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Solid phase chemistry at a modified cathode surface. First synthesis of a polyamine precursor

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Abstract

The synthesis of a polyamine precursor was performed at a modified electrode interface. The chemical behaviour of the polythiophene matrix appeared identical to that of polystyrene beads. The target molecule, obtained with good yield, was released from the solid support by cathodic S–N bond scission, using the conducting properties of the polymer. © 2000 Elsevier Science Ltd. All rights reserved.

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The possible use of functionalized polythiophenes in solid-phase chemistry[1] has recently been described. To validate this methodology, we have investigated the polyamine synthesis at modified electrode interfaces. Apart from the biological aspect that makes polyamine derivatives of particular interest,[2] the build-up of such entities on a solid support is known to present numerous advantages,[3] especially for their purification. Moreover, the use of fast and highly selective S–N bond cleavages previously demonstrated on a model polymer[1] should indeed provide a good alternative to usual reactions implying polystyrene beads.

The poly-[**1**] matrix, obtained from the corresponding monomer by electrodeposition on platinum plate (area=5 cm^2) at constant potential (+1.40 V vs 0.1 mol L^{-1} Ag^+/Ag electrode in CH_3CN, anodic charge=2 C), was found to present an interfacial functionalization in the order of 2μmol/cm^2. This value could be obtained, without any matrix structure change, either by direct or indirect means.[4] The synthesis of target molecule **2** was developed on this resin as shown in Scheme 1.

This three step sequence involved an azido amine[5] condensation followed by the azido group reduction[6] and subsequent benzoyl choride condensation. Electrochemical cleavage led to the desired product[7] in 60% yield and 95% purity (NMR, MS and GC analysis). The progress of each step, performed on a small area of the conducting polymer, was followed by FT-IR. Thus, a characteristic band centered at 2103 cm^{-1} observed after 30 min reaction clearly demonstrated the azido amine condensation. Moreover,

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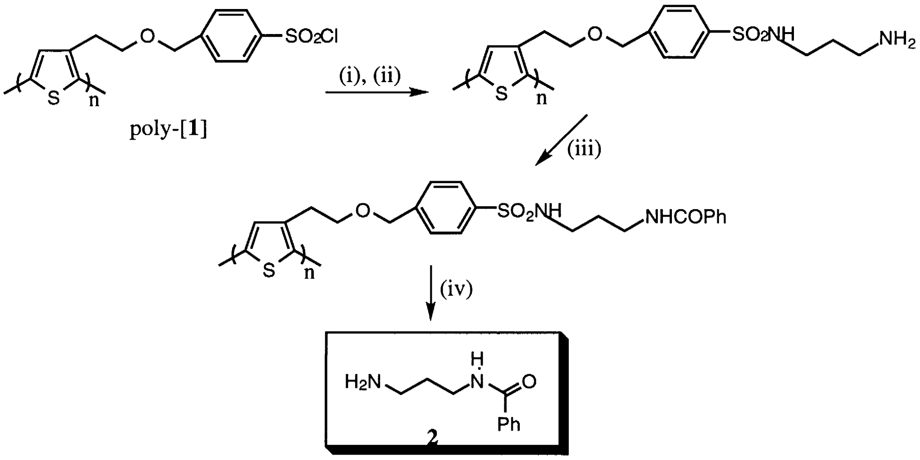

Scheme 1. (i) $H_2N(CH_2)_3N_3$, pyridine; (ii) $SnCl_2$, PhSH, Et_3N, CH_3CN; (iii) PhCOCl, Et_3N, THF; (iv) $2e^-$ $E_{red}=-2.95$ V vs 0.1 mol.L^{-1} Ag^+/Ag electrode in CH_3CN containing 0.1 mol L^{-1} Bu_4NBF_4, cathodic charge=1.4 C, rt

a total azide band disappearance by treatment of the resin with tin dichloride was observed after only 5 min indicating total reduction. Finally, the acid chloride condensation, performed under dilute conditions in order to avoid any by-products, was also followed by IR spectroscopy. Indeed, a strong band centered at 1652 cm^{-1} does attest a successful conversion. Lastly, the chemical stability of this conducting polymer was studied and compared with that of polystyrene beads. As expected, both matrixes present a similar behaviour since no polythiophene denaturation was observed along the chemical elongation. Hence, the conductivity of the recovered polymer was unchanged after each chemical step. The product release from solid support was finally performed at room temperature according to a procedure already reported.[1] This electrochemical cleavage appeared to be faster (less than 1 min) than parent chemical[8] or photochemical[9] processes. No effect on the target molecule was found owing to its low electroactivity.

In summary, a new solid phase methodology based on conducting modified electrode, has been developed. Both attachment to and cleavage from this new polymeric support can be achieved under milder and faster conditions than known procedures on polystyrene beads. It should therefore be particularly useful for fragile compounds such as acid labile derivatives. Finally, regarding the small amount of product synthesized at the cathode interface, this process seems to be of particular interest for combinatorial synthesis where only a low quantity of compounds is required.

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