Synthesis, electropolymerization, and surface morphological properties of N-derivatized pyrroles with potential application in biosensing

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Abstract

We describe the synthesis of conjugated pyrrole-based monomers and their derived polymers on different conducting surfaces for biosensing applications, containing aryl-ketone 1-[4-(1H-pyrrol-1-yl)phenyl]ethan-1-one, (compound **1**), and iodo 1-(4-iodophenyl)-1*H*- pyrrole (compound **2**) functional groups, along with their electrochemical, morphological properties. Monomer **2** shows lack of electropolymerisation, while monomer **1** is electropolymerizable monomer. SEM-EDX, and Diffuse-reflectance FT-IR (DRFT-IR) were employed for surface characterisation of the deposited polymeric film on FTO glass.

1. Introduction

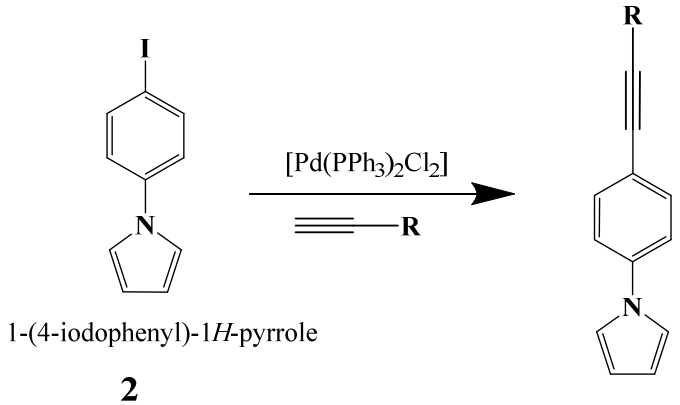
The use and application of amperometric chemical and biochemical sensor have attracted considerable attention in recent years. The fabrication and characterization of electroactive conducting polymers modified electrodes have been utilized in the design of novel amperometric biosensor devices.[1-4] Immobilization of biological active molecules on conducting surfaces via tailored electropolymers are attracting widespread interest as advanced materials. The use of such functionalized electropolymers in the modification of conducting surfaces enable the easy electrochemical control of various parameters including film thickness, film morphology, and active clusters loading. Among all others conducting polymers, polypyrrole has been widely studied and used for the immobilization of enzymes, antibodies, and nucleic acids, due to its good biocompatibility.[5-7] In 1979, Diaz *et al.* first reported the formation of conducting and high stable polypyrrole film on a platinum electrode using anodic oxidation of pyrrole monomer in acetonitrile.[8] In the last two decades, pyrrole-based polymers have been studied extensively due to their structural versatility, stability, high conductivity, electrochemical properties, ease of modification via either structural derivations or copolymerization, and finally ease of generation chemically or electrochemically on the electrode surfaces.[9]

In this study, we reported the electrochemical polymerization, and surface modification of two N-substituted functionalized pyrrole derivatives bearing different functional groups, aryl ketone (**1**) and aryl Iodo (**2**), which can be used for post-functionalization (scheme 1) allowing the introduction of biological groups within conducting films. For example, compound **2** can be used in palladium-catalysed C-C coupling reactions such Sonogashira couplings (scheme 2). While, compound **1** can be involved in the condensation reactions with Schiff-bases, and amines.[10] The resulting polymeric films were characterized using SEM-EDX, and DRFT-IR techniques.

1-[4-(1*H*-pyrrol-1-yl)phenyl]ethan-1-one **1**

1-(4-iodophenyl)-1*H*-pyrrole **2**

Scheme 1. Structures of N-substituted functionalized pyrrole derivatives **1** and **2**.



1-(4-iodophenyl)-1*H*-pyrrole **2**

Scheme 2. Proposed Sonogashira couplings of **2**.

2. Experimental

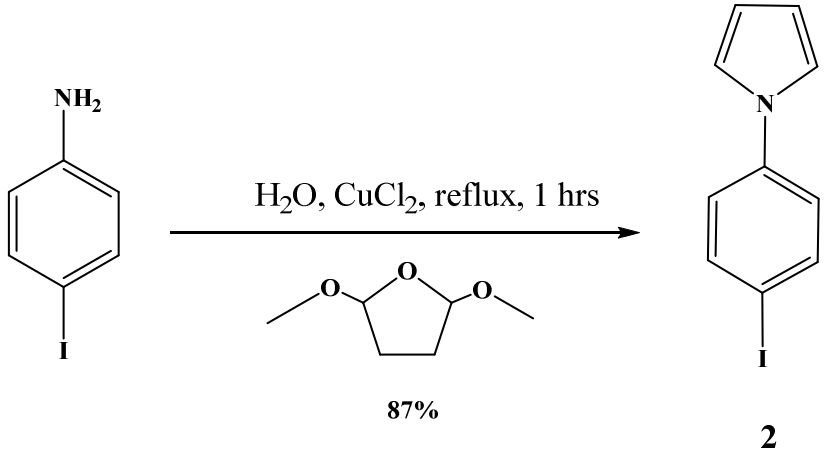
Commercial reagents were obtained as ACS grade from Sigma Aldrich, Alfa Aesar or Fisher Scientific and used without further purification. Acetonitrile (MeCN) was distilled over CaH_2 under nitrogen, deuterated acetonitrile was used as received. Tetra-n-butylammonium tetrafluoroborate (Bu_4NBF_4) were synthesised according to literature procedures[11], and kept under nitrogen. NMR spectra were recorded on a Bruker AC 300 (300 MHz) and Bruker Ascend 500 (500 MHz) spectrometers. All shifts are quoted with respect to TMS using the solvent signals as secondary standard. Electrochemical measurements and electropolymerisation (surface deposition) were made using a potentiostat/galvanostat type Autolab (PGStat 302N, and PGStat 30). Electropolymerisation of the monomers was carried out using a three-compartment cell in 0.2 M NBu_4BF_4 in MeCN under nitrogen. The polymer

films were deposited on platinum disc, glassy carbon, or Fluorine-doped tin oxide (FTO) working electrode with a Ag/AgCl reference electrode (3M NaCl, saturated AgCl).

2.1 Synthesis

Synthesis of 1-[4-(1*H*- pyrrol-1-yl)phenyl]ethan-1-one, Compound **1** was achieved following the reported method[11]; identity was checked by ^{1}H-NMR.

Synthesis of 1-(4-iodophenyl)-1*H*- pyrrole, Compound **2** was synthesized using the copper-catalyzed Clauson–Kass reaction[12] starting from 4-iodoaniline (Scheme 3). A mixture of 2,5-dimethoxytetrahydrofuran **1** (0.145 g, 1.1mmol), 4-iodoaniline (0.219 g, 1 mmol) and $CuCl_2$ (1 mol %, 0.015 g, 0.1 mol) was refluxed with stirring in H_2O (3 mL), for 1 hrs. The completion of the reaction was monitored by TLC using a mixture of ethyl acetate and hexane (5:95%). The reaction mixture was cooled to room temperature, before being diluted with ethyl acetate (20 mL). The aqueous phase was re-extracted (2 × 20 mL) with ethyl acetate and the combined organic extracts were dried over magnesium sulphate, before being concentrated and dried in a vacuum. The resulting residue was purified by silica gel column chromatography using hexane/ethyl acetate in a 95:5 % to afford yellowish solid (0.235 g, 87 %). δ_H (500 MHz, $CDCl_3$) 7.28 (d, *J* = 8.9 Hz, 2H, H-aryl), 7.15 (d, *J* = 8.9 Hz, 2H, H-aryl), 7.05 (t, *J* = 2.2 Hz, 2H, H-pyrrole), 6.35 (t, *J* = 2.2 Hz, 2H, H-pyrrole). δ_C (125 MHz, (CD_3CN) 139.4, 137.5, 121.1, 118.0, 109.8, 88.3. Anal. Calcd (found) % for $C_{10}H_{10}N_2$: C, 60.50 (60.30); H, 2.13 (2.15); N, 3.17 (3.16); I, 33.64 (33.65). FTIR: 2970 (vw); 1585 (m); 1496 (s); 1405 (w); 1330 (s); 1263 (m); 1189 (w); 1126 (w); 1064 (m); 1002 (m); 918 (m); 813 (vs); 727 (vs).



Scheme 3. Synthesis of 1-(4-iodophenyl)-1*H*-pyrrole (compound **2**).

3. Results and discussion

3.1 Synthesis

In earlier work we have reported the synthesis of compound **1**; however, we have not explored the formation of electropolymer film of this derivative.[11] The synthesis of

compound **2** was quite easy with the copper-catalyzed Clauson–Kass reaction, shown in Scheme 3. This allows large quantities to be obtained with overall yields of 87%, despite the use of silica gel column chromatography. Figure **1** shows the ^{1}H-NMR spectrum of compound **2** in deuterated- chloroform ($CDCl_3$). Both aryl protons (**a** and **b**) exhibit a pair of doublets with higher chemical shifts (downfield shift) after pyrrole-ring formation compared to the ^{1}H-NMR of the 4-iodoaniline consistent with replacement of a strong electron donor group (NH_2), with a weak electron donor (pyrrole). The pyrrole protons **c** and **d** exhibit a pair of triplet at δ 7.1 and 6.4 ppm. This was supported by 2D COSY NMR results, shown in figure 2, ^{13}C and DEPT experiments.

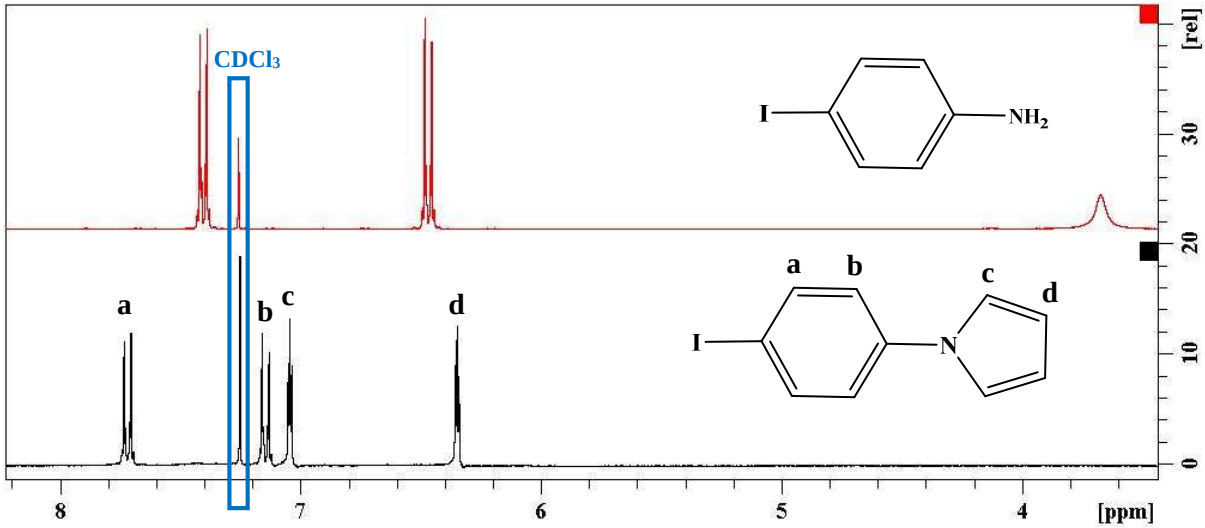


Figure 1. Stacked ^{1}H-NMR spectra of **2** (bottom, black) and its parent 4-iodoaniline (top, red), in $CDCl_3$.

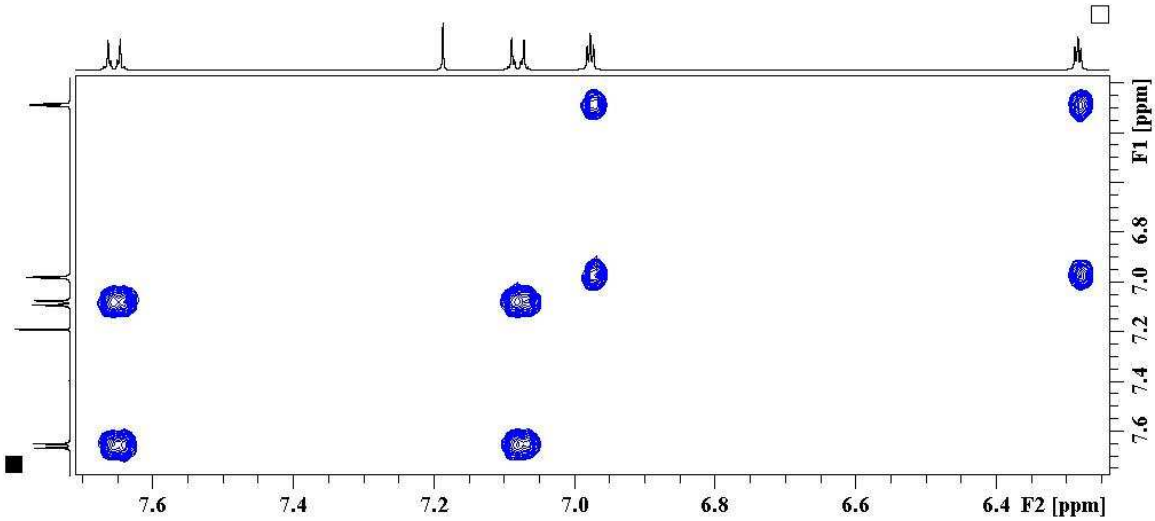


Figure 2. 2D COSY NMR spectrum of **2** in $CDCl_3$.

3.2 Electropolymerisation – polymeric film formation

All attempts to electropolymerise compound **2**, employing a variety of electrolytes, solvents and conditions have failed. However, this lack of electropolymerization is not surprising; many studies have reported this lack of polymerisation which attributed to the steric

hindrance.[13,14] Compound **1** undergoes facile electropolymerisation potentiostatically (chronoamperograms) in freshly distilled acetonitrile (MeCN) containing 0.2 M $[NBu_4][BF_4]$ at platinum, vitreous carbon, or FTO electrodes to give stable well-adherent black films, as shown in figure 3. The optimum polymerization potential of **1** is +1.2 V (vs. Ag/AgCl) for 300 seconds where 308 µA was passed, either on a Pt or a FTO glass electrode.

Figure 3. FTO surface coated with black film of poly-**1**.

3.3 Surface characterization

The morphology of the polymers was investigated using an SEM study of films coated on FTO glass electrodes, at different film thickness. However, uneven nucleation growth films have been obtained with no remarkable features (Figure 4), within the resolution limits of the microscope. EDX analysis of the deposited film on FTO shows the presence of C, Sn, Si, O, N confirming the presence of the polymeric film on FTO surface (Figure 5). Further studies using high resolution microscopy such as TEM and cross-section area analysis for film thickness determination are needed.

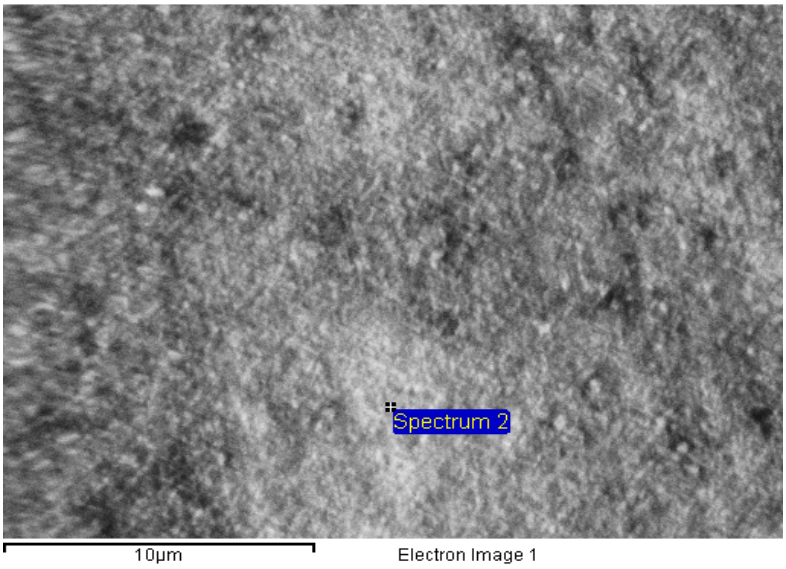


Figure 4. SEM images of poly-**1** on FTO electrode showing uneven nucleation growth film with no remarkable features.

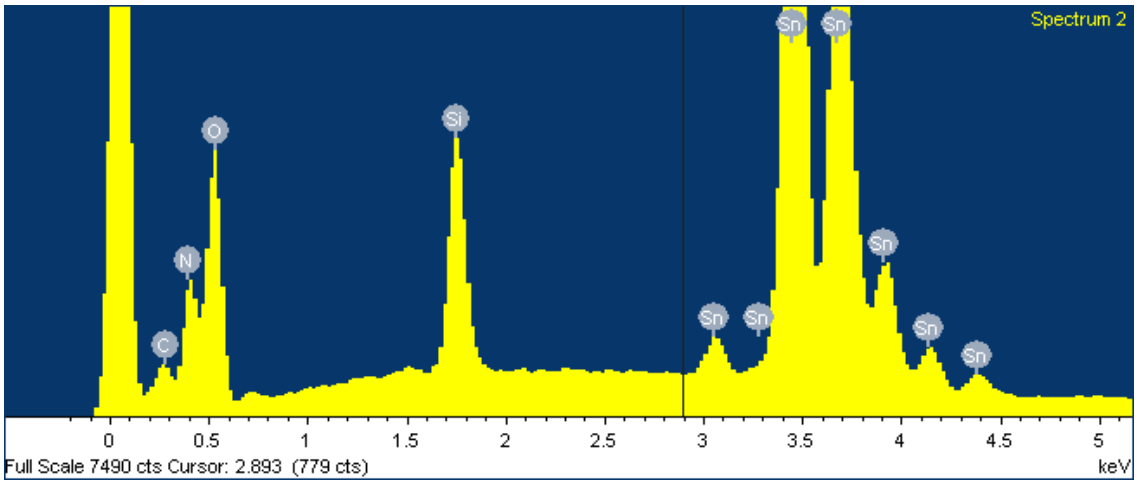


Figure 5. EDX of the surface of poly-**1** on FTO electrode.

3.4 Diffuse-reflectance FTIR spectroscopy of the polymer film

By using diffuse reflectance spectroscopy (DR), ex-situ FT-IR (DRFT-IR) spectra were recorded on films grown for 1170 seconds where 255 mC was passed, with the polished, platinum electrode providing the background spectrum. Figure 6 shows the DRFT-IR spectrum of poly-**1** where the band at 1683 cm^{-1} is the characteristic vibration of (**C=O**) carbonyl of the ketone. The band observed at 1598 cm^{-1} is the characteristic vibration of pyrrole ring, while the bands in the range of 1413 and 1000 cm^{-1} are clearly the characteristic peaks for pyrrole, and phenyl rings, which is in agreement with previous studies.[15,16] These observed bands are similar to the characteristic bands of the functional groups in the corresponding monomer **1**, shown in figure 7.

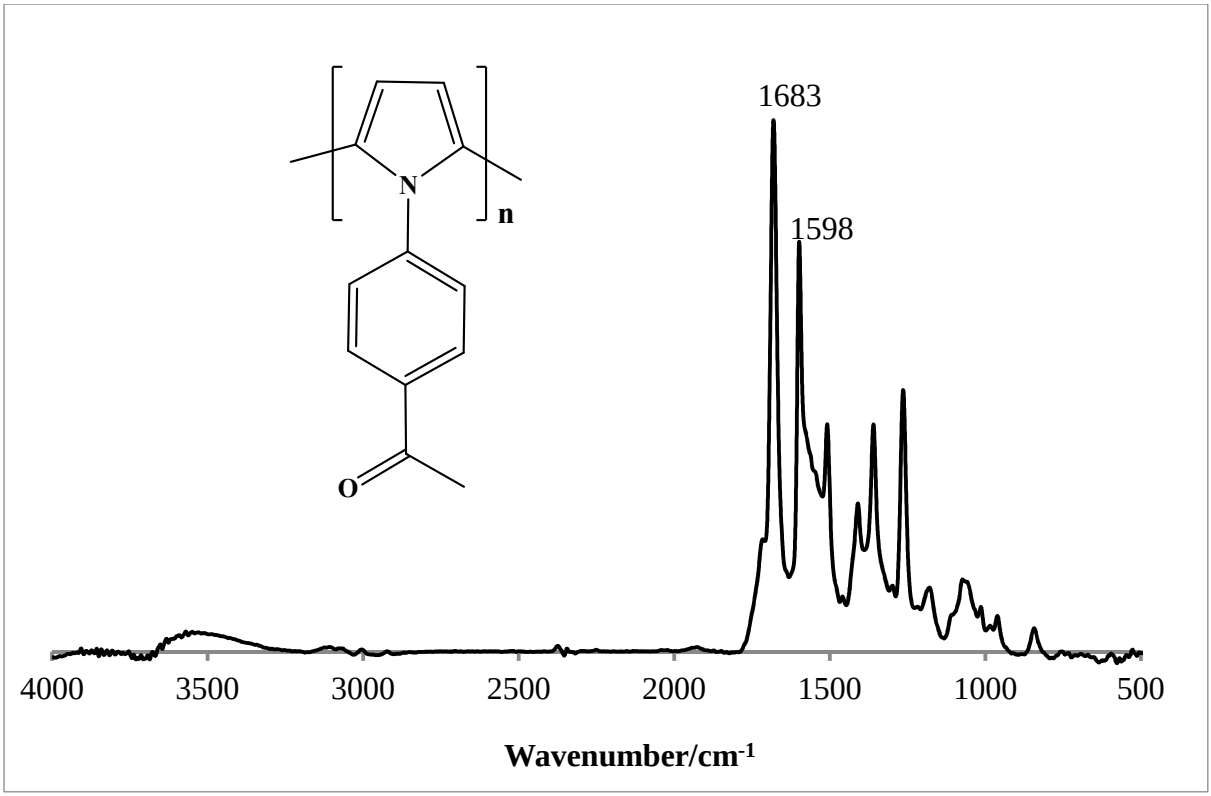


Figure 6. Reflectance FT-IR spectrum of the reduced-form film of poly-**1**.

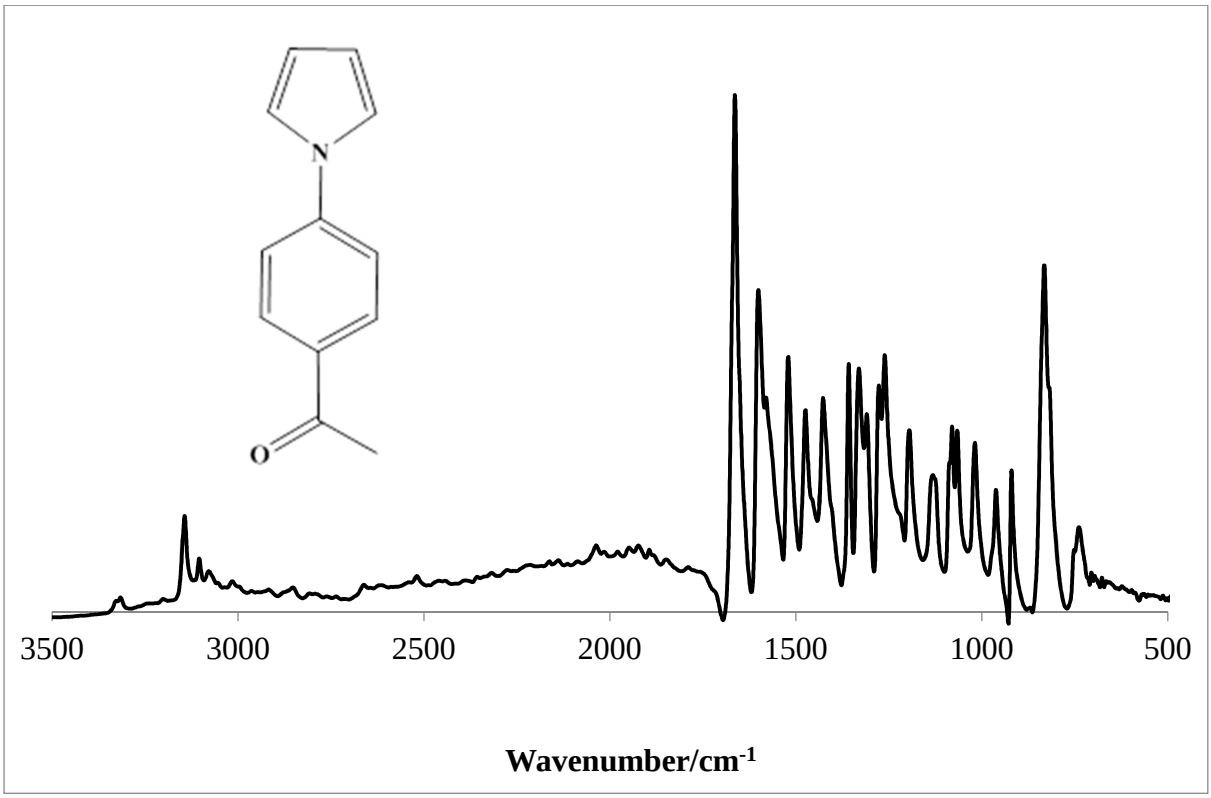


Figure 7. FT-IR spectrum of monomer **1**.

4. Conclusion

We have described the synthesis and the electrochemical study of with iodo (compound **2**), and aryl-ketone (compound **1**) groups available for further functionalization . The synthesis procedure of **2** is quite straightforward that affords the target molecules with good yields. However, only compound **1** was readily to electropolymerize potentiostatically on conducting surfaces. The surface morphology of Poly-**1** films was studied using SEM-EDX and DRFT-IR techniques. SEM results showed unremarkable features within the resolution limits of the microscope. Both EDX and DRFT-IR results confirmed the presence of the target polymeric film on conducting electrodes.

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