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Unusual Solubility Behavior of Catechol-Arginine Derivative

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ABSTRACT

Numerous literatures have been reported, catechol undergoes electrochemical oxidation in presence of different nucleophiles and yields Michael addition products. This study was aimed to synthesize catechol-arginine derivative chemically followed by two steps. The first step involves oxidation of catechol into o-benzoquinone in presence of buffer solution pH 7 containing$K_3[Fe(CN)_6]$ and the latter step is 1,4-Michael addition reaction with L-arginine. Finally, a black product was obtained which shows an unusual solubility behavior in case of almost all organic solvents as well as in water (except pH > 7). Due to abnormal solubility it was not possible to characterize the product by Nuclear Magnetic Resonance (NMR), Electron Diffusion Spectroscopy (EDS) and Inductively Coupled Plasma Mass Spectrometry (ICP-MS) techniques. Appearance of some new peaks in Fourier Transform Infrared Spectroscopy spectrum indicates the formation of catechol-arginine adduct.
KEYWORDS: Catechol, Arginine, Unusual solubility, Characterization, Chemical synthesis

INTRODUCTION

Catechol is most important building blocks in organic synthesis and the precursor of pesticides, dyes, perfumes, drugs, intermediate for antioxidants in rubber and lubricating oils, polymerization inhibitors and pharmaceuticals [1,2]. Many vital drugs, like daunorubicin, mitomycin C and doxorubicin in cancer treatment contain quinones [3]. Electrochemical oxidation of catechol generates a quite reactive o-benzoquinone intermediate [4]and that can be attacked by various nucleophiles (amine, chloride, sulfhydryl, amide, indole and imidazole substituents compounds) to form Schiff bases, N-quinonyl derivatives and S-quinonyl derivatives [5]. Beside electrochemical technique, when catechol is subjected to treat with $K_3[Fe(CN)_6]$ at 25-30 °C produces o-benzoquinone [6] that may also undergoes nucleophilic substitution reaction. Compared to other nucleophiles amino acids are relatively weak and the functional side chains of arginine, lysine, cysteine, histidine, aspartic acid, glutamic acid and tyrosine are active nucleophiles in their unprotonated state [7]. Quinone based amino acid derivatives plays a crucial role in the synthesis of different natural products, medicinal compounds having antimalarial and antitumor activities [8-10]. Some biological processes like cross-linking of DNA and enzyme inhibition are also associated with the alkylamino derivatives [11]. Numerous groups of researcher have investigated electrochemical oxidation in presence of different nucleophiles[12-16]that has motivated us to synthesize catechol-arginine derivative chemically. None of them reported the unusual solubility behavior of o-benzoquinone derivatives in presence of amino acids.

MATERIALS AND METHODS

The chemicals and reagents were purchased from commercial supplier and used without further purification. Oxidation of catechol (1g, 9.08 mmol) was carried out by using$K_3[Fe(CN)_6]$ in presence of buffer solution (pH 7)and the resulting mixture was stirred for 24 hat 25-30 °C[6]. Then arginine (1.56 g, 9.08 mmol) was added into this mixture and continued stirring overnight. The resulting product was washed several times by buffer solution (pH 7) and dried in an oven at 80°C for 6 h, to obtain black powdered compound in30% (0.77 g) yield (**Scheme 1**).

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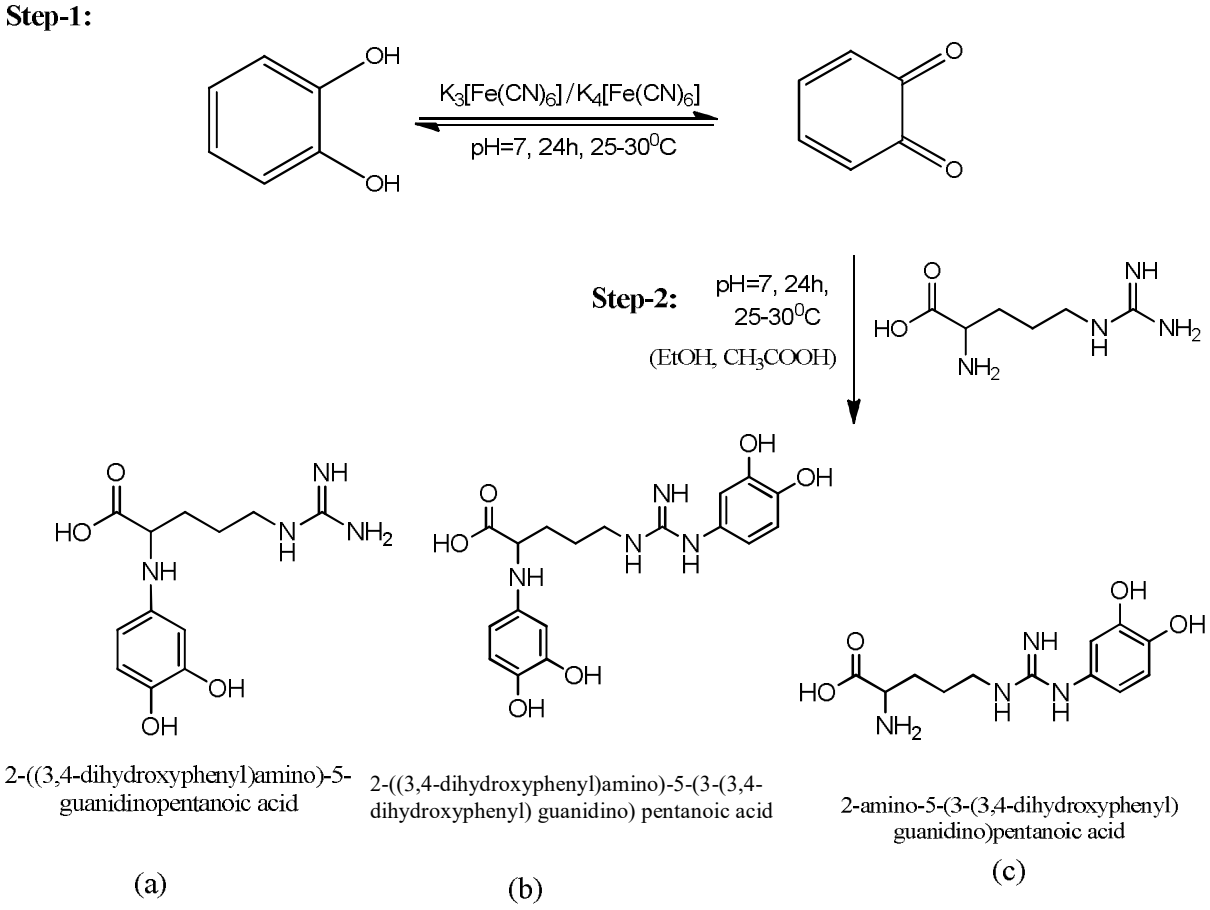

Scheme 1. Probable structures of (a) 2-((3,4-dihydroxyphenyl)amino)-5-guanidinopentanoic acid (b) 2-((3,4-dihydroxyphenyl)amino)-5-(3-(3,4- dihydroxyphenyl) guanidino) pentanoic acid and (c) 2-amino-5-(3-(3,4-dihydroxyphenyl) guanidino) pentanoic acid

RESULTS AND DISCUSSION

Catalytic or enzymatic oxidation of catechol generates o-benzoquinone that may undergo crosslinking with different nucleophiles to yield Schiff base and 1,4-Michael addition adducts [17-19]. Juan et al. synthesized 4-propylamino-5-methyl-o-quinone by the treatment of 4-methylcatechol with propylamine catalyzed by $NaIO_4$. Mason and Peterson studied the reaction between catechol and L-proline and the product formation was confirmed by the oxygen consumption [20]. Kehrmann and Cordon reported non-enzymaticoxidation catechol in presence aniline using silver oxide [21]. Physical, chemical and biological properties of o-quinone-amino acid adducts were extensively studied by Bitner [5]. In this study we have synthesized catechol-arginine adduct which is insoluble in the most of organic solvents (**Table 1**) whereas catechol and arginine are soluble in listed solvent. We studied this reaction in buffer solution of pH 7. The synthesized compound was also insoluble in pH 7 buffer solution. The blackish product was only soluble in NaOH, KOH, $NaHCO_3$, Na_2CO_3 and Buffer solution of pH > 7. Due to insolubility behavior makes it difficult to purify this compound by column chromatography. We tried to characterize this compound by ICP-MS, EDS and NMR spectroscopy. But this product was insoluble in $CDCl_3$ and DMSO as a result it was not possible to characterize the product by these techniques. The FTIR spectroscopy is used to investigate the presence of different functional groups in desired compound. IR spectrum (**figure 1**), υ, cm^{-1}: 3383 (N-H), 3174 (O-H, -COOH), 1669 cm^{-1}(Ar-C=O), 1653 (C=N), 1622, 1472 (C=C). On the basis of this data we are expecting that the newly synthesized compound would be any of **a**, **b** or **c** in the displayed **Scheme 1.**

Table 1. Solubility of starting materials (catechol and arginine) and product

Solvents	Reagents and Product		
	Catechol	Arginine	Product
Pentane	PS[a]	I[b]	I
n-hexane	I	I	I
Heptane	I	I	I
Cyclohexane	I	I	I
Cyclobenzene	I	I	I
DCM	I	I	I
CCl_4	I	I	I
$CHCl_3$	S[c]	I	I
Benzene	I	I	I
Toluene	I	I	I
Ether	S	I	I
Acetone	PS	S	I
2-butanone	PS	I	I
Ethyl acetate	S	I	I
Acetic acid	S	PS	I
Methanol	S	PS	I
Ethanol	S	PS	I
1-butanol	S	I	I
2-butanol	S	I	I
1-propanol	PS	I	I
2-propanol	PS	I	I
t-butyl alcohol	PS	I	I
$CDCl_3$	S	PS	I
DMSO	S	S	I
Ethylene glycol	PS	I	I
Glycerin	I	I	I
DMF	I	S	I
D_2O	PS	PS	I
Pyridine	PS	I	I
NaOH	S	S	S
$NaHCO_3$	S	S	PS
$Na_2(CO_3)$	S	S	S
KOH	S	S	S
pH 7	S	S	I
< pH 4	S	S	PS
> pH 7	S	S	S

[a]PS= Partially Soluble,[b]I= Insoluble and [c]S= Soluble

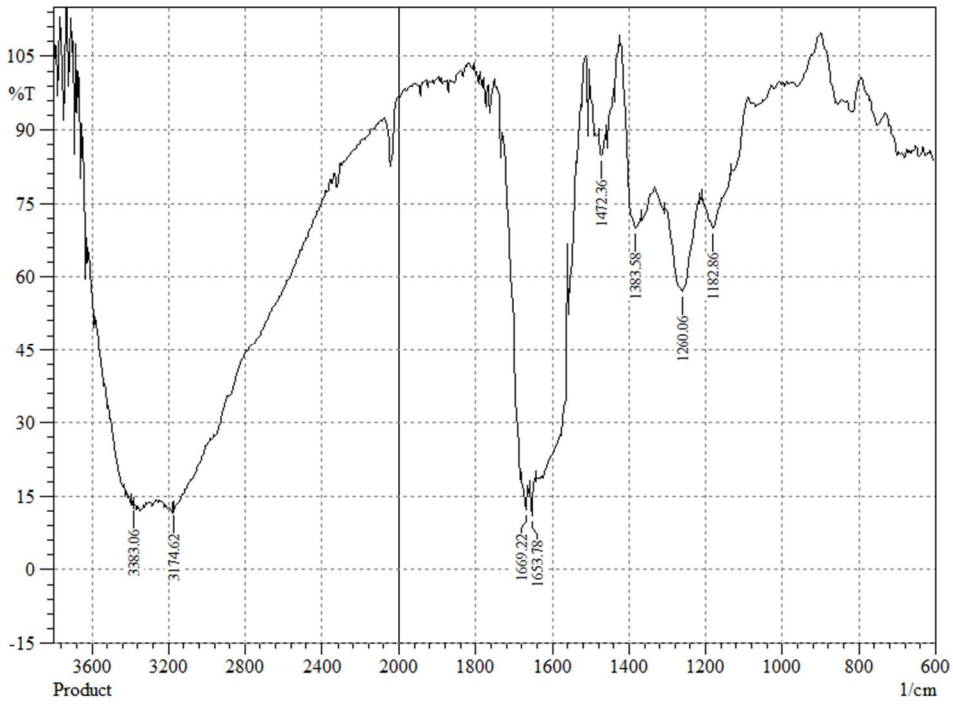

Fig 1. FTIR spectrum of catechol-arginine derivative

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