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TEMPO-modified graphite felt electrodes: attempted enantioselective oxidation of *rac*-1-phenylethanol in the presence of (−)-sparteine

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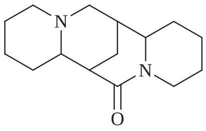
At a TEMPO-modified graphite felt electrode (TMGFE) *rac*-1-phenylethanol 2 is not enantioselectively oxidised in the presence of (−)-sparteine 1, but instead 1 is dehydrogenated to its iminium salt; 2 is oxidised in solution by the oxoammonium salt 6 in the absence of 1, but not on the TMGFE in the range 0–1.0 V *vs.* Ag/AgNO$_3$.

Oxoammonium[1] salts, generated by oxidation of aminoxyl radicals by chemical oxidants or at the anode, have been successfully used for the selective oxidation of alcohols. Of particular interest in this connection was the invention of TEMPO-modified graphite felt electrodes (TMGFE).[2–7] In the presence of (−)-sparteine **1**, it was reported that a TMGFE can oxidise enantioselectively (*S*)-1-phenylethanol (*S*-**2**) in *rac*-**2** leaving 46.2% of **2** as the (*R*)-isomer with 99.6% ee.[7] We failed to reproduce these very interesting results and therefore studied this conversion by cyclic voltammetry and controlled potential electrolysis.[8]

Fig. 1 shows voltammograms recorded at the TMGFE in 0.2 M NaClO$_4$ MeCN solution.[9] The charge, Q_P, involved during oxidation of TEMPO and reduction of TEMPO$^+$ is equal and stable within 30 cycles. Deconvolution and integration of these peaks permits evaluation of the concentration, $C_{NO^\cdot}$, of the active aminoxyl radicals at the electrode.[10] It was found that $C_{NO^\cdot}$ never exceeds 1 μmol cm^{-3} ($0.4 < C_{NO^\cdot} < 0.6$ μmol cm^{-3}).[11] By potential controlled coulometry a density of 0.43 μmol cm^{-3} of active radicals was found, which is consistent with the results obtained *via* cyclic voltammetry.

Electrolysis in a divided cell (Nafion® 117 membrane) under previously reported conditions[7] (10 mmol of **1**, 10 mmol of *rac*-**2** and 5 mmol of tetraline **3** used as standard in 25 ml of 0.2 M NaClO$_4$ MeCN solution) afforded after consumption of 752.6 C, which is sufficient to oxidise about 80% of (*S*)-**2**, no acetophenone **4**, but **2** was almost quantitatively recovered (96%). However, 78% of **1** was oxidized, presumably into the corresponding iminium salt. It has been reported[12–14] that tertiary amines can be dehydrogenated to iminium salts by oxoammonium salts.

With a five-fold lower concentration of *rac*-**2**, **1** and **3** under otherwise the same conditions, the current decreased to 5% after consumption of 64 C. GC of the crude product gave 0.03 mmol of α-tetralol and 0.01 mmol of α-tetralone from **3** and 0.11 mmol of aphylline[15] **5** from **1**, which corresponds to more than 80% of the experimental quantity of electricity. The amount of iminium salt of **1** is difficult to evaluate, but it corresponds approximately to the missing quantity of electricity. Compound **4** could not be detected. In an undivided cell no conversion of **2** was found in the presence of **1** at oxidation potentials ranging from 0.53 to 1.10 V *vs.* Ag/AgNO$_3$.



Aphylline **5**

These results led us to investigate the electrochemical behaviour of **1** by cyclic voltammetry (Fig. 2). As expected, **1** is oxidized both on graphite felt and on TMGFE. Under potentiodynamic conditions the TMGFE are inactive towards the *rac*-**2** oxidation between 0 and 0.8 V *vs.* Ag/AgNO$_3$ (Fig. 3), but at 1.0 V *vs.* Ag/AgNO$_3$ an oxidation wave starts even in the absence of the chiral base. It is well known that secondary alcohols are readily oxidised by oxoammonium salts in solution.

This is also found with 4-acetylamino-2,2,6,6-tetramethyl-1-oxopiperidinium **6** as a tetrafluoroborate salt. Species **6** was selected for the homogeneous oxidation because of its similar structure to the immobilized aminoxyl radical, which is also substituted with an amide group at C-4. In the absence of **1** with 1 mmol of *rac*-**2** and 1 mmol of **6** (tetrafluoroborate salt) in 5 ml of MeCN, 50% acetophenone **4** was obtained after 10 min. When **6** (2 mmol) was added to a mixture of *rac*-**2** (2 mmol) and **1** (2 mmol) in 5 ml of MeCN the solution turned immediately to an orange colour, however no *rac*-**2** was converted. The orange

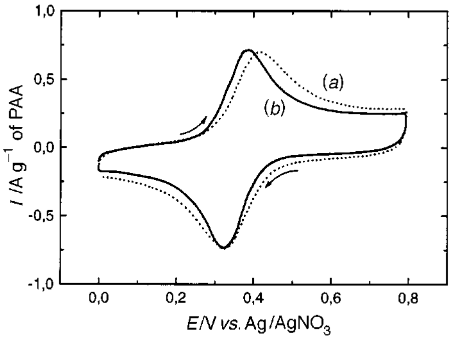


Fig. 1 Voltammograms recorded at 10 mV s^{-1} in 0.2 M NaClO$_4$–MeCN unstirred solution: (*a*) non-crosslinked and non-methylated TMGFE and (*b*) crosslinked and methylated TMGFE (0.5 × 1 × 1 cm^3).

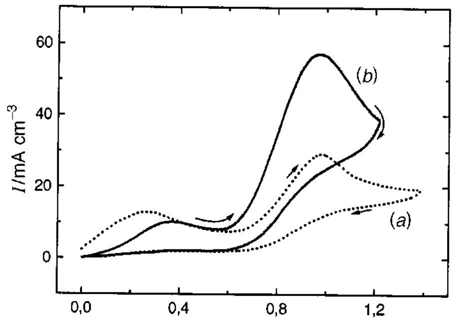


Fig. 2 Voltammograms recorded in 0.2 M NaClO$_4$–MeCN unstirred solution at 10 mV s^{-1} in the presence of 2 mmol (−)-sparteine: (*a*) on a graphite felt electrode and (*b*) on TMGFE (0.5 × 1 × 1 cm^3).

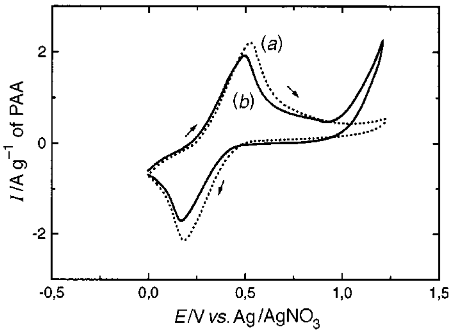
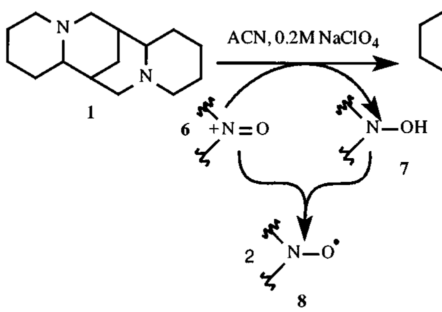


Fig. 3 Voltammograms of a TMGFE (0.5 × 1 × 1 cm^3) recorded in 0.2 M NaClO$_4$–MeCN stirred solution at 10 mV s^{-1} (*a*) in the absence and (*b*) in the presence of 1 mmol of phenylethanol.



Scheme 1

colour is due to the formation of the radical *via* a fast symproportionation[1] (Scheme 1).

The results above demonstrate that the TMGFEs are not active below 0.8 V *vs.* Ag/AgNO$_3$ towards *rac*-**2** oxidation, which is easily oxidised in solution by **6**, whereby 4-acetamido-2,2,6,6-tetramethyl-1-hydroxypiperidine **7** is formed as a reduction product of **6**. The difference in these two processes is that in homogeneous oxidation **8** is regenerated *via* a base catalysed symproportionation of **6** and **7**, whilst at the TMGFE the immobilised **7** has to be oxidized.

In the absence of a base, the inactivity of the TMGFE towards the oxidation of *rac*-**2** could be due to a slow oxidation of immobilised **7**. Therefore we investigated the electrochemical behaviour of **7** by cyclic voltammetry (Fig. 4). In an unstirred solution, the CV exhibits during the first cycle a very weak oxidation of **7** into **6**, which is reduced during the negative sweep at 0.32 V *vs.* Ag/AgNO$_3$ into **8**. The current of **7** amounts to only 0.5% of that of **8** at the same concentration. In the presence of lutidine **9**, the current increases about twenty-fold, however it is still only 10% of that of **8** at the same concentration. The role of the added base appears to be connected with the regeneration of the active oxidant immobilised onto the electrode,[16] because we demonstrated that in solution **6** can oxidise *rac*-1-phenylethanol without any organic or mineral base.

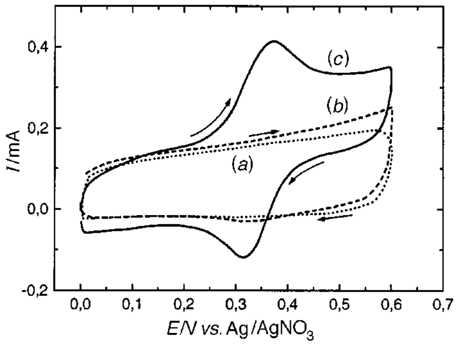


Fig. 4 Voltammograms of a graphite rod electrode recorded in 0.2 M NaClO$_4$–MeCN solution at 10 mV s^{-1} (*a*) in supporting electrolyte only, (*b*) in the presence of 0.2 mmol of **7** and (*c*) in the presence of both 0.2 mmol of **7** and 0.2 mmol of lutidine **9**.

The TMGFE is thus active for alcohol oxidation, but only in the presence of an electrochemically inert base which can be used in acetonitrile. (−)-Sparteine as base appears to be unsatisfactory, because it is oxidized by **6** prior to the alcohol.

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Notes and references

1 A. E. J. de Nooy, A. C. Besemer and H. van Bekkum, *Synthesis*, 1996, 1153; and references cited therein.

2 T. Osa, Y. Kashiwagi, K. Mukai, A. Oshawa and J. Bobbitt, *Chem. Lett.*, 1990, 75.

3 Y. Kashiwagi, A. Ohsawa, T. Osa, Z. Ma and J. M. Bobbitt, *Chem. Lett.*, 1991, 581.

4 Y. Kashiwagi, H. Ono and T. Osa, *Chem. Lett.*, 1993, 257.

5 T. Osa, Y. Kashiwagi, Y. Yanagisawa and J. Bobbitt, *J. Chem. Soc., Chem. Commun.*, 1994, 2535.

6 Y. Yanagisawa, Y. Kashiwagi, F. Kurashima, J.-I. Anzai, T. Osa and J. Bobbitt, *Chem. Lett.*, 1996, 1043.

7 Y. Kashiwagi, Y. Yanagisawa, F. Kurashima, J.-I. Anzai, T. Osa and J. M. Bobbitt, *Chem. Commun.*, 1996, 2745.

8 The preparation of TEMPO-modified graphite felt electrodes (TMGFE) was carried out following a previously described procedure (ref. 2–7). The graphite felt electrodes (Le Carbone Lorraine, VG 4000) were refluxed in MeOH for 4 h, dried and dipped in a 0.25% polyacrylic acid (PAA, Aldrich)–methanol (Merck) solution and then carefully dried. Subsequently, the coated electrodes were treated with 4 equiv. of 4-amino-2,2,6,6-tetramethylpiperidin-1-oxyl [with respect to the amount of carboxylic acid (evaluated by weight) at the electrode] in the presence of 4.8 equiv. of DCC (ACROS) in DMF (ACROS) at room temperature for 80–90 h. Thereafter the electrodes were crosslinked with 3.3 equiv. of 1,6-diaminohexane (Fluka) in the presence of DCC for 80 h and were subsequently alkylated (CH_2N_2 or Me_2SO_4 or Et_2SO_4). Following this procedure, no difference was found between the electrodes alkylated in ethereal Et_2O or Me_2SO_4 or Et_2SO_4. If alkylation is carried out before the amide linkage formation, the concentration, $C_{NO^\cdot}$, of the active aminoxyl radical decreases but the electrochemical behaviour is similar to that observed with the other electrodes. Increasing PAA thickness did not increase significantly $C_{NO^\cdot}$ and did not improve the activity of the electrode even if the reaction time of each preparative step was increased proportionally. Amide linkage formation was also carried out before the coating procedure but the resulting film was very unstable.

Electrochemical measurements and electrolyses were performed in a 0.2 M NaClO$_4$ (ACROS)–MeCN (Merck) solution (dried on molecular sieves 3Å) using a HEKA PG28 generator-potentiostat. Chromatographic analyses were carried out using a Shimadzu chromatograph equipped with a capillary column [HP5 (Hewlett Packard) or FS Hydrodex β-PM (Macherey Nagel)]. *rac*-1-Phenylethanol, acetophenone, tetraline and (−)-sparteine were purchased from Aldrich. The work-up of the electrolyses solution consisted of evaporating the MeCN, then the residue was dissolved in EtOAc, filtered and subjected to chromatography.

9 Conversely to the results reported by Osa *et al.* (ref. 2), no large difference was observed between the peak potentials when the PAA on the electrode was crosslinked and methylated or untreated.

10 $C_{NO^\cdot} = Q_P/nFV$, where n is the number of electrons, F is the Faraday equivalent and V the volume of the graphite felt electrode.

11 According to Osa and co-workers, the density evaluated by titration was 50 times higher (24 μmol cm^{-3}) and seems to be very stable from one article to the other (ref. 3–7). However, the quantity of electricity estimated from their voltammogram (ref. 5) is equal to 33.6 mC and corresponds to 0.7 μmol cm^{-3}.

12 D. H. Hunter, D. H. R. Barton and W. J. Motherwell, *Tetrahedron Lett.*, 1984, **25**, 603.

13 D. H. Hunter, J. S. Racok, A. W. Rey and Y. Z. Ponce, *J. Org. Chem.*, 1988, **53**, 1278.

14 J. M. Bobbitt and Zhenkun Ma, *Heterocycles*, 1992, **33**, 641.

15 Structure assignment was performed by comparison of the mass spectra obtained by GC–MS with spectra from the NIST library.

16 A. Deronzier, D. Limosin and J. C. Moutet, *Electrochim. Acta*, 1987, **32**, 1643.

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