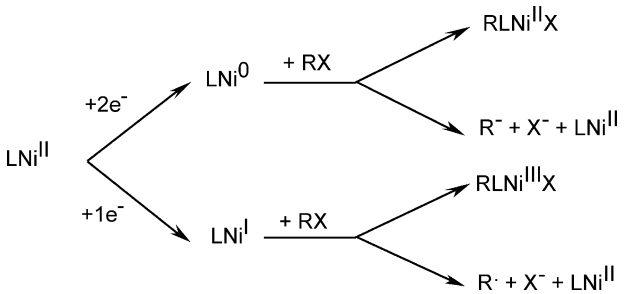


Scheme 2 Indirect electroreduction of an organic halide R–X (Med = organic mediator; M = organometallic species).

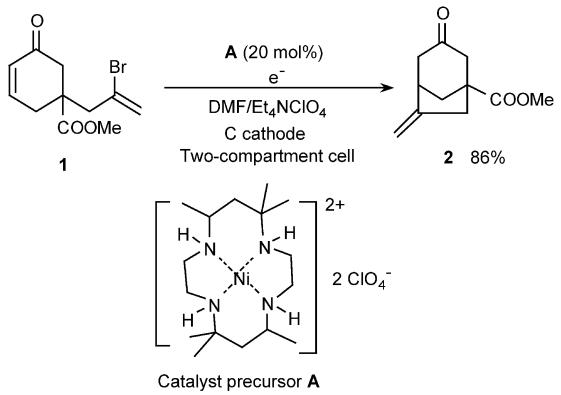
X^-. The direct one-electron reduction is also possible, generating intermediate radical species $R^\bullet$.

When the carbon–halogen bond is reductively cleaved with electron-transfer mediators or catalysts (Scheme 2), the potentials correspond to those of the reduction of the mediator, generally more positive that those required for direct reduction of the carbon–halogen bond. The one-electron transfer from the mediator affords intermediate radical species $R^\bullet$, that can react as such or be further reduced to the corresponding carbanion R^-.

In the field of electrosynthesis *via* organometallic reagents, palladium(II), nickel(II) and cobalt-(II) and -(III) complexes have been mostly used as the catalyst precursors for the reduction and further reactivity on carbon–halogen bonds.[7] In Pd-catalysed coupling reactions, electrogenerated Pd^0 complexes are formed from Pd^{II}, generally in the presence of phosphine ligands. Pd^0 complexes undergo further oxidative addition with the organic halides.[5,8] Cobalt-(II) and -(III) complexes can be reduced in a one- or two-electron processes.[9] In the case of Ni^{II} complexes, reductive coupling reactions have been reported that involve the *in situ* generation of Ni^0 or Ni^I species. Whether Ni^0 or Ni^I species are formed mainly depends on the nature of the ligands associated with the Ni^{II} complex.[10] In particular, salen and tetraaza-macrocyclic ligands such as cyclam or porphyrin derivatives generate Ni^I species and further radical-type intermediates (Scheme 3).[11] The reduction of Ni^{II}-phosphine complexes proceeds either through the formation of Ni^I intermediates with further reduction to Ni^0, or through the direct formation of Ni^0



Scheme 3 Electroreduction of L–Ni^{II} complexes in the presence of organic halides (L = ligand).



Scheme 4 Ni^{II}-precursor-catalysed electroreductive intramolecular vinyl bromide addition to an enone.

complexes by a two-electron reduction.[12] With other ligands, such as 2,2′-bipyridine or mono- or diamines, a direct Ni^{II} reduction to Ni^{0} occurs, with further oxidative addition of the organic halide.[4]

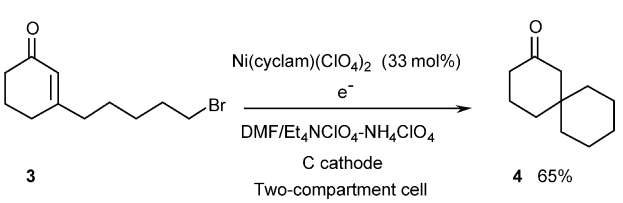
2.1. Addition of monohalides to activated olefins

Classical organometallic 1,4-alkylation and alkenylation of electron-deficient olefins generally involves the introduction of the alkyl or alkenyl moiety with the previous preparation of organocopper,[13] organoboron,[14] organomanganese,[15] organozirconium[16] or other reagents in nucleophilic-type additions.[17] Electrosynthesis enables the direct reductive coupling with no preparation of the intermediate organometallic species. Reported examples mainly concern the catalytic use of Ni^{II} or Co^{III} complexes associated to macrocyclic ligands in radical-type processes.[18]

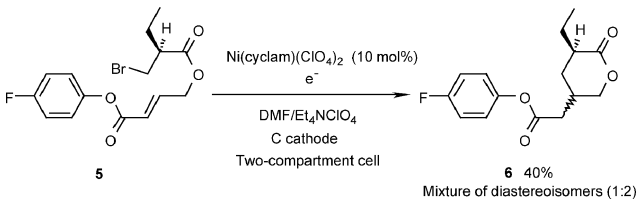
The intramolecular version of a reductive addition of a vinyl bromide to an enone has been reported in the cyclisation of **1**, to give the bicyclic structure **2** in 86% yield (Scheme 4).[19] This cyclisation was catalysed by an electrogenerated Ni^{I} complex derived from Ni(Me_6-cyclam)$(ClO_4)_2$ (Me_6-cyclam = 5,7,7,12,14,14-hexamethylcyclam, catalyst precursor **A**) in DMF and was carried out at −2.0 V *vs.* SCE in a two-compartment cell with a carbon graphite cathode.

The intramolecular 1,4-addition of alkyl bromides for the synthesis of bicyclic ketones has also been performed using various Ni^{II} and Co^{III} complexes as the catalyst precursors (Scheme 5).[20] Thus, the addition of electrogenerated alkyl radicals from alkyl bromide derivative **3** afforded spirolactone **4** in 65% yield with Ni(cyclam)$(ClO_4)_2$ in DMF.

The electrochemical intramolecular 1,4-addition of alkyl bromides to unsaturated esters has been reported for β-bromoester derivatives such as **5** (Scheme 6).[21] The cyclisation was catalysed by Ni(cyclam)$(ClO_4)_2$ precursor and run in DMF at a controlled potential of −1.5 V *vs.* Ag/AgCl.



Scheme 5 Electrosynthesis of spirolactones.



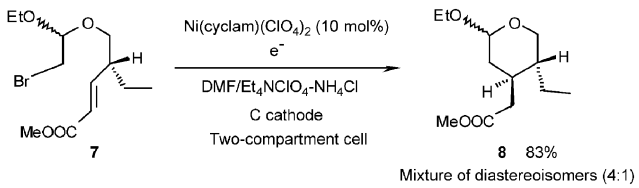
Scheme 6 Electroreductive cyclisation of alkyl bromides on activated olefins.

Electrogenerated Ni^{I}-catalysed electrochemical reactions have been extended to the cyclisation of unsaturated α-bromoacetals to the corresponding functionalised cyclic ethers. Thus, the Ni^{I}(cyclam)(ClO_4)-catalysed electroreduction of substituted 2-bromoacetal **7** led to the six-membered ring ether **8** in 83% yield (Scheme 7).[21,22] Differently substituted pyrans were obtained in a highly regio- and stereoselective manner, giving stereoselectivities up to 99 : 1 for the corresponding lactones, after acetal oxidation with Ag_2CO_3/Celite.

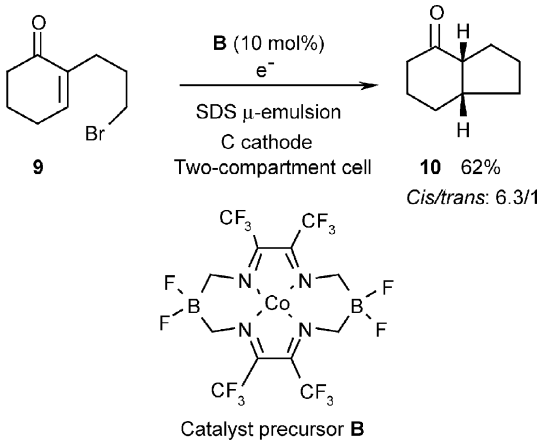
Applications to the stereoselective synthesis of Ipecac and Corynanthe alkaloids and to a lactal precursor of tacamonine were described.[21] By conventional methods, tetrahydropyrans such as **8** could also be formed from **7** by using over-stoichiometric amounts of Bu_3SnH.[23]

The use of vitamin B_{12}, with a reduction potential at −0.9 V *vs.* SCE, is important among Co^{I}-catalysed electrochemical reactions. Electrochemical catalysis using vitamin B_{12} essentially concerns alkylation and acylation of Michael acceptors.[24] Vitamin B_{12} and [bis[μ-[(2,3-butanedione dioximato)(2−)-*O*:*O*′]]tetrafluorodiborato(2−)-*N*,*N*′,*N*″,*N*‴]-cobalt, (catalyst **B**), were used in bicontinuous microemulsions containing cetyltrimethylammonium bromide (CTAB) or sodium dodecyl sulfate (SDS)[25] to convert 2-*n*-bromoalkyl-2-cyclohexenones **9** into the bicyclic ketones **10** in good yields (Scheme 8).[26,27]

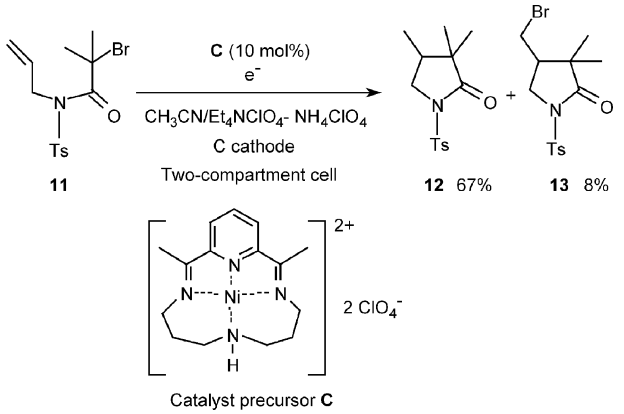
The reaction was proposed to proceed through the electrogenerated L–Co^{I} insertion into the aliphatic C–Br bond of **9** with the formation of a R–Co^{III} intermediate,[28] which reacts as a R^{-} nucleophile in a 1,4-addition process. Increased current efficiencies and high turnover rates (up to 85-fold) were attained for the cyclisation of **9** using metallopolyion films of cobalt corrin derivatives, covalently attached to the carbon electrode, in microemulsion systems.[29]



Scheme 7 Ni^{II}-cyclam precursor-catalysed electroreductive cyclisation of unsaturated α-bromoacetals.



Scheme 8 Electrochemical intramolecular cyclisation in microemulsions.



Scheme 9 Electroreductive cyclisation of *N*-allylic-α-bromo amides using Ni^{I} complexes as the catalysts.

2.2. Cyclisation of monohalides to non-activated C–C double and triple bonds

Electroreductive intramolecular addition of organic halides R–X to carbon–carbon double or triple bonds has been thoroughly investigated. The electroreductive addition of R–X to non-activated C–C multiple bonds generally requires the generation of radical R• species or the presence of an organometallic complex able to activate both the organic halide and the unsaturated bond. Most reported examples use electrogenerated Ni^{I} or Co^{I} intermediates, generally with tetraaza macrocyclic ligands. This methodology involves the formation of $RNi^{III}X$, $RCo^{III}X$ or R• radicals (Scheme 3) and has been extended to numerous cyclisations.

Conventional chemically related one-electron reductants for carbon–halogen bonds are notably tributyltin hydride and samarium diiodide.[30] The use of tin hydrides requires attention to avoid hydrogenation of the intermediate radicals and alkene hydrostannylation.[31] Moreover, the tin hydride is used in stoichiometric amounts and is toxic. SmI_2 in THF solutions has been reported for several selective coupling reactions and generally requires the use of 2 equivalents or more of Sm^{II}.[32]

(a) Electroreductive cyclisation of unsaturated α-bromoesters and α-bromoamides. The electroreduction of α-bromoesters and α-bromoamides generates a stabilised radical (or anion) in the α position of the carbonyl group. Whereas the direct electroreduction of these substrates involves a two-electron reduction and generally forms the corresponding anions that react as nucleophiles (as in the electrochemical Reformatsky reaction),[33] the Ni^{I}-mediated generation of intermediate radicals allows the further intramolecular coupling with non-activated olefins.

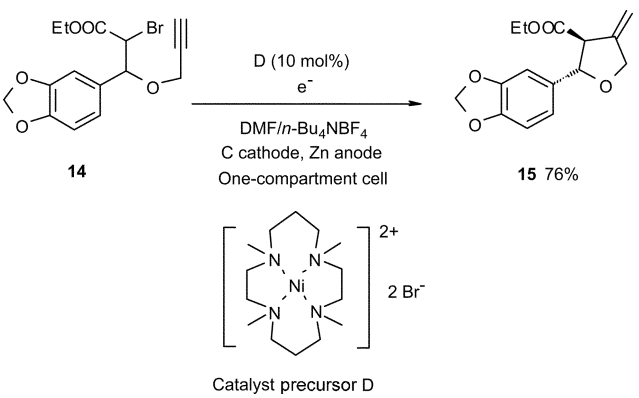
The Ni^{I}-catalysed electroreduction of *N*-allyl- and *N*-propargyl-α-bromo amides provided five-membered lactams in DMF or acetonitrile (Scheme 9).[34] The Ni^{I}-catalyst electrogenerated from precursor **C** at −0.70 V *vs.* SCE, was a Ni^{I} tetraazamacrocyclic complex containing a pyridine moiety. As a typical example, the electroreduction of *N*-allyl-*N*-(bromoacetyl)-*p*-toluene sulfonamide, **11**, afforded 4-methylpyrrolidinone **12** and 4-(bromomethyl)pyrrolidinone **13** in 75% overall yield.

The product distribution is affected by the ability of the solvent to donate hydrogen atoms. The analogous *N*-allyl-α-iodoamides give mainly the iodinated pyrrolidinones (analogous to **13**), indicating a strong reactivity difference of the halogenated substrates according to the transfer rates of the halogen atoms.[35]

The electrochemical intramolecular cyclisation of α-bromoesters containing propargyloxy or allyloxy moieties (Scheme 10) has been shown to afford highly functionalised unsaturated cyclic ethers in good yields.[36,37] In particular, the reductive cyclisation of **14** led to **15** in a highly regio- and stereoselective process using $Ni(Me_4\text{-cyclam})Br_2$ as the catalyst precursor (catalyst precursor **D**), using an undivided cell with a Zn anode in DMF.

The construction of tetrahydrofuran derivatives of type **15** by conventional methods has been recently reported by the use of 2 equivalents of Cp_2TiCl.[38] Other conventional cyclisations of unsaturated α-bromoesters and α-bromoamides have also been reported using Bu_3SnH in over-stoichiometric amounts.[39]

The mechanism of these electrochemical allyl α-bromoester cyclisations has been examined with $Ni(cyclam)^{2+}$.[40] After the reversible one-electron reduction of $Ni(Me_4\text{-cyclam})^{2+}$ to $Ni(Me_4\text{-cyclam})^{+}$ and the further electron-transfer to **14** with



Scheme 10 Electrochemical intramolecular cyclisation of propargyloxy bromoesters.

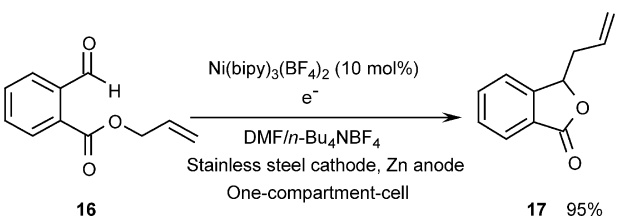
carbon–bromine bond cleavage, the proposed radical intermediate undergoes a rapid intramolecular cyclisation to yield the cyclic ether **15**. In the absence of the nickel catalyst, an elimination reaction to an acrylate derivative of **14** occurs without cyclisation.

The reductive cyclisation of propargyloxy and allyloxy α-bromoesters has recently been carried out in more friendly ethanol and ethanol–water mixtures as the solvents.[41] For example, 97% cyclisation was obtained from **14** (Scheme 10) in EtOH–H_2O (9 : 1) with Ni(Me_4-cyclam)Br_2 (catalyst precursor **D**) using a consumable Mg anode. In these protic media, a radical reaction based on the one-electron reduction of Ni^{II} was also proposed.

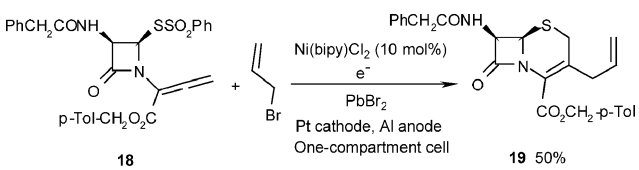
(b) Cyclisations involving allyl halide reductions. Electrochemical reactions involving the reduction of allyl halides, acetates or phenolates in the presence of carbonyl compounds—leading to the synthesis of homoallyl alcohols—have been extensively studied. In particular, direct[42] and catalysed electrochemical allyl coupling reactions with tin(IV),[43] samarium(III)[44] and nickel(II)[45] precursors have been described. Electrochemical intramolecular allyl transfer reactions have also been reported.[46] The electrochemical allyl transfer processes have been applied to the reductive cyclisation of *ortho*-carbonylated allylic esters **16** to form bicyclic lactones **17** (Scheme 11).[47] Reactions were catalysed by $Ni(bipy)_3(BF_4)_2$ precursor (bipy = 2,2′-bipyridine) and run in DMF in a single-compartment cell with a Zn anode, affording the corresponding lactones in yields up to 95%.

Intermediate π-allyl-Ni^{II} species have been proposed to be formed from electrogenerated Ni^0-bipy complexes and the allyl substrates.[48,49] Allyl transfer from the ester to the carbonyl group of **16**, followed by lactonisation of the hydroxy acid intermediate, occurred in a one-pot reaction. In conventional allylations, stoichiometric Ni^0 reactions with aldehydes involving (π-allyl)Ni^{II} species have been reported,[50] but no example of allyl transfer or of lactone formation (as in Scheme 11) by conventional methods has been reported.

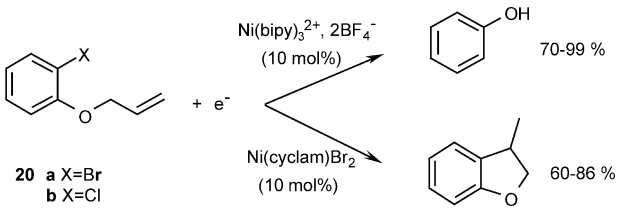
The allylation of allenic esters involving further cyclisation has been reported for the electrosynthesis of cephalosporin derivatives (Scheme 12).[51,52] The catalytic precursor system



Scheme 11 Ni^0-catalysed allyl transfer process to benzolactones.



Scheme 12 Electrosynthesis of cephalosporin skeletons.



Scheme 13 Strong influence of the ligand on the selectivity of the electroreduction of α-halogenated allyloxy benzenes.

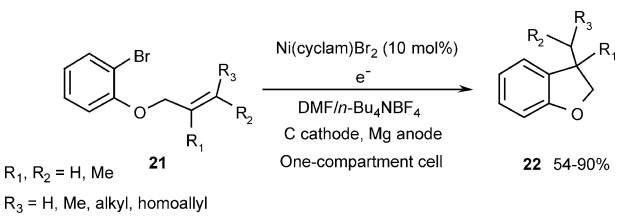
was a combination of Ni(bipy)Cl_2 and $PbBr_2$ to obtain bicyclic lactams of type **19**.

(c) Reductive cyclisation of unsaturated aryl halides. The electroreduction of *ortho*-allyloxyhalobenzenes such as **20** in view of intramolecular cyclisations has been thoroughly examined in the presence of nickel(II) complexes. It was shown that the nature of the ligand associated with the metal strongly determines the reactivity and selectivity of reactions of such halogenated allyl ether substrates. Whereas Ni^{II}-bipy complexes [such as $Ni(bipy)_3(BF_4)_2$ or Ni(bipy)Br_2] led to selective C–O bond cleavage of the allyloxy moiety of **20** affording phenol derivatives (Scheme 13), the use of Ni^{II}-cyclam-type complexes selectively afforded cyclic compounds.[10] In the absence of catalyst, the main processes were dehalogenation and isomerisation of the double bond to the corresponding enol ethers.[53]

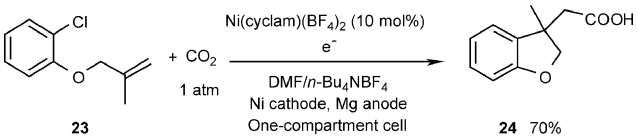
In the presence of Ni^{II} with tetraaza macrocyclic ligands, the electrochemical cyclisation of 2-allyloxyhalobenzenes **21** led selectively to 3-methyldihydrobenzofurans **22** in good yields. No six-membered ring benzopyran derivatives were formed.[19,54] Reactions could be efficiently carried out at constant current in DMF in single-compartment cells with a consumable Mg anode at room temperature (Scheme 14).[55] Thus, allyl bromoaryl ethers **21** reductively afforded benzofurans derivatives **22** in 54–90% yields.

Chloro-, bromo- and iodoaryl derivatives were used with different allyl substitutions. The possibility to cyclise progargyl analogues of **21** leading to substituted benzofuran structures has also been reported.[55] Other macrocyclic ligands derived from cyclam, such as Me_4-cyclam, as well as N-tetradentate ligands such as bis-pyridine bis-oxazolines,[56] showed also high efficiency in these cyclisations. Interestingly, allyloxy chlorobenzene derivatives, difficult to activate by conventional methods, could also be efficiently cyclised in yields up to 77%.

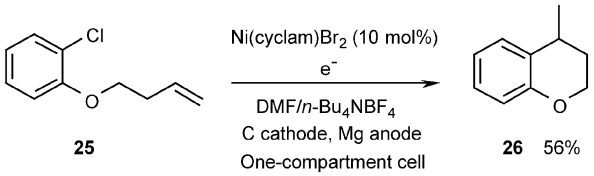
The electrochemical tandem cyclisation–carboxylation process of functionalised aryl halides **23** in the presence of CO_2 has been described in $Ni^I(cyclam)^+$-catalysed reactions, to



Scheme 14 Electrochemical intramolecular cyclisation of 2-allyloxybromobenzenes catalysed by Ni(cyclam)Br_2 precursor.



Scheme 15 Electrochemical tandem cyclisation–carboxylation of functionalised aryl halides.



Scheme 16 Electroreductive synthesis of 1-dihydrobenzopyran derivatives.

afford regioselectively carboxylic acids such as **24** in bicyclic structures (Scheme 15).[57]

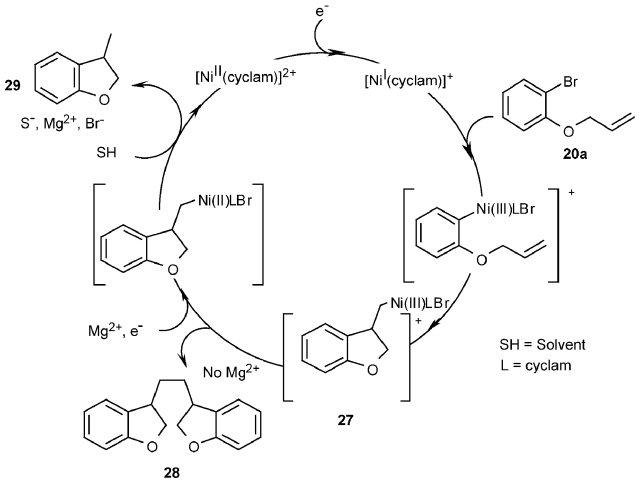
The electroreductive cyclisation of aryl halides bearing homoallylic alcohols at the *ortho* position allowed the synthesis of six-membered ring ethers. Thus, 1-dihydrobenzopyran structures **26** were obtained in yields of 40–68% (Scheme 16).[55,56] The position of the double bond on the aryl side-chain determined the five- *vs.* six-membered-ring cyclisation. These cyclisations used Ni^{II}-cyclam and Ni^{II}-bis-pyridine bis-oxazolines as the catalyst precursors in DMF in single-compartment cells.

The analogous cyclisation of allyl halobenzyl ethers afforded the corresponding 2-dihydrobenzopyrans in 52–56% yields, with either chloro or bromo starting aryl derivatives.[55,56]

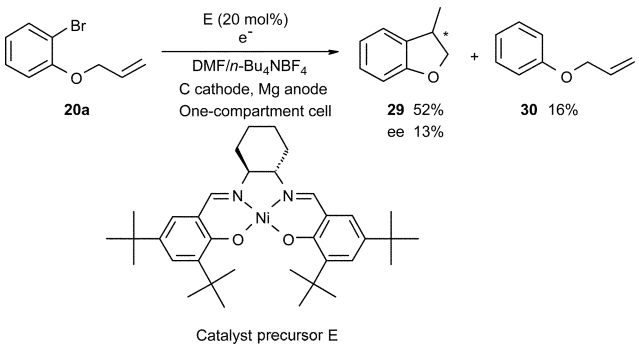
The mechanism of the aryl halide cyclisations on side-chain double bonds has been examined with Ni(cyclam)Br_2.[58] Cyclic voltammetry indicated that the initial Ni^{II}/Ni^{I} reversible reduction at −1.45 V *vs.* Ag/AgCl in DMF solutions led to an irreversible catalytic current upon addition of halide **20a**. This behaviour is indicative of electron transfer from the electrogenerated Ni^{I} complex to the substrate. It was proposed that the electrogenerated Ni^{I} species oxidatively add to the aryl-halogen bond to form a $ArNi^{III}X$-type intermediate (Scheme 17). The radical character of the aryl moiety of this Ni^{III} complex allowed for its addition on the side-chain double bond to form intermediate **27**; a further one-electron reduction regenerated the Ni^{II} species.

It was also shown that the presence of Mg^{2+} ions (which were issued from the oxidation of the Mg anode) had an important effect in controlling the reactivity and the selectivity of the catalytic system. In the absence of Mg^{2+}, an increased ratio of dimers **28** was observed.[58]

The electrochemical intramolecular cyclisation of allyl 2-bromophenyl ethers has also been developed using Ni^{I}(salen)-type complexes as electron-transfer mediators, including chiral complexes.[59,60] Ni^{I}(salen) was shown to be an efficient catalyst for these reductive cyclisations, run under controlled-potential conditions in DMF. Dihydrobenzofuran derivatives were obtained in good yields (Scheme 18). An asymmetric induction up to 13% enantiomeric excess was achieved.



Scheme 17 Catalytic cycle for the reductive cyclisation of **20a** catalysed by Ni(cyclam)Br_2 precursor.



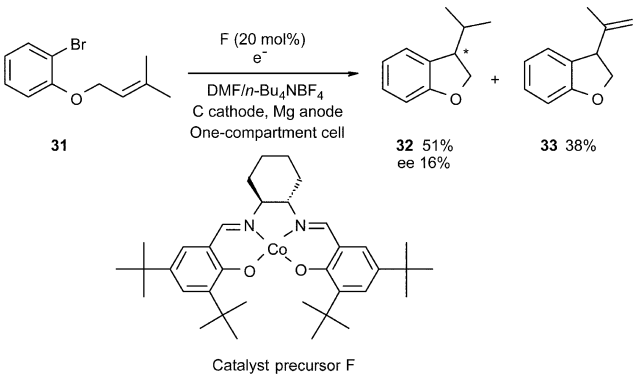
Scheme 18 Ni(salen)-catalysed electrochemical cyclisation of allyl 2-bromophenyl ethers.

Interestingly, the electroreduction of allyl *o*-haloaryl ether substrates in the presence of Pd^{II} complexes with tetraaza ligands underwent a different reaction pathway, involving selective cleavage of the C–O bond of the allyl ethers with no cyclisation, to afford the corresponding phenol derivatives in quantitative yields, as in Scheme 13.[61] This Pd^{II} cleavage process may constitute an alternative catalytic deprotection method for allyl ethers.[62]

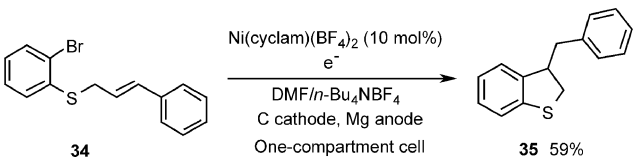
Attempts of asymmetric induction in these electrochemical cyclisations have been reported using Co^{II} complexes associated with a chiral salen derivative as the catalyst precursors.[59,60] The Co-salen complex **F** was shown to be an efficient catalyst precursor for the reductive cyclisation. Cyclic benzofuran derivatives **32** and **33** were obtained in up to 89% overall yields from **31**. Reactions were run in DMF at room temperature, in a single-compartment cell with a Mg anode. Enantiomeric excesses up to 16% have been reported (Scheme 19).

The extension of the electrochemical synthesis to dihydrobenzothiophene derivatives, *via* the reductive cyclisation of *o*-haloaryl allyl thioethers, has been reported with Ni^{I}(cyclam) as the catalyst (Scheme 20).[63] Bromo- and chloroaryl substrates were reduced in DMF and cyclic sulfides were obtained in 40–73% yields.

The conventional chemical preparation of analogous benzo[*b*]thiophene derivatives has been reported with iodoaryl substrates in the presence of stoichiometric amounts of



Scheme 19 Co-catalysed electrochemical cyclisation of allyl 2-bromophenyl ethers.



Scheme 20 Electrochemical synthesis of dihydrobenzothiophene derivatives.

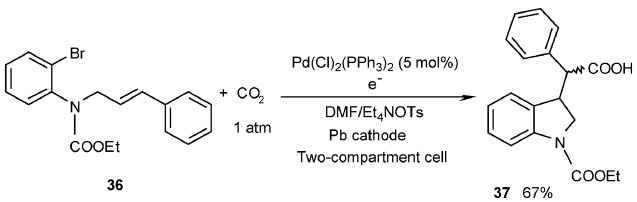
tributyltin hydride and AIBN,[64] and in Pd(0)-catalysed intramolecular Heck-type cyclisations.[65]

In related reactions, the electrosynthesis of N-heterocycles has been reported for the cyclisation of *N*-allyl 2-bromo-4-methoxybenzene to cyclic amines using Ni(Me_6-cyclam)$(ClO_4)_2$.[19] The cyclisations were carried out under controlled potential in two-compartment cells. The reduction of unsaturated aryl thioesters catalysed by Ni^I(salen) and Ni^I(Me_6-cyclam) led to the formation of cyclic ketones and indanones in yields up to 63%.[66]

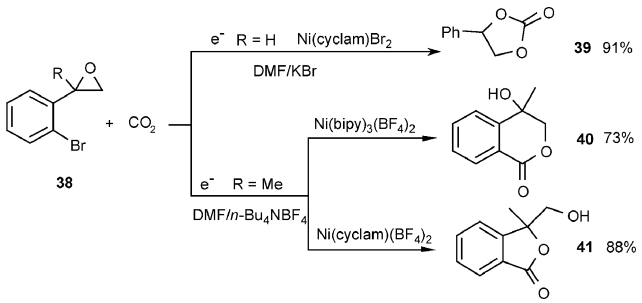
The electroreductive cyclisation–carboxylation of *N*-alkenyl-2-bromoamides leading to indoline derivatives **37** in the presence of CO_2 has been reported in a $PdCl_2(PPh_3)_2$-catalysed tandem process. Reactions were carried out in two-compartment cells with a lead cathode in DMF (Scheme 21).[67]

The catalytic use of Ni^{II} complexes in the electroreduction of aryl halides bearing epoxide groups at the *ortho* position has been studied in the presence of carbon dioxide for the synthesis of cyclic carbonates and benzolactones.[68] The CO_2 incorporation into 2-haloaryl epoxides such as **38** led chemoselectively to different carboxylated products **39–41**, according to the nature of the substrate and of the catalytic system (Scheme 22). Electrolyses were run in DMF using one-compartment cells with a Mg anode.

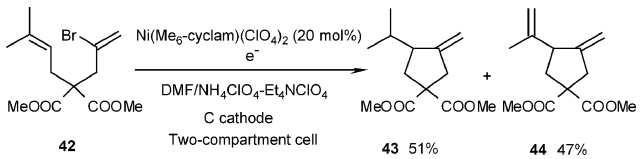
Whereas terminal epoxides led to cyclic carbonates **39** in excellent yields,[69,70] 1,1-disubstituted epoxides first reacted through electrocarboxylation of the carbon–halogen bond of



Scheme 21 Electrosynthesis of indoline derivatives.



Scheme 22 Electrosynthesis of benzolactones and cyclic carbonates from epoxide-functionalised aromatic halides.



Scheme 23 Electrochemical cyclisation of unsaturated vinyl bromides with Ni^I as the catalyst.

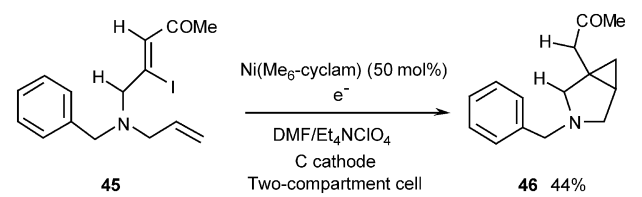
38 followed by the oxirane ring opening.[71] Five-membered-ring benzolactones were formed with cyclam as the ligand on nickel, whereas six-membered-ring isocoumarin derivatives were obtained using 2,2′-bipyridine (Scheme 22).[68]

The analogous insertion of carbon dioxide into aziridines for the synthesis of cyclic carbamates has also been described in Ni^I(cyclam)-catalysed reactions.[72]

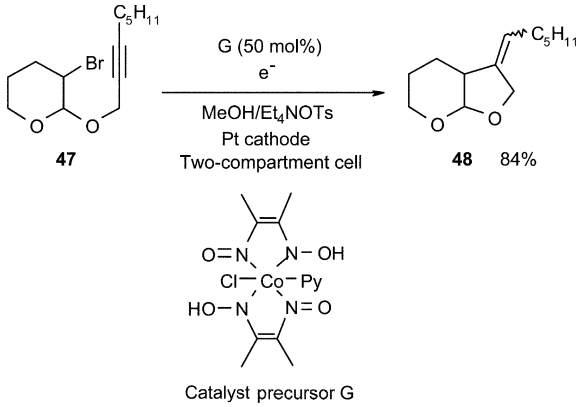
(d) Reductive cyclisation of unsaturated vinyl halides. Radical-type cyclisations of electrogenerated vinyl radicals have been reported to give mono- and bicyclic compounds in good yields.[19] Examples of addition of vinyl bromides **42** to non-activated double bonds have been performed with Ni(Me_6-cyclam)$(ClO_4)_2$ (catalyst precursor **A**) in DMF at controlled potential in two-compartment cells. Electrolyses proceeded preferentially in a 5-*exo* mode to form five-membered-ring methylene derivatives **43** and **44** (Scheme 23).

In connection with this work, a tandem radical cyclisation affording bicyclic cyclopropane derivatives has been investigated.[73] Thus, a vinyl iodide such as **45** reacted through a proposed cyclopropylcarbinyl radical intermediate that underwent electroreduction and further protonation to afford **46** in 44% yield (Scheme 24). The bis-cyclisation used by Ni(Me_4-cyclam)$(ClO_4)_2$ or Ni(Me_6-cyclam)$(ClO_4)_2$ catalyst precursors and could be run in DMF or DMSO.

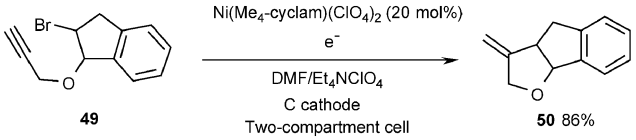
(e) Electroreduction of unsaturated α-bromoacetals. The Co-catalysed cyclisation of allylic and propargylic bromoacetals



Scheme 24 Tandem radical electrochemical cyclopropanation of unsaturated vinyl halides catalysed by Ni^I complexes.



Scheme 25 Electrochemical radical cyclisation of α-bromoacetals on alkyne moieties by Co^{I}.



Scheme 26 Cyclisation of unsaturated alkyl bromide derivatives by electrogenerated Ni^{I} complexes.

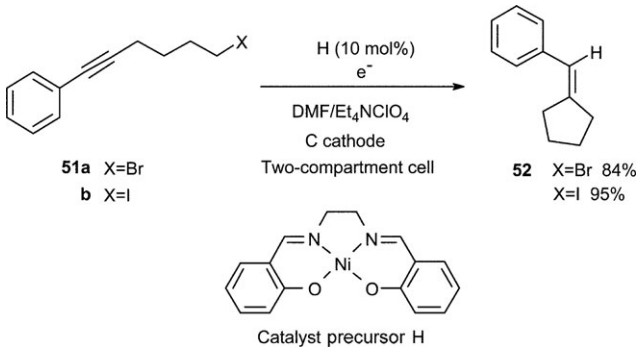
such as **47** afforded the *exo*-methylene bicyclic ethers **48** in good yields, according to Scheme 25.[74]

These Co^{I}-catalysed reductive reactions have been extended to the synthesis of some natural, biologically interesting compounds.[75] The procedure was further improved with the use of a zinc plate as the sacrificial anode in an undivided cell.[75] The proposed catalytic species involved an electrogenerated cobaloxime(I), acting as an electron-transfer agent to the bromoacetal. The first radical intermediate was able to cyclise through an *exo*-type ring-closure on the unsaturated ether chain. A related cyclisation of cyclohexenyl bromoacetals was reported in a microemulsion medium.[76]

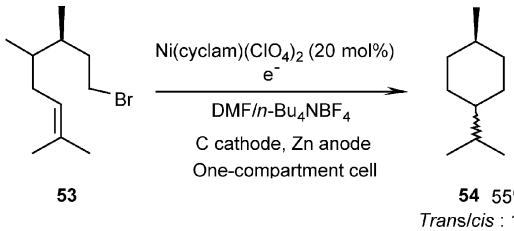
(f) Unsaturated aliphatic monohalides. The methodology using electrogenerated Ni^{I} intermediates for intramolecular cyclisations has also been extended to alkyl halides possessing non-activated olefins or C–C triple bonds, as illustrated in Scheme 26.[54] Alkyl bromides such as **49** could be cyclised *via* the 5-*exo*-trig mode to the corresponding tetrahydrofuran **50** in 86% yield. Several Ni^{II} tetraaza macrocyclic complexes were tested in controlled-potential electrolyses (at the reduction potential of the nickel(II) complexes ranging from −0.95 to −1.38 V *vs.* SCE) in DMF at room temperature.

The electroreduction of 5-alkynyl iodides and bromides using Ni^{II}(salen) (catalyst **H**), under controlled-potential conditions in two-compartment cells afforded vinyl cycloalkanes in good yields. Thus, the reduction of 6-iodo- or 6-bromo-1-phenyl-1-hexyne, **51a,b**, led to benzylidenecyclopentane **52** in 84–95% yields (Scheme 27) in reactions carried out in DMF or acetonitrile.[77]

Mechanistic studies have been performed with substrates **51**.[78,79] Ni^{I}(salen) species was generated at −1.75 V *vs.* SCE, a potential where the haloalkynes were not electroactive. The substrates were reduced catalytically to form radical intermediates, which regioselectively afforded benzylidenecyclo-



Scheme 27 Electrochemical reduction of 6-bromo- and 6-iodo-1-phenyl-1-hexyne using Ni^{II}(salen) as the catalyst precursor.



Scheme 28 Electroreductive cyclisation of citronnellyl bromide.

pentane.[80,81] The direct, non-catalysed electrochemical reduction of these acetylenic halides led to reductive dehalogenation without cyclisation.[82]

The electrochemical reductive cyclisation of 6-bromo-1-hexene and of citronellyl bromide **53** (Scheme 28) was reported using Ni(cyclam)$(ClO_4)_2$[83] and Ni^{II}(salen)[84] as catalyst precursors.

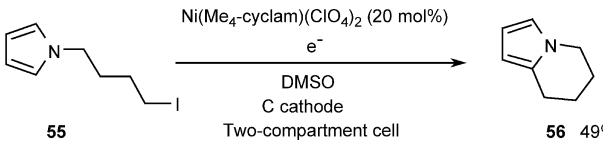
Cyclic compounds (methylcyclopentane and *p*-menthane **54**, respectively) were obtained in one step in yields up to 65%; the main by-products were formed from the reductive dehalogenation of the substrates.[85] Mechanistic studies including the effect of proton donors have been carried out.[86,87]

2.3. Electroreduction of organic halides and coupling to aromatic systems

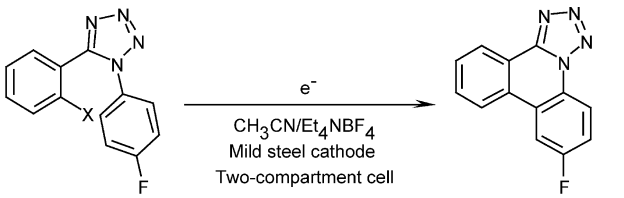
The intramolecular electroreductive addition of 1-(ω-iodoalkyl)pyrroles **55** to bicyclic ring systems **56** has been studied in a catalysed reaction using Ni(Me$_4$-cyclam)$(ClO_4)_2$ (catalyst precursor **D**) (Scheme 29).[88]

The direct synthesis of aryl–aryl bonds involving cyclisations has been reported *via* the non-catalysed electrolytic cleavage of aryl–halogen bonds,[89,90] for the preparation of bicyclic and tricyclic structures.[91,92] Thus, the electroreduction of tetrazoles **57** afforded phenanthridine **58** in high yields (Scheme 30).[93]

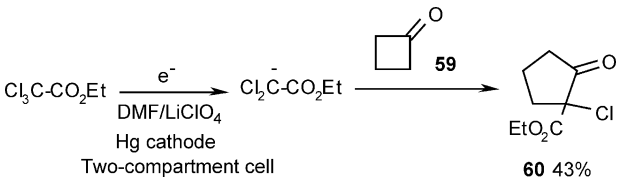
The cyclisation could be run in an undivided cell using a mild-steel cathode and a sacrificial magnesium anode.



Scheme 29 Electroreductive alkyl halide addition to heteroaromatic rings.



Scheme 30 Electrochemical radical cyclisation of aryl halides **57** to the tricyclic structure **58**.



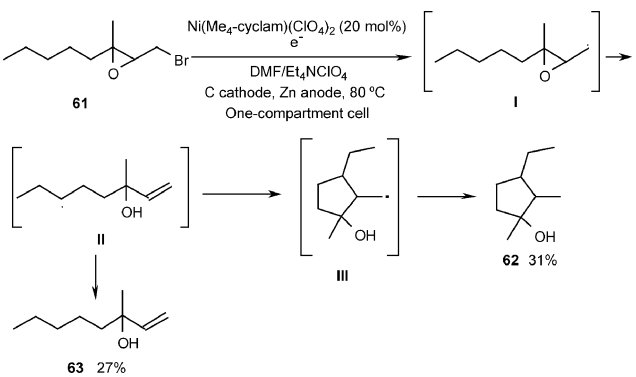
Scheme 31 Electroreductive cyclisation with ring expansion.

Aryl radical intermediates, formed by reduction of the carbon–halogen bond of **57**, were proposed.[94,95] Conventional related biaryl-forming reactions have been described using tributyltin hydride or low-oxidation-state transition-metal complexes, under stoichiometric conditions.[96]

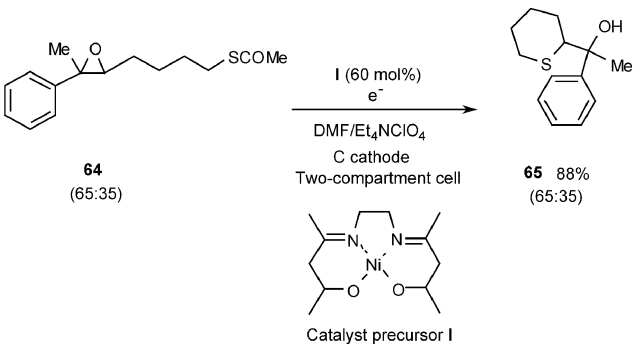
2.4. Electroreduction of organic halides and coupling to carbonyl derivatives and epoxides

The electroreductive addition of an organic halide to carbonyl compounds for the synthesis of alcohols has been extensively investigated.[4,97] A particular example with an addition-cyclisation process concerns the electroreductive coupling of ethyl trichloroacetate to cyclic carbonyl compounds with ring expansion to afford the (n + 1) cyclic ketones (Scheme 31).[98]

An interesting electroreductive cyclisation of α-bromoepoxides with ring expansion to five-membered-ring cyclic alcohols has been reported in a Ni^{I}-catalysed process.[99] Thus, the reaction of 1-bromo-2,3-epoxyalkane **61** led to substituted cyclopentanol **62** in 31% yield as a mixture of diastereomers (Scheme 32). Allyl alcohols **63** were obtained as the side-products. Reactions were performed in DMF with Ni(Me$_4$-cyclam)(ClO$_4$)$_2$ as the catalyst precursor (catalyst precursor **D**) at constant current in an undivided cell with a Zn anode.



Scheme 32 Electrochemical reduction of 2,3-epoxybromides catalysed by Ni(Me$_4$-cyclam)(ClO$_4$)$_2$ precursor.



Scheme 33 Intramolecular reductive ring-opening of epoxy-thioacetates catalysed by Ni^{I}.

The proposed mechanism involves the radical fragmentation of 2,3-epoxybromides. The first Ni^{II} to Ni^{I} reduction with formation of an α-epoxy radical affords an allyloxy radical **I** that undergoes a 1,5-hydrogen shift to **II**. Further radical-type 5-*exo*-cyclisation on the double bond forms **III**. The further reduction or disproportionation of **II** and **III** affords the observed reaction products **62** and **63**.

The nickel-catalyzed electroreduction of the thioacetates **64**, bearing an epoxy group at the γ- or δ-positions of the thioacetate moiety, also allowed for cyclisation (Scheme 33).[100]

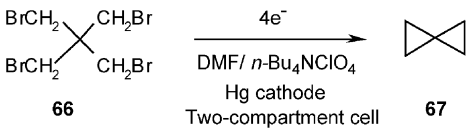
Five- and six-membered ring thioethers (such as **65**) were obtained in good yields in electrolyses run in DMF in a divided cell.[101] These functionalised cyclic sulfides are useful intermediates for the synthesis of biologically active compounds.[102]

2.5. Electroreduction involving di- and trihalides

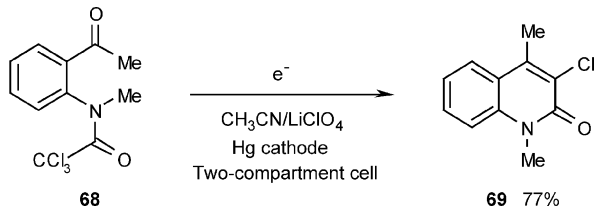
While 1,2-dihalides generally afford olefins upon electroreduction, small-ring compounds such as cyclopropane and cyclobutane derivatives can be obtained from the corresponding 1,3- and 1,4-dihalides, respectively.[103,104] Highly strained bicyclobutanes were obtained from dihalogenated cyclobutanes. The example of Scheme 34 illustrates the synthesis of spiropentane **67** from the electrolysis of 1,3-dibromo-2,2-bis(bromomethyl)propane **66** at a mercury cathode.[105]

More recent work concerning the direct reduction of α,ω-dihaloalkanes in DMF confirmed that, while the direct electrolyses of 1,3-dihalopropanes afforded cyclopropanes in high yields,[106] the direct reduction of higher 1,ω-dihaloalkanes[107–109] gave the corresponding cyclic derivatives in very low yields. However, in the presence of electrogenerated Ni^{I}(salen), 1,6-dibromohexane affords cyclohexane in up to 78% yield in DMF.[110]

The electrochemical version of the Darzens reaction for the synthesis of epoxides has been examined.[33,111,112] The electroreduction of trichloroacetamides with further intramolecular

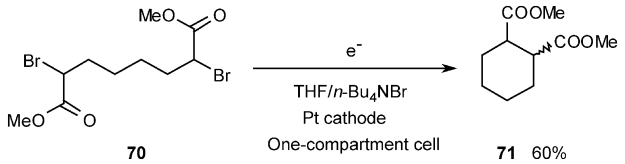


Scheme 34 Electrosynthesis of spiropentane.



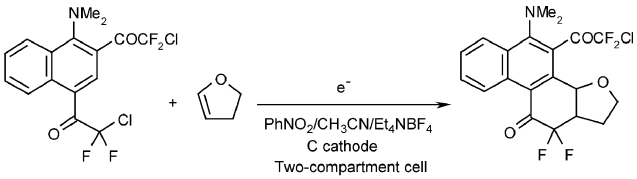
68 69 77%

Scheme 35 Electrosynthesis of substituted quinolinones.



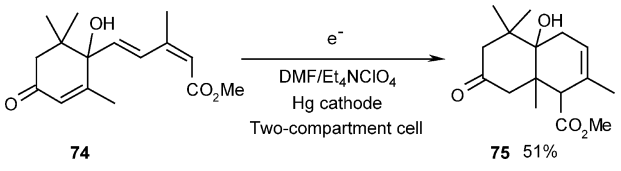
70 71 60%

Scheme 36 Electrosynthesis of cyclised 1,2-diesters.



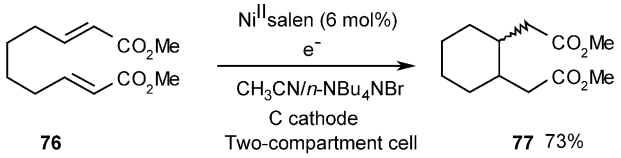
72 73 60%

Scheme 37 Electrosynthesis of cyclised α,α-difluoroketones.



74 75 51%

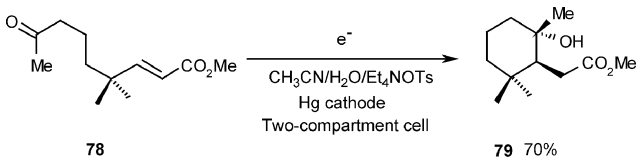
Scheme 38 Electrosynthesis of decalin derivatives.



76 77 73%

Trans/cis: 3.1/1

Scheme 39 Electrosynthesis of cyclic 1,2-diesters.



78 79 70%

Trans/cis : 1/2.9

Scheme 40 Electrochemical reductive coupling involving unsaturated esters.

coupling with a carbonyl group has been reported for the synthesis of substituted quinolinones and dioxindoles.[113] Thus, the cathodic reduction of trichloro-*N*-methylacetamide **68** at −1.2 V *vs.* SCE afforded quinolinone **69** in 77% yield after reduction of the epoxide intermediate (Scheme 35).

Concerning intramolecular reductive α-bromoester coupling, the electrolysis of α,α′-dibromoalkanedioates afforded cyclised 1,2-diesters of various ring sizes.[114] Thus, 1,6-dibromide **70** was reduced to give cyclohexanedicarboxylate derivative **71** in 60% yield (Scheme 36).

Cyclisations proceeded in THF in a single-compartment cell with two platinum plate electrodes; *cis*/*trans* ratios were very dependent on the reaction conditions.

In the field of fluorinated compounds, the electrochemical cyclisation of α,α-difluoroketones has been reported.[115] The reductive coupling of chlorodifluoro ketone **72** with electron-rich olefins afforded polycyclic **73** in 60% yield (Scheme 37).[116] Reactions proceeded under controlled-potential electrolysis at −1.3 V *vs.* SCE.

A free-radical addition of the electrogenerated difluoro ketone radicals to the olefinic substrates followed by an intramolecular cyclisation has been proposed.[115] Some of these fluorine-containing heterocycles have potential biological activity.[117]

3. Cyclisations involving electroreduction of carbonyl derivatives

3.1. Coupling of conjugated carbonyl derivatives

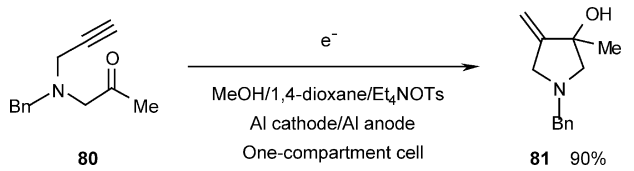
The electrochemical reductive dimerisation of acrylate and acrylonitrile derivatives has been particularly developed for the synthesis of Nylon 6–6 and generally affords the 3,3′-coupling compounds in neutral media and increased 1,1′- and 1,3′-dimers in acidic media.[118,119] The intramolecular version of this coupling hydrodimerisation process generally allows one to obtain *trans* stereoisomers, although the stereochemistry was shown to be highly dependent on the electrolysis conditions.[120–122] Ring-closure has been reported, for example, for the 6-*exo*-trig reduction of methyl abscicate **74** to the decalin **75** (Scheme 38).[123]

The β,β′-coupling of α,β-unsaturated esters has been reported for the preparation of cyclic 1,2-diesters.[124,125] In a recent study, diester **77** was obtained in 73% yield from **76** (Scheme 39), in a Ni^{I}(salen)-catalysed electrohydrocyclisation run in acetonitrile at −2.1 V *vs.* $Ag/AgNO_3$.[126]

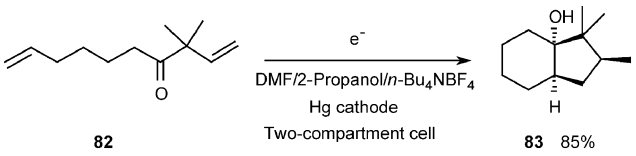
The intramolecular coupling of unsaturated esters or nitriles tethered to carbonyl groups has been reported by direct electrochemical reaction[125] and more recently with Ni^{I}(salen) as the catalyst.[126] In both catalysed and non-catalysed processes, cyclic hydroxylated compounds **79** were obtained in yields ranging from 70 to 94% and regioselectivities up to 11.4 : 1 (Scheme 40). Recent studies indicated the possibility to reductively alkylate the imine group of the salen ligand.[126]

3.2. Cyclisation of carbonyl compounds on non-activated C–C double and triple bonds

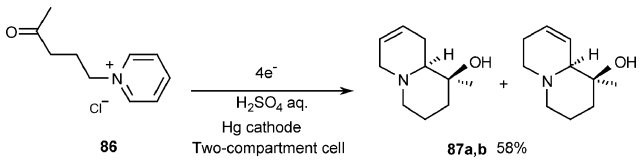
The intramolecular reduction of a carbonyl group and its further coupling with unsaturated systems has been reported with non-activated carbon–carbon double[127–129] or triple bonds,[130] to afford the corresponding cyclic alcohols. The direct, non-catalysed process was proposed to proceed through the initial one-electron reduction of the carbonyl group, with further radical coupling on the unsaturated moiety (Scheme 41). Biologically active intermediates have



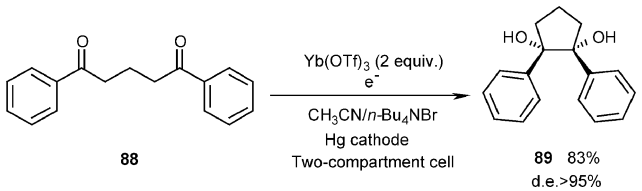
Scheme 41 Electroreductive cyclisation of unsaturated ketones to functionalised heterocycles.



Scheme 42 Stereoselective intramolecular electroreductive cyclisation of unsaturated ketones to bicylic structures.



Scheme 44 Electroreductive cyclisation of the 1-(4-oxopentyl)pyridinium chloride **86** to quinolizidine **87**.



Scheme 45 Electrosynthesis of cyclic *cis*-1,2-diols.

been prepared from unsaturated nitrogen or sulfur derivatives.[131] For example, carbonyl compound **80** underwent a stereoselective reductive cyclisation to afford regioselectively the corresponding heterocyclic alcohols **81** in 90% yield (Scheme 41).[132]

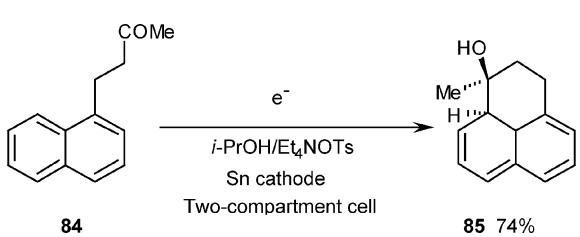
Highly stereoselective cyclisations of non-conjugated unsaturated ketones have been reported in direct electrolyses in DMF–2-propanol mixtures at a mercury cathode in the presence of *N*,*N*-methylquinuclidinium salts.[133] Bicyclic structures such as **83** were obtained in tandem cyclisations (Scheme 42).

Interesting selectivities were obtained by the electrochemical method as compared to conventional reductive cyclisations of unsaturated carbonyl compounds using stoichiometric amounts of reducing agents. Allenic ketones were also reported to undergo electrochemical cyclisation to allylic alcohols.[134]

3.3. Cyclisation of carbonyl compounds with aryl groups

The intramolecular ketone coupling with aromatic groups has also been examined (Scheme 43).[135,136] Thus, naphthyl ketone **84** was directly reduced to afford regio- and stereoselectively the *cis*-isomer of the unsaturated bicyclic alcohol **85** in 74% yield. Reactions were run at room temperature in *i*-PrOH in a two-compartment cell.

The proposed mechanism involved the formation of the ketyl anion radical generated by one-electron reduction, followed by its intramolecular attack on the aromatic ring.[135] The conventional reduction of **84** with Na in HMPA–THF



Scheme 43 Electroreductive intramolecular coupling of ketones with aromatic rings.

(2 : 1) at 0 °C gave the same cyclised alcohol **85** though with a lower yield of 42%.[136]

The cathodic cyclisation of carbonyl-containing pyridinium salts such as **86** has been examined for the synthesis of quinolizidine derivatives **87**, obtained in 58% yield and a diastereoisomeric 1.3 : 1.0 ratio (Scheme 44).[137]

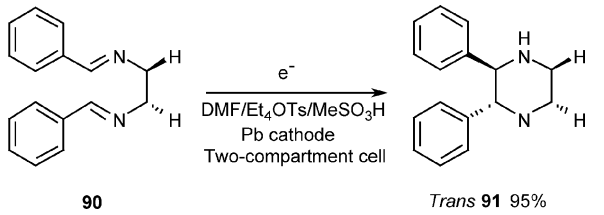
3.4. Coupling of carbonyl compounds, imines and acid derivatives

The preparative-scale electroreductive intramolecular cyclisation of diketones to the corresponding 1,2-diols, the electrochemical intramolecular pinacol reaction, has been thoroughly examined, in particular for aromatic diketones.[138,139] The direct, non-catalysed reduction is efficient for activated carbonyl derivatives, with 1,2-diol stereoselectivities highly influenced by the electrolysis conditions.[140] This electrochemical intramolecular pinacol coupling has also been reported with the use of samarium(III)[141] and ytterbium(III)[142] as the catalyst precursors. Interesting selectivities were reported for the coupling of **88** to afford *cis*-cyclised diol **89** in 83% yield and >95% diastereoselectivity (Scheme 45).[142]

The proposed mechanism involved the reduction of Yb^{III} or Sm^{III} to Yb^{II} or Sm^{II}, respectively, with further electron transfer to the ketone and biradical ketyl coupling. The lanthanide(III) species could be recycled. The electrochemical Sm^{III} coupling constituted the first example in which the more classical SmI_2-mediated pinacol reaction (needing two equivalents)[143] could be run catalytically.

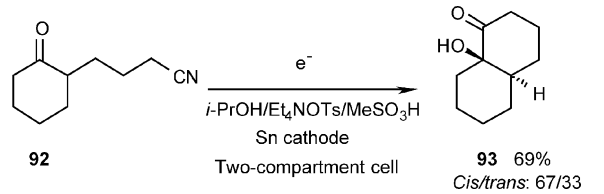
The electroreductive intramolecular coupling of aromatic diimines to the corresponding 2,3-diarylpiperazines has been reported in yields of 40–95%.[144] The reduction of *N*,*N*′-dibenzylideneethylenediamine **90** afforded *trans*-**91** in 95% yield, in electrolysis carried out with a lead cathode in DMF containing methanesulfonic acid (Scheme 46).

Seven- and eight-membered cyclic diamines were obtained stereoselectively by the same procedure, with yields ranging from 30 to 79%. The coupling of chiral diimines derived from chiral ethylenediamines was also investigated and led stereoselectively to chiral diarylpiperazines, which were used as chiral ligands in diethylzinc additions to aldehydes with enantiomeric excesses up to 99%.[144]



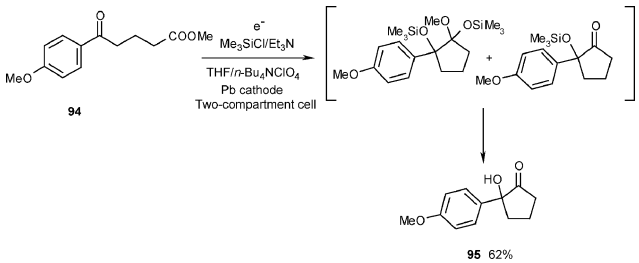
90 *Trans* **91** 95%

Scheme 46 Electroreductive intramolecular coupling of aromatic diimines.



92 **93** 69%
Cis/trans: 67/33

Scheme 47 Electroreductive intramolecular coupling of ketones with nitriles.



94 **95** 62%

Scheme 48 Electroreduction of aromatic δ-keto ester **94**.

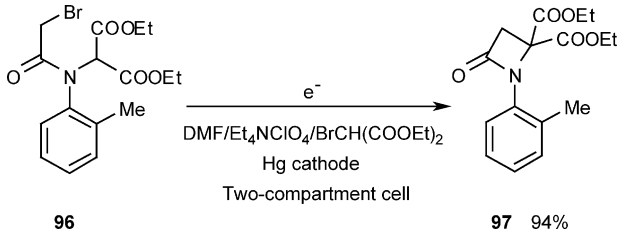
The direct C–C coupling of diesters has also been reported in the case of aryl derivatives to afford 1,2-diketones.[145] Improved yields were obtained using $SmCl_3$[146] or freshly deposited Cd cathodes.[147]

The electroreductive intramolecular coupling of carbonyl compounds with nitriles[148,149] or *o*-methyl oximes[150] afforded stereoselectively the corresponding cyclised compounds. Thus, the direct electroreduction of γ- or δ-cyano ketones such as **92** in *i*-PrOH gave α-hydroxyketones of type **93** in yields of 55–76% (Scheme 47).

The proposed mechanism involved the initial reduction of the carbonyl group to its anion radical or its protonated analogue, with further intramolecular attack on the cyano group and subsequent one-electron transfer and protonation of the α-hydroxy imine.

The analogous electrochemical coupling of carbonyl compounds with non-conjugated ester groups has also been reported, in particular in the case of more easily reducible aryl ketones. Electroreductive cyclisation of aromatic δ- or ε-keto esters such as **94** led to five- or six-membered ring hydrolysed products **95** in the presence of chlorotrimethylsilane and triethylamine (Scheme 48).[151] The corresponding α-hydroxy ketones were obtained in yields up to 95%, this reaction providing an alternative method for the synthesis of α-hydroxy cycloalkanones.

Conventional reductive intramolecular coupling of keto esters for the synthesis of cyclic hydroxy ketones has been described using low-valent titanium as the reducing agent.[152]



96 **97** 94%

Scheme 49 Electrosynthesis of β-lactams using a probase approach.

4. Cyclisations involving electrogenerated bases

Cyclisations have also been reported to proceed through electrogenerated bases and further intramolecular reactions.[153,154] In this approach, the cathodic reduction of a suitable probase R–X or RH yields an electrogenerated base R^-, able to deprotonate the target organic substrate.

This cyclisation methodology has been successfully applied, for example, to the electrosynthesis of a large series of β-lactams.[155,156] Probases such as diethyl bromomalonate have been used, which are able to react with β-bromoacetamides through N–H abstraction and further ring closure and N-C4 bond formation.[157] Deprotonation α to the amide nitrogen in the case of ω-bromoalkanamides or amide-malonate derivatives such as **96** proceeded in excellent yields at a mercury pool cathode in DMF (Scheme 49).[158,159]

The yield of the cyclisation reaction decreased in the order β-lactams > γ-lactams > δ-lactams. By conventional chemical routes in the presence of the same basic conditions, the δ-lactams were not formed, emphasising the advantage of the electrochemical procedure for the preparation of six-membered-ring lactams in good yields.

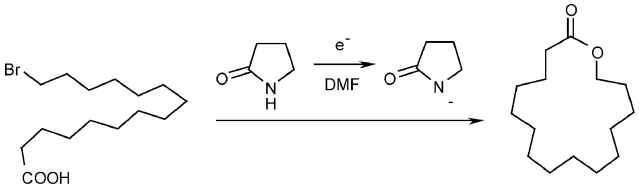
Tetrachloromethane has also been used as a probase for the intramolecular cyclisation of ω-bromoalkyl malonates in high yields. S_N2 reactions of electrogenerated CCl_3^- may compete in this case with proton abstraction.[160]

The use of 2-pyrrolidone as a probase in DMF has been proposed for the synthesis of esters and for the cyclisation of ω-halocarboxylic acids to macrolides, as illustrated in Scheme 50.[161]

5. Other electrochemical cyclisations

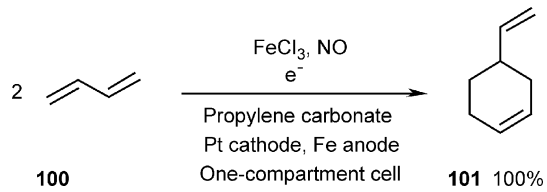
The cyclodimerisation of conjugated dienes to 4-vinylcyclohexene **101** has been reported by the use of an electrogenerated dinitrosyliron(0) complex (Scheme 51).[162]

In the case of butadiene, the reaction was highly selective and the electrogenerated Fe^0 intermediate showed a high catalytic activity, with a turnover frequency of 20 000 h^{-1}.

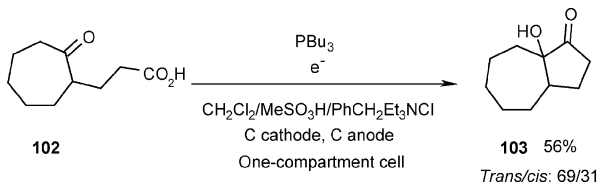


98 **99** 84%

Scheme 50 Electrochemical macrocyclic lactone formation.



Scheme 51 Fe-catalysed electrochemical cyclodimerisation of conjugated dienes.



Scheme 52 Electrochemical preparation of α-hydroxy cycloalkanones from keto acids.

The electroreduction of δ-oxocarboxylic acid such as **102** in the presence of PBu_3 enabled the preparation of bicyclic hydroxy ketone **103** in a stereoselective reaction (Scheme 52).[163]

Electrochemically generated tungsten and molybdenum active species have been reported for olefin metathesis.[164] The process has mainly been applied to ring-opening polymerisation reactions.

6. Perspectives

The development of new reactions and improved synthetic methodologies for the controlled formation of C–C bonds lies at the heart of modern preparative organic chemistry. In this context, recent results highlight the potential synthetic utility of intramolecular C–C bond forming reactions at the cathode. Over the past years, intramolecular electroreductive processes have increased in terms of number and types of transformations reported. These reductive cyclisations afford products ranging from simple monocyclic ring systems to more complex polycyclic skeletons. The compatibility with functional groups appears as an interesting feature of the electrosynthetic methodology.

Despite the high synthetic utility and the environmental advantages of electrosynthesis, this methodology has not yet expanded to a large community of synthetic chemists or to wide industrial applications.

The ease of electrochemical generation of active catalytic species under controlled conditions enables a very large spectrum of regio- and stereoselective syntheses, generally in single-step reactions under mild conditions, generally at room temperature. The scale-up of electrochemical organic reactions has been proven possible, in particular by the use of undivided cells. Significant progress has been made in the recent years, in particular in electroreductive reactions using consumable anodes. This simple and efficient electrochemical methodology should see further development, in particular in the field of transition-metal-catalysed reactions. The combined use of transition-metal complexes and electrosynthesis should allow the generation of novel intermediates able to modulate and better control chemical reactivity. The catalytic use of redox systems in electroreductive processes may offer a wide applicability. This field of indirect electrolysis with specifically reactive metal complexes should expand with synthetic applications and increased selective processes.

Electrosynthesis may offer efficient and controlled reactions in close connection with economic and environmental concerns. The electrode presents some advantages over chemical redox reagents; multifunctional compounds with several electroactive groups can be more selectively converted by the adjustment of the electrode potential and the reaction specificity is generally parallel to the use of mild reaction conditions, avoiding low temperatures and multi-step reactions. Moreover, the use of the electron as reductant avoids the use of stoichiometric amounts of inorganic and metal-based reagents (mostly metal hydrides), making cleaner reactions with easier work-up and less waste, avoiding often expensive reagents.

From an environmental point of view, electrosynthesis should provide in a near future more applications in terms of safe and clean alternative methodology.

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