ELECTROCHEMICAL OXIDATION OF PYRROLE DERIVATIVES IN ALCOHOLIC MEDIUM

Farouk Tedjar[a], Salah Ymmel[a], Miroslav Janda[b], Petr Duchek[b],
Petr Holý[c] and Ivan Stibor[c]

[a] Department of Electrochemistry, Setif University, Setif, Algeria
[b] Department of Organic Chemistry,
   Prague Institute of Chemical Technology, 166 28 Prague 6, Czechoslovakia and
[c] Institute of Organic Chemistry and Biochemistry,
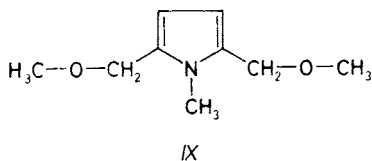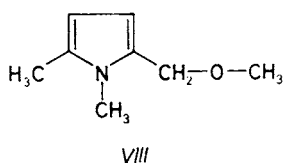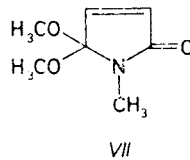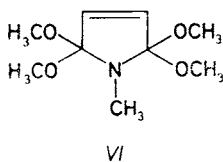   Czechoslovak Academy of Sciences, 166 10 Prague 6, Czechoslovakia

Electrochemical oxidation of pyrrole (I), 1-methylpyrrole (II), 1,2,5-trimethylpyrrole (III), methyl 1-methyl-2-pyrrolecarboxylate (IV) and diethyl 3,5-dimethyl-2,4-pyrroledicarboxylate (V) has been studied. An advantageous method of preparation of polypyrroles (PP) and conductive PVC–PP composites has been elaborated, permitting a 20 fold starting concentration of the monomer. Electrooxidation of II in methanol leads either to 5,5-dimethoxy-1-methyl-3-pyrrolin-2-one (VII) or 1-methyl-2,2,5,5-tetramethoxy-3-pyrroline (VI), their ratio depending on water content in the alcohol used. Oxidation of IV affords the analogous 5-carbomethoxy-5-methoxy-1-methyl-3-pyrrolin-2-one (X), oxidation of III and V leads to products of substitution at the methyl groups.

Electropolymerization of pyrrole was discovered[1] in 1981 and studied in detail later by other authors[2,3]. The reaction was carried out in acetonitrile using various metals (Pt, Pd, Au, Ni, Cr, In, Al, Ag) as material for working electrodes and tetraalkylammonium perchlorates and tetrafluoroborates as auxiliary electrolytes. The concentration of pyrrole was usually of the order 10^{-2} moll^{-1} and that of the auxiliary electrolyte one order of magnitude higher. Although the thus-obtained polymers are conductive (specific conductivity $\sigma = 30-100\,\Omega^{-1}\,cm^{-1}$), they have unsuitable mechanical properties. Later it has been found that electrolysis on a PVC-coated working electrode can furnish composites of advantageous conducting as well as mechanical properties[4,5].

Compared with furan and thiophene analogues, surprisingly little is known about the electrochemistry of pyrrole derivatives[6]. Apart from porphyrines and pentaarylpyrroles, the only simple pyrrole derivative studied was 1-methylpyrrole (II) which was electrooxidized[7] on a platinum anode in methanolic KOH. The reaction gave 1-methyl-2,2,5,5-tetramethoxy-3-pyrroline (VI). In more detail was studied the anodic cyanation of simple pyrrole and indole derivatives, performed in methanolic solution of sodium cyanide[8].

I, $R^1 = R^2 = R^3 = R^4 = R^5 = H$

II, $R^1 = CH_3$; $R^2 = R^3 = R^4 = R^5 = H$

III, $R^1 = R^2 = R^5 = CH_3$; $R^3 = R^4 = H$

IV, $R^1 = CH_3$; $R^2 = COOCH_3$; $R^3 = R^4 = R^5 = H$

V, $R^1 = H$; $R^2 = R^4 = COOC_2H_5$; $R^3 = R^5 = CH_3$

VI

VII

VIII

IX
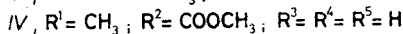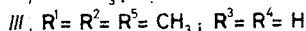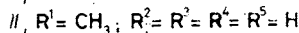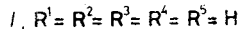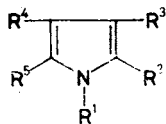
In the present communication we describe the results of electrochemical polymerization of pyrrole in methanol, which has several practical advantages compared with the existing methods. We also report on the results of electrochemical oxidation of some pyrrole derivatives, again in an alcoholic medium. The aim of the study of pyrrole derivatives has been to compare their behaviour with that of the furan and thiophene analogues under conditions of electrochemical alkoxylation because in the furan and thiophene series this reaction is of great synthetic significance, as seen from many original papers and reviews[6,9,10,11].

EXPERIMENTAL

The melting and boiling points are uncorrected. Solid samples were dried for 12 h at 14 Pa prior to analysis. IR spectra were recorded in chloroform on a Perkin–Elmer 325 instrument. NMR spectra were measured in deuterochloroform with tetramethylsilane as internal standard; ^{1}H NMR on a Varian XL-100 (CW mode; 100 MHz) and ^{13}C NMR on a Bruker WP-80 (FT mode; 20·1 MHz) instrument. Chemical shifts are given in ppm (δ-scale), coupling constants (J) in Hz. Mass spectra were obtained with a Gas Chromatograph — Mass Spectrometer LKB-9000, gas-liquid analyses were performed on a Chrom 31 (Laboratorní přístroje, Prague) instrument,

using 5% butanediol succinate, XE-60 and Carbowax 20M on Chromaton. Cyclic voltametry and chronopotentiometry were run using a PAR 173 potentiostat, combined with an APPLE II computer. A commercial electrolytic cell (PAR) was equipped with a working platinum electrode (disc, 0.125 cm^2), a commercial reference electrode and a nickel auxiliary electrode. Preparative electrolyses were performed in a 200 ml all-glass electrolyser with magnetic stirring and external cooling. The cathode space was separated with sintered glass (S-3). The anodes were made of a platinum sheet or gauze with a surface area of 1.8, 6.12 or 45 cm^2. The cathode was made of a nickel sheet (working area 30 cm^2). Coating with a film of PVC was performed by immersion of the pre-cleaned working electrode into a solution of low-molecular-weight PVC (mean molecular weight 3 000) in tetrahydrofuran (10 g dm^{-3}).

The starting compounds were either purchased (*I*) or prepared according to the described procedures (*II* (ref.[17]), *III* (ref.[18]), *IV* (ref.[19]), *V* (ref.[20])).

2,2,5,5-Tetramethoxy-1-methyl-3-pyrroline (*VI*)

A solution of *II* (1.60 g; 20 mol) and potassium hydroxide (3.0 g) in absolute methanol(300 ml) in the anode space and potassium hydroxide (1.6 g) in absolute methanol (80 ml) in the cathode space were electrolyzed at constant current $I = 0.5$ A at $10-15°C$, the total amount of electricity being 1.6 F mol^{-1}. The content of the anode space was then taken down, and the residue was extracted with ether (3 × 100 ml). The combined extracts were dried over anhydrous potassium carbonate, the solvent was evaporated and the crude product *VI* (1.3 g; purity 95%, according to g.l.c.) was distilled, b.p. $78-80°C/267$ Pa; yield 1.0 g (25%) of pure *VI*, m.p. $37-41°C$ (after sublimation $41-43°C$). For C$_9$H$_{17}$NO$_4$ (203.2) calculated: $54.19%$ C, $8.43%$ H, $6.89%$ N, $61.10%$ OCH$_3$; found: $53.35%$ C, $8.57%$ H, $6.84%$ N, $61.03%$ OCH$_3$. ^{1}H NMR spectrum: 2.43 s, 3 H (N-CH$_3$); 3.30 s, 12 H (OCH$_3$); 6.23 s, 2 H (H-3, H-4). IR spectrum 3 000, 2 935, 2 830, 1 715, 1 686, 1 460, 1 436, 1 388, 1 344, 1 325, 1 220, 1 080, 1 035, 1 010, 983. Mass spectrum, m/z (relative intensity, %): 203 (M$^+$, 2.6), 172 (78), 166 (22), 159 (16), 158 (20), 156 (17), 126 (100), 105 (18), 98 (18), 72 (63), 59 (25), 55 (33), 45 (17).

5,5-Dimethoxy-1-methyl-3-pyrrolin-2-one (*VII*)

The title compound was prepared in the same manner as compound *VI* except that the methanol used contained 5% of water. Distillation afforded 1.80 g (58%) of viscous liquid, b.p. $78-80°C/260$ Pa. For C$_7$H$_{11}$NO$_3$ (157.2) calculated: $53.49%$ C, $7.05%$ H, $8.91%$ N, $39.00%$ OCH$_3$; found: $53.77%$ C, $7.36%$ H, $8.82%$ N, $40.44%$ OCH$_3$. ^{1}H NMR spectrum: 2.63 s, 3 H (N-CH$_3$); 3.12 s, 6 H (OCH$_3$); 6.33 d, 1 H (H-4, $J(3, 4) = 6$); 6.91 d, 1 H (H-3, $J(3, 4) = 6$). IR spectrum: 3 005, 2 940, 2 840, 1 712, 1 604, 1 433, 1 390, 1 329, 1 264, 1 215, 1 140, 1 110, 1 080, 1 005, 924, 809. Mass spectrum, m/z (relative intensity, %): 157 (M$^+$, 0.5), 127 (8), 126 (100), 98 (6), 85 (10), 67 (6), 66 (11), 59 (7), 55 (13), 54 (8), 53 (6).

1,5-Dimethyl-2-methoxymethylpyrrole (*VIII*) and
2,5-Bis(methoxymethyl)-1-methylpyrrole (*IX*)

The electrooxidation of *III* (1.10 g; 10 mmol) was performed similarly as described for compound *VI* ($5°C$, 0.3 A, 2 F mol^{-1}). Analogous work-up of the reaction mixture gave 1.0 g of the crude product which on distillation afforded 0.60 g (43%) of monomethoxy derivative *VIII* (b.p. 56 to $58°C/267$ Pa) and 0.21 g (12%) of dimethoxy derivative *IX* (b.p. $70-75°C/267$ Pa). Compound *VIII*: For C$_8$H$_{13}$NO (139.2) calculated: $69.03%$ C, $9.41%$ H, $10.06%$ N; found: $69.23%$ C, $9.41%$ H, $9.86%$ N. ^{1}H NMR spectrum: 2.17 s, 3 H (5-CH$_3$); 3.24 s, 3 H (1-CH$_3$); 3.43 s, 3 H (OCH$_3$); 4.30 s, 2 H (CH$_2$); 5.74 d, 1 H (H-4, $J(3, 4) = 3$); 5.98 d, 1 H (H-3, $J(3, 4) = 3$);

^{13}C NMR spectrum: 12·3 (5-CH$_3$); 30·5 (1-CH$_3$); 56·9 (OCH$_3$); 66·3 (CH$_2$); 106·2 (4-C), 109·7 (3-C), 129·4 (5-C), 131·1 (2-C). IR spectrum: 3 010, 2 930, 2 831, 1 695, 1 654, 1 509, 1 470, 1 447, 1 436, 1 410, 1 367, 1 355, 1 304, 1 215, 1 180, 1 173, 1 078, 1 020, 975, 938, 890. Mass spectrum, m/z (relative intensity, %): 139 (M$^+$, 89), 109 (28), 108 (100), 107 (45), 92 (14), 65 (19), 52 (17), 51 (20).

Compound *IX*: For C$_9$H$_{15}$NO$_2$ (169·2) calculated: 63·88% C, 8·93% H, 8·28% N; found: 63·97% C, 8·70% H, 8·01% N. ^{1}H NMR spectrum: 3·24 s, 3 H (1-CH$_3$); 3·43 s, 6 H (OCH$_3$); 4·30 s, 4 H (CH$_2$); 5·97 s, 2 H (3-H, 4-H). ^{13}C NMR spectrum: 30·5 (1-CH$_3$); 57·1 (OCH$_3$); 66·8 (CH$_2$), 110·0 (3-C, 4-C), 311·7 (2-C, 5-C). Mass spectrum, m/z (relative intensity, %): 169 (M$^+$, 35), 139 (11), 138 (100), 122 (10), 107 (75), 94 (10), 45 (15).

Methoxycarbonyl-5-methoxy-1-methyl-3-pyrrolin-2-one (*X*)

Electrolysis of ester *IV* (1·39 g; 10 mmol) in methanol (200 ml) containing NaClO$_4$ (12·2 g) under galvanostatic conditions ($I = 1$ A; 8 F mol^{-1}) at $-10°$C, followed by the work-up described in the preceding experiments, afforded 1·65 g of crude product which on distillation (b.p. 80 to 100°C/1·5 Pa) furnished 0·35 g (19%) of compound *X*. For C$_8$H$_{11}$NO$_4$ (185·2) calculated: 51·89% C, 5·99% H; found: 51·48% C, 5·80% H. ^{1}H NMR spectrum: 2·86 s, 3 H (1-CH$_3$); 3·14—3·80 m, 6 H (5-OCH$_3$ and COOCH$_3$), 6·34 d 1 H (H-4, $J(3, 4) = 6$); 6·84 d, 1 H (H-3, $J(3, 4) = 6$). IR spectrum: 3 010, 2 968, 2 950, 2 910, 2 843, 1 774, 1 726, 1 438, 1 387, 1 322, 1 248, 1 195, 1 106, 1 082, 1 025, 923. Mass spectrum, m/z (relative intensity, %): 185 (M$^+$, 3), 154 (32), 125 (54), 110 (34), 98 (56), 85 (58), 67 (100), 66 (98), 59 (41), 54 (44), 53 (46).

Diethyl 5-Ethoxymethyl-3-methyl-2,4-pyrroledicarboxylate (*XIa*)
or Diethyl 3-Ethoxymethyl-5-methyl-2,4-pyrroledicarboxylate (*XIb*)

Diester *V* (4·2 g; 17 mmol) and tetraethylammonium perchlorate (0·8 g; 3·5 mmol) in a mixture of absolute ethanol (80 ml) and dichloromethane (20 ml) were electrolyzed at constant current ($I = 0·2$ A; 8 F mol^{-1}) at 0—5°C. The usual work-up gave crude product consisting mainly of the unreacted diester *IV*. Column chromatography on silica gel in chloroform afforded 0·2 g (6%) of a fraction whose spectral data corresponded to structure *XIa* or *XIb*. ^{1}H NMR spectrum: 1·1—1·5 m, 9 H (3 × CH$_3$CH$_2$); 2·51 s, 3 H (3- or 5-CH$_3$); 3·60 q, 2 H (3- or 5-CH$_2$CH$_3$); 4·15—4·45 m, 4 H (2 × COOCH$_2$CH$_3$); 4·90 s, 2 H (3- or 5-CH$_2$–O). Mass spectrum, m/z (relative intensity, %): 283 (M$^+$, 3), 256 (26), 208 (100), 183 (19), 181 (40), 164 (27), 162 (47), 136 (17), 99 (17), 85 (37), 83 (51), 45 (51).

RESULTS AND DISCUSSION

Electrochemical methoxylation of unsubstituted pyrrole invariably afforded only a polymer (PP) similar to the product obtained in acetonitrile[1−3]. Cyclic voltametry found an oxidation peak at 900 mV (SCE). Infrared spectrum of the obtained polymer exhibited a strong band at 1 470 cm^{-1} due to pyrrole nucleus vibrations and a band in the region 1 100 cm^{-1} corresponding to the perchlorate anion (perchlorate as the auxiliary electrolyte) which is in accord with the known[1−3] protonation of the pyrrole nucleus in PP. Analogous results were also obtained with lithium and potassium hydroxides as auxiliary electrolytes. The reaction proper is obviously diffusion-controlled because the linear relationships $I_p = kv^{1/2}$ and $E_p = k'v^{1/2}$ can be found.

Working with PVC-coated platinum electrode, we used only potassium hydroxide as auxiliary electrolyte because of best results in the preceding experiments. Using chronopotentiometry we determined the diffusion coefficient to be $D = 0.81$ . . 10^{-10} cm^2 s^{-1}; this showed that the permeability[5] of the PVC film in methanol is lower than in acetonitrile $(D = 3 . 10^{-8}$ cm^2 s$^{-1})$. The infrared spectrum of the thus-obtained composite exhibited the expected bands at 1 470 cm^{-1} $(=$C—H bonds of the heterocyclic nucleus) and at 1 425 cm^{-1} (deformation vibrations of methylene groups in PVC). Since the properties of polymers and composites obtained by oxidation in methanol are practically identical with those described for products of electropolymerization in acetonitrile, the use of methanol appears to be more advantageous. Starting concentration of pyrrole can be 20 times higher, methanol dissolves better the auxiliary electrolytes and the requirements concerning purity, and particularly water content, are substantially lower.

Because of the great polymerization ability of pyrrole derivatives, we performed a series of orientational experiments with 1-methylpyrrole (II) in order to obtain low-molecular electrooxidation products. The obtained results can be summarized into the following points: 1) As auxiliary electrolytes one may use basic (KOH, CH$_3$ONa) as well as neutral (NaClO$_4$, LiClO$_4$, (C$_2$H$_5$)$_4$NClO$_4$ and NH$_4$Br) compounds. 2) For this type of oxidation, platinum appears to be the material of choice for the working electrode. 3) Separation of the cathode and anode space by a diaphragm markedly lowers the amount of polymers because the separation suppresses cathodic reactions leading to dihydro derivatives which enter in polycondensation reactions. This explanation was supported by the fact that the extent of polymerization increased on addition of 2-pyrroline to the electrolyzed solution. 4) Electrolysis under constant potential of the working electrode brings no preparative advantage. 5) In the case of alkyl-substituted pyrroles the alkyl on the heterocyclic nitrogen atom represents a necessary condition for an at least partial suppression of polymerization and for formation of low-molecular oxidation products.

When reproducing the described methoxylation of 1-methylpyrrole (II) we obtained results that quantitatively, and particularly qualitatively, differed from those described. In addition to polymeric material, we repeatedly isolated $30-40\%$ of a product, consisting of two components, as shown by gas-liquid chromatography. The ratio of these components was different in different experiments. The reason of this behaviour has been found in varying content of water in the methanol used. In absolute methanol the only product was 1-methyl-2,2,5,5-tetramethoxy-3-pyrroline (VI), in agreement with the published results[7]. However, in the presence of 5% of water the reaction led almost exclusively to the product of partial hydrolysis, 5,5-dimethoxy-1 methyl-3-pyrrolin-2-one (VII). This result apparently is connected with the different reactivity of carbonyl groups in the Lukeš reaction[12] (addition of Grignard reagent to N-methylsuccinimide). The oxidation degree of both compounds VI and VII is the same and corresponds to a six-electron oxidation process.

Thus, compared with the two-electron oxidation common in the furan and thiophene series, the pyrrole nucleus undergoes a more profound oxidation.

Electrolysis of 1,2,5-trimethylpyrrole (*III*) was carried out under conditions which had been optimized in experiments with 1-methylpyrrole (*II*) (methanolic KOH, diaphragm, platinum anode). Gas-liquid chromatography-mass spectrometry identified four compounds in the crude product: one monomethoxy derivative, two dimethoxy derivatives and one trimethoxy derivative of the starting compound. After distillation we isolated and identified two of them − both were the products of substitution on the methyl groups: 1,5-dimethyl-2-methoxymethylpyrrole (*VIII*) and 2,5-bis(methoxymethyl)-1-methylpyrrole (*IX*). This result is logically related with the reported[8] course of anodic cyanation.

In the study of pyrrole derivatives with carbonyl-containing substituents we could not perform the electrooxidation of pyrrolealdehydes and acetylpyrroles without complete polymerization, even with the 1-methyl compounds. On the other hand, oxidation of methyl 1-methyl-2-pyrrolecarboxylate (*IV*) gave some low-molecular oxidation products of which 5-methoxycarbonyl-5-methoxy-1-methyl-3-pyrrolin-2--one (*X*) was isolated sufficiently pure for identification.

Under analogous conditions, the tetrasubstituted pyrrole diester *V* was substantially more resistant to electrochemical oxidation. After passage of 8 F mol^{-1} most of the starting compound still remained unreacted. We isolated small amount of a product for which we suggest the structure *XIa* or *XIb*. The available spectral data could not distinguish between these two similar structures.

X

XI a   *XI b*
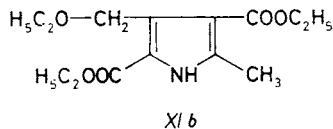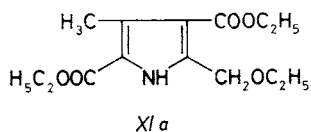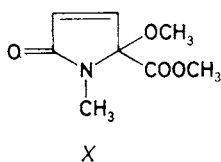
The N-methylated derivative of diester *V* was so stable toward the electrolysis that even after passage of 16 F mol^{-1} no oxidation product could be detected in the reaction mixture.

The study of preparative electrooxidation of pyrrole and indole derivatives containing substituents of various type[13] allows us to make some general conclusions on the course of electrolysis of these nitrogen heterocycles and to compare these

systems with the furan and thiophene analogues. For pyrrole and indole derivatives, substitution of the nitrogen atom leads to a higher stability toward electrochemical oxidation, making thus possible to isolate low-molecular oxidation products. Structures of the oxidation products show a more profound oxidation of pyrrole and indole derivatives as compared with derivatives of furan[6,9,10], benzofuran[14], thiophene[15] and benzothiophene[16].

For pyrrole compounds, two different types of oxidation attack were found. The first, observed with compounds with unsubstituted α-position of the pyrrole nucleus, affords 3-pyrrolin-2-one derivatives. Also oxidation products of indole derivatives correspond to the formation of this stabilized imide grouping. In the second type of oxidative effect, the anodic substitution at the methyl groups leads to alkoxymethyl derivatives.

REFERENCES

1. Diaz A. F., Castillo J. I., Logan J. A., Lee W. Y.: J. Electroanal. Chem. Interfacial Electrochem. *129*, 115 (1981).
2. Tourillon G., Garnier F.: J. Electroanal. Chem. Interfacial Electrochem. *135*, 173 (1982).
3. Prejza J., Lundström I., Skotheim T.: J. Electrochem. Soc. *129*, 1685 (1982).
4. Niwa O., Tamamura T.: J. Chem. Soc., Chem. Commun. *1984*, 817.
5. De Paoli M., Waltman R. J., Diaz A. F., Bargon J.: J. Chem. Soc., Chem. Commun. *1984*, 1015.
6. Lund H. in: *Organic Electrochemistry* (M. M. Baizer and H. Lund, Eds), p. 530. M. Dekker, New York 1983).
7. Weinberg N. L., Brown E. A.: J. Org. Chem. *31*, 4054 (1966).
8. Kunihisa Y.: J. Am. Chem. Soc. *101*, 2116 (1979).
9. Elming N. in: *Advances in Organic Chemistry* (R. A. Raphael and E. C. Taylor, Eds), Vol. 2, p. 67. Wiley, New York 1960.
10. Beck F.: *Elektroorganische Chemie*, p. 247. Chemie, Weinheim 1974.
11. Šrogl J., Janda M., Stibor I.: Collect. Czech. Chem. Commun. *39*, 185 (1974).
12. Lukeš R.: Collect. Czech. Chem. Commun. *1*, 119 (1929).
13. Janda M., Šrogl J., Holý P.: Collect. Czech. Chem. Commun. *46*, 3278 (1981).
14. Šrogl J., Janda M., Stibor I., Rozinek R.: Synthesis *1985*, 717.
15. Janda M.: Collect. Czech. Chem. Commun. *28*, 2524 (1963).
16. Šrogl J., Janda M., Stibor I., Kos J., Vyskočil V.: Collect. Czech. Chem. Commun. *43*, 2015 (1977).
17. Heaney H., Ley S. V.: J. Chem. Soc., Perkin Trans. 1, *1973*, 499.
18. Whipple E. B., Chiang Y., Hinman R. L.: J. Am. Chem. Soc. *85*, 26 (1963).
19. Hodge P., Rickards E. W.: J. Chem. Soc. *1963*, 2543.
20. Fischer H.: Org. Synth., Coll. Vol. *2*, 202 (1969).