

Electroreductive Intramolecular Cyclization of Bromoalkoxylated Derivatives Catalyzed by Nickel(I) Tetramethylcyclam in "Green"

Media

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Abstract

The (1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetra-decane)nickel(I), [Ni(tmc)]⁺, electrogenerated at glassy carbon cathodes is shown to be an effective catalyst for the intramolecular radical-type cyclisation of bromoalkoxylated derivatives **1** in alcohol and / or alcohol/water mixtures as well as in microemulsions made with cationic and anionic surfactants. The results obtained indicate that the reaction proceeds *via* cleavage of the carbon-bromine bond to form a radical-type intermediate that undergoes cyclisation on the unsaturated C-C bond to afford substituted tetrahydrofurans. The reactions are more selective and take place at higher current density than when carried out in conventional aprotic solvents.

Keywords: Microemulsions; Electrosynthesis; Catalytic reduction; Intramolecular cyclisation; Nickel(II) complex.

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1. Introduction

The formation of carbon-carbon bonds by radical cyclisation has become an invaluable synthetic tool in organic chemistry especially in the total synthesis of complex natural products [1]. Although tributyltin hydride has been a choice as the radical reducing agent and has wide applications in radical cyclisations for the construction of various organic molecules, its toxicity and the difficulties associated with purification of the products from tributyltin halides tend to limit the widespread use of these methods [1].

Therefore, an area of continuing and important research is to develop new methods of radical generation, which avoid the use of the toxic alkyl tin hydrides. Hence, the indirect electrochemical radical cyclisation [2] catalysed by nickel(II) complexes has been considered as a convenient "green" alternative way to carry out such reactions.

This process is based on an EC' mechanism:



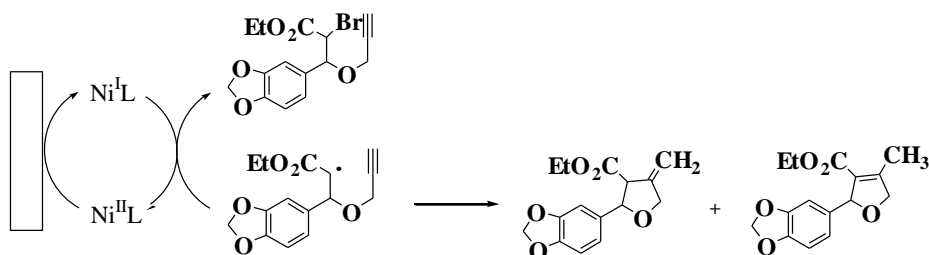
in which $\text{Ni}^{\text{II}}\text{L}$ has a reduction potential positive to the substrate (RBr) and it is reduced at the electrode. The reduced mediator diffuses into the solution and reduces the substrate. The catalytic reaction recycles the mediator back to the electrode according to the kinetics of the system and the relative concentration of the substrate and the mediator (called the excess factor, $\gamma = [\text{RBr}]/[\text{Ni}^{\text{II}}\text{L}]$).

Usually, organic solvents are more fitted to organic reactions, giving higher selectivity as well as allowing the use of higher substrate concentration. However, due to environmental and health issues, the search for non-toxic fluid alternatives to such organic solvents for chemical synthesis are currently receiving attention. Electrolytic organic synthesis in non-toxic fluids would be a valuable, environmentally sound method of chemical production. Water and/or aqueous solvents are a desirable media for electrosynthesis for both economic and environmental reasons, although those solvents cannot always dissolve all the organic substrates in sufficient amounts. Another attractive alternative to organic solvents is to employ microemulsions prepared from water, hydrocarbon oils and surfactants for synthetic organic processes [3]. Microemulsions have attracted wide interest because they have lower toxicity and cost than usual organic solvents, present good solubility for polar and non-polar compounds and allow the possibility of recycling of microemulsion components. They have been widely used in domestic and industrial applications ranging from detergency to cosmetics and pharmaceuticals to tertiary oil recovery [3].

The electrolysis medium is always an issue and non-toxic microemulsions could combine the advantages of aqueous electrochemistry and an appropriate medium for organic chemistry in an environmentally acceptable way.

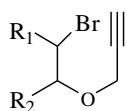
In our previous work, we reported the electrochemical studies of intramolecular cyclisation of propargyl and allyl bromoesters in microemulsions catalysed by electrogenerated nickel(I) at carbon cathodes on bicontinuous microemulsions prepared from water, hydrocarbon oils and surfactant [4]. It was demonstrated that the electroreduction reaction of bromo propargyloxy and bromo allyloxy esters carried out in microemulsions was catalyzed by the electrogenerated Ni(I) complexes (Scheme 1).

Only cyclisation to the five-membered-ring ethers was obtained in moderate to good yields as the main products. Functionalized tetrahydrofurans are important intermediates in the synthesis of natural products such as lignans [5].



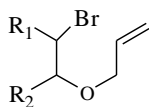
Scheme 1

These results encouraged us to undertake further studies on analogues/derivatives of bromoalkoxy-substituted substrates. Following this approach, in this research we have explored the use of electrogenerated $[\text{Ni}(\text{tmc})]^+$ complex, [(1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane)nickel(I)], to catalyse the reduction of bromoalkoxy-substituted derivatives **1a–1c**. Reactions in bicontinuous microemulsions are compared with those in homogeneous solvents.

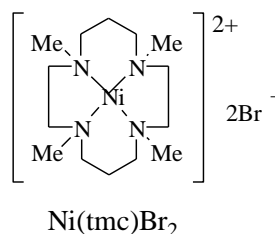


1a: $\text{R}_1 = \text{phenyl}$; $\text{R}_2 = 4\text{-methoxyphenyl}$

b: $\text{R}_1 = \text{phenyl}$; $\text{R}_2 = \text{methoxy}$



1c: $\text{R}_1 = \text{ethoxycarbonyl}$; $\text{R}_2 = 3,4\text{-dimethoxyphenyl}$



2. Experimental Section

2.1. Reagents

Each of the following chemicals was used as received: nickel(II) bromide (Aldrich, 98%), 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (tetramethylcyclam, tmc, ACROS, 97%), *n*-tetradecane (ACROS, 99%), cyclohexane (Lab-Scan, 99%), 1-pentanol (ACROS, 99%), 1-butanol (ACROS, 99%), dodecane (Aldrich, 99%), cetyltrimethylammonium bromide (CTAB) (ACROS, 99%), tetradecyltrimethylammonium bromide (MTAB) (ACROS, 99%), sodium dodecylsulfate (SDS) (Fisher Scientific, 99%) and *n*-hexadecane (Aldrich, 99%), ethanol (EtOH) (Riedel-de-Häen, Analytical Reagent) and 1-propanol (Riedel-de-Häen, Analytical Reagent). We purchased tetraethylammonium bromide (TEABr) with a purity of 98% from Fluka; this electrolyte was stored in a vacuum oven at 80°C to remove traces of water. Deaeration procedures were carried out with zero-grade argon (Air Products).

Published procedures were employed for the preparation of [Ni(tmc)]Br₂ [6] and of, 1-[2-bromo-2-phenyl-1-(prop-2'-nyloxy)ethyl]-4-methoxybenzene (**1a**) [7], [1-bromo-2-methoxy-2-(prop-2'-nyloxy)ethyl]benzene (**1b**) [7] and ethyl 2-bromo-3-(3',4'-dimethoxyphenyl)-3-(allyloxy)propanoate (**1c**) [7].

Synthesis of and 2-(4'-methoxyphenyl)-4-methylene-3-phenyltetrahydrofuran (**2a**), 2-methoxy-4-methylene-3-phenyltetrahydrofuran (**2b**) and 2-(3',4'-dimethoxyphenyl)-3-ethoxycarbonyl-4-methyltetrahydrofuran (**2c**) was based on the method published by McCague *et al.* [8].

The product **2c** is known and it was identified by comparison of their spectroscopic data with those reported [9]. The compounds **2a** and **2b** were

characterized from their spectroscopic data and elemental analysis. These data are presented below:

2-(4'-methoxyphenyl)-4-methylene-3-phenyltetrahydrofuran (**2a**): ^1H NMR (CDCl_3) δ 3.64-3.70 (1H, m, 3-H); 3.78 (3H, s, OCH_3); 4.66 (1H, dq, J 13.2 and 2.4, 5- H_a); 4.72 (1H, app q, J = 2.4, $\text{C}=\underline{\text{CHH}}$); 4.79 (1H, d, J = 9.3, 2-H); 4.84 (1H, broad d, J = 13.2, 5- H_b); 5.09 (1H, app q, J = 2.1, $\text{C}=\underline{\text{CHH}}$); 6.81 (2H, app d, J = 8.5, 2'-H and 6'-H); 7.14 (2H, app d, J = 8.5, 3'-H and 5'-H); 7.22-7.34 (5H, m, Ph). ^{13}C NMR (CDCl_3) δ 55.18, 59.33, 71.96, 88.26, 106.04, 113.62, 126.86, 127.43, 128.48, 129.07, 132.05, 139.10, 152.82, 159.20. Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$ (266.34): C, 81.17, H, 6.81. Found: C, 81.02; H, 6.78.

2-methoxy-4-methylene-3-phenyltetrahydrofuran (**2b**): ^1H NMR (CDCl_3) δ 3.41 (3H, s, OCH_3); 3.81 (1H, broad s, 3-H); 4.61 (2H, app q, J = 2.0, 5- H_2); 4.99 (1H, app q, J = 2.0, $\text{C}=\underline{\text{CHH}}$); 5.02 (1H, broad s, 2-H); 5.12 (1H, app q, J = 2.0, $\text{C}=\underline{\text{CHH}}$); 7.20-7.40 (5H, m, C_6H_5). ^{13}C NMR (CDCl_3) δ 54.78, 56.74, 69.94, 107.38, 110.84, 126.80, 127.61, 128.67, 141.05, 149.83. Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2$ (190.24): C, 75.76; H, 7.42. Found: C, 75.62; H, 7.38.

2-(3',4'-dimethoxyphenyl)-3-ethoxycarbonyl-4-methyltetrahydrofuran (**2c**): ^1H NMR (CDCl_3) δ 1.07 (d, J = 6.9 Hz, 2.55 H, 4- CH_3), 1.18 (d, J = 6.6 Hz, 0.45 H, 4- CH_3), 1.25 (t, J = 7.0 Hz, 0.45 H, OCH_2CH_3), 1.28 (t, J = 7.2 Hz, 2.55 H, OCH_2CH_3), 2.55 (apparent t, J = 9.0, 8.7 Hz, 0.15 H, 3-H), 2.70-2.85 (m, 1 H, 4-H), 3.00 (apparent dd, J = 9.0, 7.8 Hz, 0.85 H, 3-H), 3.66 (apparent dd, J = 8.7, 6.6 Hz, 1 H, 5- H_a), 3.87 (3H, s, OCH_3), 3.89 (s, 3 H, OCH_3), 4.12-4.24 (m, 2 H, OCH_2CH_3), 4.28 (dd, J = 8.4 and 6.6 Hz, 1 H, 5- H_b), 5.05 (d, J = 9.0 Hz, 0.15 H, 2-H), 5.19 (d, J = 7.8 Hz, 0.85 H, 2-H), 6.83 (d, J = 9.0 Hz, 1 H, 5'-H), 6.88-6.92 (m, 2 H, 2'-H and 6'-H).

The compounds 2a–2c were utilized as standards for the determination of gas chromatographic response factors.

In the preparation of the microemulsions each component was added by weight and the mixture was mechanically stirred until clear and homogeneous. The basic composition for cationic bicontinuous microemulsions containing MTAB, CTAB and anionic bicontinuous microemulsions containing SDS were taken from the literature [10,11]. Typically, 50 g of the cationic microemulsion was prepared by dissolving 8.75 g of CTAB in 6.25 g of oil and 17.5 g of water then the liquid became turbid. To this 17.5 g of co-surfactant was added with constant stirring until the mixture became clear and stable. The anionic microemulsion was prepared similarly.

2.2. *Electrodes*

Electrodes for cyclic voltammetry were fabricated from 3-mm-diameter glassy carbon rods (Tokai Electrode Manufacturing Company, Tokyo, Japan, Grade GC-20) press-fitted into Teflon shrouds to provide planar, circular working electrodes with areas of 0.071 cm². Before use, the electrodes were cleaned with an aqueous suspension of 0.05- μ m alumina (Buehler) on a Master-Tex (Buehler) polishing pad. Working electrodes for controlled-potential electrolyses were disks (0.2 cm in thickness, 2.4 cm in diameter, and approximately 100 cm² in total area) sliced from reticulated vitreous carbon logs (RVC 2X1-100S, Energy Research and Generation, Oakland, CA) and graphite felt (2 cm x 2 cm x 0.5 cm) (China Yangzhou Guo Tai Fiberglass Co.,LTD) while a carbon rod was the counter electrode. Procedures for cleaning and handling of these electrodes have been described previously [12].

All potentials are quoted with respect to a Ag/AgCl/3 M KCl in water reference electrode (-0.036 vs SCE).

2.3. Cells and instrumentation

Cyclic voltammograms were recorded in a three-electrode, two-compartment cell as described in earlier publications [13]. All solutions were deoxygenated with a fast stream of argon before each experiment. For controlled-potential electrolysis and product analysis, a divided cell with an anodic and a cathodic compartment separated by a glass sinter (as have been described in earlier publications [14]) was used. The catholyte and anolyte compartments were each 16 cm³. All preparative electrolyses were carried out in an atmosphere of argon, owing to the extreme sensitivity of Ni(I) complexes to oxygen [15], and the catholyte solutions were stirred with a magnetic bar. Cyclic voltammograms were obtained and controlled-potential electrolyses were carried out with the aid of an AUTOLAB model PGSTAT12 potentiostat–galvanostat. The data from the above experiments were acquired and stored by GPES 4.9 software, which controlled a data acquisition board installed in a personal computer.

Elemental analyses were performed with a Leco CHNS-932 analyser. NMR spectra were obtained on a Varian Unity Plus Spectrometer at an operating frequency of 300 MHz for ¹H NMR and 75.4 MHz for ¹³C NMR using the solvent peak as internal reference at 25 °C. Identities of the electrolysis products were confirmed by means of a Hewlett-Packard 5890 Series II gas chromatograph coupled to a Hewlett-Packard 5971 mass-selective detector.

2.4. Identification and determination of products

Gas chromatographic analyses were accomplished with the aid of a Chrompack, type CP 9000, instrument equipped with flame ionization detector. Products were separated with a 25 m x 0.25 mm i.d. capillary column (WCOT fused silica) with a stationary phase of poly(methylphenylsiloxane). A known quantity of an electroinactive internal standard (*n*-hexadecane and/or *n*-tetradecane) was added to a

solution before each experiment to allow quantitative determination of the electrolysis products. Gas chromatographic response factors were measured experimentally with authentic samples of each product, and all product yields tabulated in this paper represent the absolute percentage of starting material incorporated into a particular product.

In order to purify the products, the reaction mixtures were submitted to flash chromatography over silica gel (70-230 mesh) using ethyl acetate for **2a**, diethyl ether-petroleum ether (1:2, v/v) for **2b** and ethyl acetate-hexane (1:5, v/v) for **2c** as eluent. Surfactant or supporting electrolyte and Ni(II) complex are retained on the silica gel columns. After concentration to 16 cm³ under vacuum, the eluent was analyzed by gas chromatography. To isolate the products, the eluent from the first silica gel column should be concentrated and passed through a second silica gel column, and the solvent from the second effluent should be evaporated completely to yield the products [10b].

Identities of the electrolysis products **2** derived from controlled-potential electrolyses were confirmed by means of a Hewlett-Packard 5890 Series II gas chromatograph coupled to a Hewlett-Packard 5971 mass-selective detector: (a) for **2a**, m/z (70 eV) 266, M^+ (10); 129, $[M-CH_3OC_6H_4CHOH]^+$ (100); 91, $[C_6H_5CH_2]^+$ (8); 77, $[C_6H_5]^+$ (18); (b) for **2b**, m/z (70 eV) 290, M^+ (0.5); 159, $[M-CH_3O]^+$ (8); 129, $[M-CH_3OCHOH]^+$ (100); 91, $[C_6H_5CH_2]^+$ (32); 77, $[M-C_6H_5]^+$ (11); and (c) for **2c**, m/z (70 eV) 294, M^+ (84); 279, $[M-CH_3]^+$ (26); 265, $[M-C_2H_5]^+$ (69); 220, $[M-CO_2C_2H_5-H]^+$ (10); 205, $[M-CO_2C_2H_5-CH_3-H]^+$ (35); 165, $[(CH_3O)_2C_6H_3CO]^+$ (100); 29, $[COH]^+$ (16). These identifications were checked by comparison of gas chromatographic retention times for the suspected products, under carefully controlled conditions, with those of the authentic compounds prepared above.

3. Results and discussion

Cyclic voltammetric studies of $[\text{Ni}(\text{tmc})]\text{Br}_2$ complex were performed at scan rates in the range 20 to 400 mV s^{-1} at a vitreous carbon electrode in alcohol and/or alcohol/water mixtures containing Et_4NBr as supporting electrolyte as well as in microemulsions made with cetyltrimethylammonium bromide (CTAB), tetradecyltrimethylammonium bromide (MTAB) and sodium dodecylsulfate (SDS) as surfactants.

As it was shown in earlier studies in ethanol [16], in microemulsions [4] and in organic solvents [15,17-22], the Ni(II) complex always underwent a reversible one-electron reduction to a stable product and that no further reduction occurred within the potential range of the medium. The formal electrode potentials are insensitive to the medium, see Table 1.

The cyclic voltammetric studies of bromoalkoxylated derivatives **1a** – **1c** carried out in alcohol and alcohol/water mixtures containing 0.10 M Et_4NBr and in several microemulsions showed that the bromoalkoxylated compounds present a irreversible reduction wave at potentials in the range -1.41 to -1.50 V vs Ag/AgCl, which corresponds to the reductive cleavage of the carbon-bromine bond. From these data, it can be seen that $[\text{Ni}(\text{tmc})]^{2+}$ complex reduces in a potential region where the bromoalkoxylated derivatives **1a** – **1c** themselves do not undergo reduction.

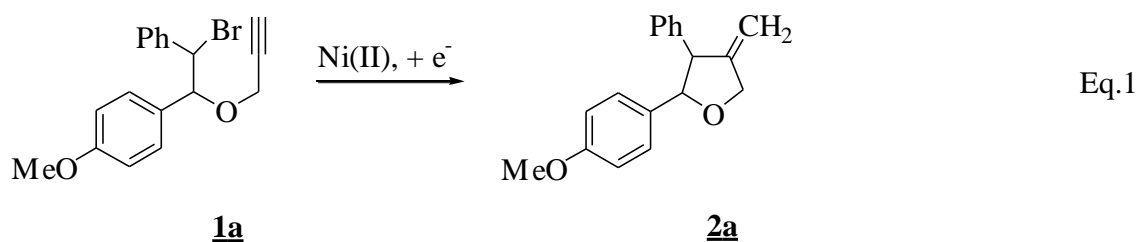
Upon addition of the bromoalkoxylated compounds to the Ni(II) complex mixtures in both alcohol and microemulsions, the experiments showed an increase of the reduction peak height of the complex as the concentration of the substrate increased and the anodic peak for the re-oxidation of $[\text{Ni}(\text{tmc})]^+$ complex was no longer observed due to its chemical consumption. The catalytic current observed result from the

regeneration of the $[\text{Ni}(\text{tmc})]^{2+}$ complex by the rapid homogeneous reaction of the electrogenerated $[\text{Ni}(\text{tmc})]^+$ complex with **1** close to the surface of the cathode. The comparative data obtained from these experiments for different bromoalkoxylated derivatives-to- $[\text{Ni}(\text{tmc})]^{2+}$ ratios are reported in Table 2. It can be seen that the extent of the catalytic reaction increases with increasing the concentration of the substrates **1** for a given mediator concentration and the results are similar in both media. The catalytic cycle is a faster chemical reaction in these media when compared to that observed in aprotic solvents [17-19]. Moreover, the rates of the catalytic cycles are high enough to enable the electrolyses of compounds **1** in the presence of $[\text{Ni}(\text{tmc})]^{2+}$ to occur at current densities acceptable for efficient electrosyntheses. These results are also consistent with our previously reported investigations in both ethanol [16] and microemulsions [4].

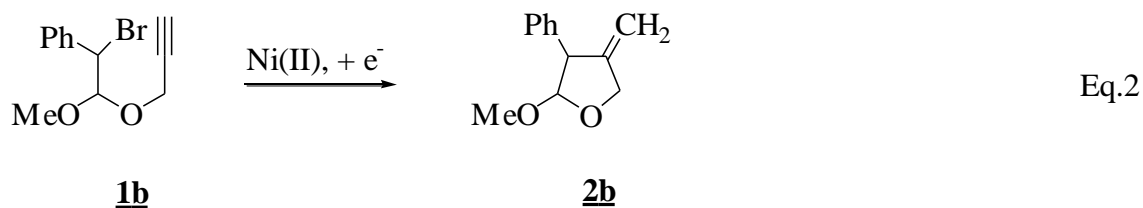
A series of controlled-potential electrolyses of $[\text{Ni}(\text{tmc})]\text{Br}_2$ at both reticulated vitreous carbon (RVC) and carbon felt (CF) cathodes in the presence of different concentrations of **1a** – **1c** in 1-PrOH and 1-PrOH/H₂O mixtures containing 0.1 M Et₄NBr and in several microemulsions were performed at ~ -1.0 V vs Ag/AgCl/ 3M aqueous KCl. Experimental parameters, such as the ratio of substrate to catalyst and the influence of water were examined to evaluate their effect on the product yields. Compiled in Table 3 are the coulometric *n* values (based on the consumption of substrates) and product yields obtained from these experiments; each entry represents the average of two or three separate runs. For every electrolysis, the current was monitored as a function of the charge passed until all of the starting material was consumed and the products were separated, identified, and quantified by gas chromatography. The current-time data were used to find the number of electrons per molecule of **1** consumed during the electrolyses. The electrolysis times are also reported

and it can be seen that complete conversions are possible rather rapidly due to the higher current densities possible for the reactions in these media.

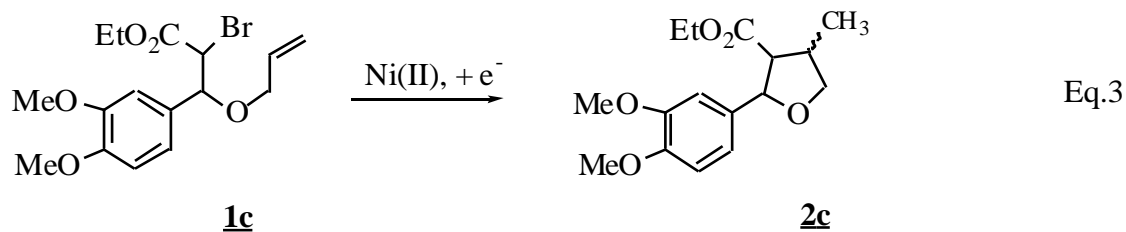
Several conclusions can be reached on the basis of results presented in Table 3. First, a *n*-value of essentially one was observed for the catalytic reduction of **1a** – **1c**. Second, gas chromatographic analysis of electrolyzed mixtures reveals the presence of 2-(4'-methoxyphenyl)-4-methylene-3-phenyltetrahydrofuran (**2a**) for **1a** (Eq.1):



2-methoxy-4-methylene-3-phenyltetrahydrofuran (**2b**) for **1b** (Eq.2):



and finally, two major products—both isomers of 2-(3',4'-dimethoxyphenyl)-3-ethoxycarbonyl-4-methyltetrahydrofuran (**2c**)—from **1c** (Eq.3):



Third, the yields of cyclic compounds **2** seem to be not sensitive to changes in the initial concentration of **1** and of $[\text{Ni}(\text{tmc})]^{2+}$ complex and in the nature of medium.

Although the sum of the yields of cyclic compounds **2a–2c** accounts for less than 100% of the original starting material in some experiments, we found no evidence (*e.g.*, additional gas chromatographic peaks) for any other products.

From the results presented, it is clear that the reduction of the bromoalkoxylated derivatives **1** is occurring at the potentials for the $[\text{Ni}(\text{tmc})]^{2+}/[\text{Ni}(\text{tmc})]^+$ couple and hence the first step in the catalytic reduction of the unsaturated halides **1** studied is the electrogeneration of nickel(I) complex which reacts with the bromoalkoxylated derivatives **1**.

Halcrow and Christou [23] published an extensive review of catalytic processes involving nickel(I) complexes and alkyl halides where they reported the detailed mechanistic study carried out by Bakac, Espenson and co-workers [24-32] of the electroreduction of alkyl halides by $[\text{Ni}(\text{tmc})]^+$ in aqueous media. According to this study, the nickel(I) complex can transfer one electron to an alkyl halide *via* an inner-sphere mechanism, and an alkylnickel intermediate might be formed, the subsequent decomposition of which could generate alkyl radicals. In fact, all the products obtained in the present study in both alcoholic and microemulsions media are consistent with radical intermediates as it was also observed in our previous work [4,16]. Once produced, the radicals intermediates would be expected to undergo rapid intramolecular cyclisation on the side-chain unsaturated to yield cyclised radicals and regenerating the starting $[\text{Ni}(\text{tmc})]^{2+}$ complex. The cyclised radicals can after be reduced or to abstract a hydrogen radical atom from a hydrogen radical atom donor in the medium, to afford the corresponding tetrahydrofuran derivatives **2** in moderate to good yields. Similarly,

Rusling *et al.*[33] reported the H-atom abstraction by the radical from a donor in the fluid medium in the formation of 1-decalone *via* the radical pathway.

Such a mechanism [24-32] is consistent with the cyclic voltammetry and controlled-potential electrolyses results reported above and in our earlier studies [4,16-19].

The results of the present study involve a selective radical-type activation and reactivity of the carbon-halogen bond of the substrates and enable a selective formation of expected tetrahydrofuran derivatives **2** in an environmentally friendly media as compared to the results obtained in earlier investigations carried out in *N,N'*-dimethylformamide (DMF) [17-19].

It should be noted that the initial *threo* stereochemistry of compounds **1a** and **1c** was kept in the cyclised *trans* products **2a** and **2c**, respectively, according to NMR and by comparison with an authentic sample. There is evidence in the literature [34] that the bromoalkoxylation reaction, as well as the formation of the cyclic compounds of type **2**, stereoselectively afford the more stable *trans* isomers in agreement with NMR data. Moreover, a review chapter by Renaud [35] discusses the factors that govern the stereochemistry of radical cyclization reactions. However, as revealed in Table 3, the electroreductive ring closure of **1c** to **2c** affords a diastereoisomeric mixture of the *cis:trans* isomers involving the ester and the methyl groups (Table 3, entries 21-26). NOED experiments showed that in the major stereoisomer, the ester and methyl groups are in a *cis* relationship [9].

Our principal purpose was to optimize the preparation of tetrahydrofuran derivatives **2** in maximal yield by indirect electrochemical reduction of **1** in non-toxic media. Although the scale of our electrochemical procedure is relatively small, nothing

should preclude adjusting the amounts of bromethers and Ni(II) complex, as well as the solution volume, to prepare the carbocycle in larger quantities, by carrying out a workup involving treatment of the reaction mixtures by passing twice through silica gel columns and evaporating the solvent [10b] (see Experimental Section).

4. Conclusions

In conclusion, it has been shown that : (i) alcohol and alcohol/water mixtures as well as microemulsions are synthetically useful media for carbon–carbon bond formation mediated by electrochemically generated $[\text{Ni}(\text{tmc})]^+$ complex from $[\text{Ni}(\text{tmc})]^{2+}$ complex; (ii) yields of heterocyclic products from **1** in microemulsions were similar to those found in alcohol and in *N,N*-dimethylformamide (DMF) [16-19]; (iii) but the rates of conversion are higher and the media are more acceptable; (iv) when compared with $\text{Bu}_3\text{SnH-AIBN}$, which is the most widely employed stoichiometric reagent to effect intramolecular cyclisations based on the alkyl radicals intermediates, electrogenerated $[\text{Ni}(\text{tmc})]^+$ complex seems to be a viable catalytic alternative; (v) another advantage of the catalytic electroreductive cyclisation of the bromoalkoxylated derivatives **1** by $[\text{Ni}(\text{tmc})]\text{Br}_2$ complex is that the carbon–halogen bond can be effectively reduced at a much less negative potential, avoiding the formation of carbanionic intermediates which do not cyclise.

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Footnotes and References

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Table 1. Standard redox potentials for [Ni(tmc)]Br₂ in EtOH, 1-PrOH and in several microemulsions.

FLUID (wt %)	-E° (V) vs Ag/AgCl
EtOH / 0.1M TEABr	0.86 ^[a]
1-PrOH / 0.1M TEABr	0.87
CTAB ^[b] / C ₁₂ H ₂₆ /H ₂ O/1-pentanol (17.5/12.5/35/35)	0.95
CTAB ^[b] / Cyclohexane/H ₂ O/1-butanol (17.5/12.5/35/35)	0.94
SDS ^[c] / C ₁₂ H ₂₆ /H ₂ O/1-pentanol (6.5/4.5/76/13)	0.94

^[a]Data from Ref. [16]; ^[b]cetyltrimethylammonium bromide (CTAB); ^[c]sodium dodecylsulfate (SDS).

Table 2. Data of the ratio I_c/I_d obtained from the cyclic voltammetry experiments of 1.0 mM [Ni(tmc)]Br₂ in the presence of different concentrations of **1 in different media. Potential scan rate 200 mV/s.**

Microemulsions (wt %)	$I_c/I_d^{[a]}$		
	$\gamma = 2^{[b]}$	$\gamma = 5^{[b]}$	$\gamma = 10^{[b]}$
RBr = 1-[2-Bromo-2-phenyl-1-(prop-2'-ynyloxy)ethyl]-4-methoxybenzene (1a)			
EtOH / 0.10 M TEABr	2.7	6.2	8.9
1-PrOH / 0.10 M TEABr	2.2	5.4	8.8
CTAB ^[c] /C ₁₄ H ₃₀ /H ₂ O/1-pentanol (17.5/12.5/35/35)	6.2	13.6	21.5
CTAB ^[c] /C ₁₄ H ₃₀ /H ₂ O/1-butanol (17.5/12.5/35/35)	3.4	8.1	13.3
SDS ^[d] / C ₁₄ H ₃₀ /H ₂ O/1-pentanol (13.3/8/52/26.7)	2.8	7.0	13.2
RBr = [1-Bromo-2-methoxy-2-(prop-2'-ynyloxy)ethyl]benzene (1b)			
EtOH / 0.10 M TEABr	2.1	5.2	9.7
CTAB ^[c] / C ₁₂ H ₂₆ /H ₂ O/1-pentanol (17.5/12.5/35/35)	6.6	14.7	25.9
CTAB ^[c] /Cyclohexane/H ₂ O/1-butanol (17.5/12.5/35/35)	3.1	8.3	12.1
SDS ^[d] / C ₁₂ H ₂₆ /H ₂ O/1-butanol (6.5/4.5/76/13)	2.4	6.3	12.5
RBr = Ethyl 2-bromo-3-(3',4'-dimethoxyphenyl)-3-(allyloxy)propanoate (1c)			
EtOH / 0.10 M TEABr	2.0	4.5	8.0
1-PrOH / 0.10 M TEABr	2.6	5.5	7.0

^[a] I_c - catalytic peak current intensity of the catalyst in the presence of substrate and I_d - peak current intensity of the catalyst in the absence of substrate; ^[b] $\gamma = [\text{RBr}] / [\text{Ni(II)}]$; ^[c] cetyltrimethylammonium bromide (CTAB); ^[d] sodium dodecylsulfate (SDS).

Table 3. Coulometric data and product yields for catalytic reduction of **1 by [Ni(tmc)]⁺ electrogenerated at reticulated vitreous carbon or graphite felt cathodes in different media.**

Entry	[Ni(tmc)] ²⁺ , mM	[1a], mM	Time, h ^[a]	<i>n</i> ^[b]	Product yield, % ^[c]
RBr = 1-[2-Bromo-2-phenyl-1-(prop-2'-ynyloxy)ethyl]-4-methoxybenzene (1a)					2a
EtOH / 0.10 M Et₄NBr^[d]					
1	0.30	2.7	0.6	1.0	79
2 ^[e]	0.30	2.7	2.0	0.9	100
1-PrOH / 0.10 M Et₄NBr					
3	0.40	1.9	0.6	1.0	94
4	0.19	1.9	0.3	1.0	91
5 ^[e]	0.38	1.9	0.3	1.1	99
6 ^[e]	0.20	1.9	0.9	1.1	93
MTAB^[f]/Tetradecane/H₂O/1-pentanol (17.5/12.5/35/35)					
7	0.38	1.9	0.9	1.3	97
8	0.26	2.5	0.8	1.3	98
CTAB^[g]/Tetradecane/H₂O/1-pentanol (17.5/12.5/35/35)					
9	0.39	1.9	0.7	1.3	97
10	0.26	2.5	0.7	1.3	86
SDS^[h]/Tetradecane/H₂O/1-pentanol (13.3/8/52/26.7)					
11	0.38	1.9	0.6	1.0	97
12	0.26	2.5	1.2	1.1	89
RBr = [1-Bromo-2-methoxy-2-(prop-2'-ynyloxy)ethyl]benzene (1b)					2b
EtOH / 0.10 M Et₄NBr^[d]					
13	0.28	2.7	0.6	1.0	99
14 ^[e]	0.30	2.9	2.3	0.9	94
CTAB^[g]/Dodecane/H₂O/1-pentanol (17.5/12.5/35/35)					
15	0.38	1.9	1.3	1.1	86
16	0.26	2.5	0.8	1.1	80
CTAB^[g]/Cycohexane/H₂O/1-butanol (17.5/12.5/35/35)					
17	0.38	1.9	0.2	1.0	94
18	0.26	2.5	0.5	1.1	87
SDS^[h]/Dodecane/H₂O/1-butanol (13.3/8/52/26.7)					
19	0.38	1.9	0.5	1.0	96
20	0.26	2.5	1.0	1.0	94
RBr = Ethyl 2-bromo-3-(3',4'-dimethoxyphenyl)-3-(allyloxy)propanoate (1c)					2c (d.r.) ^[i]
EtOH / 0.10 M Et₄NBr^[d]					
21	0.30	3.0	0.6	1.0	53 (95:5)
22 ^[e]	0.30	3.0	2.3	1.0	82 (94:6)
1-PrOH / 0.10 M Et₄NBr					
23	0.38	1.9	1.7	1.0	75 (93:7)
24	0.19	1.9	5.7	1.0	65 (93:7)
25 ^[e]	0.39	1.9	0.2	1.1	69 (94:6)
26 ^[e]	0.20	1.9	1.7	1.0	72 (93:7)

^[a] Time of electrolysis; ^[b] number of electrons per molecule of alkyl bromide, **1**; ^[c] % = yield expressed as the percentage of **1** incorporated into each product; ^[d] data from Ref.[16]; ^[e] carried out in EtOH:H₂O (9:1); ^[f] tetradecyltrimethylammonium bromide (MTAB); ^[g] cetyltrimethylammonium bromide (CTAB); ^[h] sodium dodecylsulfate (SDS); ^[i] Diastereomeric (*cis-to-trans*) ratio.