

Electrochemiluminescence detection of methamphetamine based on a Ru(bpy)₃²⁺-doped silica nanoparticles/Nafion composite film modified electrode

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ABSTRACT: An electrochemiluminescence (ECL) approach for methamphetamine determination was developed based on a glassy carbon electrode modified with a Ru(bpy)₃²⁺-doped silica nanoparticles/Nafion composite film. The monodispersed nanoparticles, which were about 50 nm in size, were synthesized using the water-in-oil microemulsion method. The ECL results revealed that Ru(bpy)₃²⁺ doped in silica nanoparticles retained its original photo- and electrochemical properties. The ECL intensity was found to be proportional to methamphetamine concentration over the range from 1.0×10^{-7} to 1.0×10^{-5} mol L⁻¹, and the detection limit was found to be 2.6×10^{-8} mol L⁻¹. The proposed ECL approach was used to analyze the methamphetamine content in drugs. Copyright © 2009 John Wiley & Sons, Ltd.

Keywords: electrochemiluminescence; Ru(bpy)₃²⁺-doped silica; methamphetamine

Introduction

Electrochemiluminescence (ECL) is a light-emitting phenomenon of excited species that are generated at an electrode surface.^[1] It has attracted considerable attention during the past several decades due to its high sensitivity, low background signal, reproducibility and good temporal and spatial control. As an important and valuable detection method, ECL has been used as a quantitative method in flow injection analysis, high-performance liquid chromatography (HPLC) and capillary electrophoresis to determine a wide range of compounds such as amine, amino acids, oxalate, NADH and nucleic acids.^[2–9] In particular, ECL based on the tris(2,2'-bipyridyl)ruthenium(II) [Ru(bpy)₃²⁺] complex has been the most thoroughly studied among various systems, since it generates strong luminescence, dissolves in both aqueous and nonaqueous media at room temperature and undergoes reversible one-electron-transfer reactions at easily attainable potential.^[1] Moreover, its oxidation–reduction reaction mechanism indicates that Ru(bpy)₃²⁺ can be regenerated on the surface of an electrode.^[10] Therefore, various efforts to immobilize Ru(bpy)₃²⁺ on an electrode surface have been made in order to fabricate an ECL sensor including: (a) a derivate Ru(bpy)₃²⁺ complex is absorbed on the electrode surface by non-covalent^[11] or covalent interaction;^[12] (b) Ru(bpy)₃²⁺ is entrapped in the network of a sol–gel film;^[14–16] (c) Ru(bpy)₃²⁺ is used as an additive to fabricate a carbon electrode;^[17,18] (d) Ru(bpy)₃²⁺ is immobilized with negatively charged nanoparticles using a layer-by-layer method;^[13] and (e) Ru(bpy)₃²⁺ is incorporated into the cation exchange membrane immobilized on an electrode surface, such as Nafion film.^[19,20] The LB film is easy to wash and the covalent method is complicated. The sol–gel film is easy to crash and has lower water solubility and conductivity. The Ru(bpy)₃²⁺-doped carbon electrode is limited by the amount of Ru(bpy)₃²⁺ on the electrode surface. The

electrostatic interaction and ion exchange methods are affected by ion strength. Although some of the above-mentioned ECL approaches are stable, the method to increase the amount of Ru(bpy)₃²⁺ on the electrode surface needs to be improved. In recent years, nanoscience and nanotechnology have opened up a promising era to synthesize nanoparticles in different shapes, sizes and compositions.^[21–23] Moreover, certain luminophors can be enriched in nanoparticles. Zhang and his co-workers report that Ru(bpy)₃²⁺-doped silica nanoparticles (RuSiNPs) could generate a bright ECL signal.^[24] In their study, Ru(bpy)₃²⁺ is enriched and restricted within the network of silica with electrostatic interactions so as to prevent its leaching, since hydroxyl groups on the surfaces of silica nanoparticles interact with the Ru(bpy)₃²⁺ cation. Some ECL sensors based on RuSiNPs have been developed to determine DNA,^[25] enzymes,^[26] amines^[27,28] and proteins.^[29]

Methamphetamine (METH) is a potent stimulant to the central nervous system. It is used to treat obesity and alcoholism, but it causes some physiological and psychological effects such as increased heart rate and blood pressure, affecting body temperature, attention and mood. As a result, the determination of METH has attracted attention. So far, many methods have been used, including gas chromatography,^[30] HPLC,^[31] gas chromatography–mass spectrometry (GC-MS),^[32] chromatography–mass spec-

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trometry (LC-MS),^[33] solid-phase microextraction–capillary zone electrophoresis^[34] and capillary electrophoresis electrochemical/electrochemiluminescence^[35] for quantifying METH in hair,^[29] plasma^[31] or urine.^[36] However, for these methods, expensive equipment and a long testing time are needed.

In our work, we produced a sensitive ECL sensor using RuSiNPs for METH detection. RuSiNPs were synthesized based on the water-in-oil microemulsion method. The photochemical and electrochemical characteristics of the RuSiNPs were examined. A glassy carbon electrode (GCE) was modified with RuSiNPs using Nafion film as a working electrode. It generated ECL signals under cyclic voltammetry (CV) scanning in a sample solution. The effects of pH and CV scan rate were studied.

Materials and methods

Chemicals

Tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate [Ru(bpy)₃Cl₂·6H₂O], Nafion and Triton X-100 were purchased from Aldrich (Milwaukee, WI, USA) and used as received. Methamphetamine hydrochloride was from the Bio-product Institute of Chinese Medicine (Beijing, China). All other chemicals were of guaranteed grade. The water used throughout was purified with a Millipore system (Millipore Co., USA). A series of METH standard solutions were prepared by diluting 1 mg mL⁻¹ METH with 0.1 mol L⁻¹ phosphate buffer solutions (PBS, pH 9.0), and the samples for METH determination were processed using the same PBS.

Apparatus

Electrochemical measurements were performed on a CHI 830 electrochemical analyzer (CHI Co., Shanghai, China). A standard three-electrode arrangement with a platinum auxiliary electrode and an Ag–AgCl reference electrode were employed. The working electrode was a GCE coated with RuSiNPs–Nafion composite film. The main body of the thin-layer electrolysis flow cell for ECL observation was constructed from two pieces of Diflon block separated by a 50 μm thick Teflon spacer. The volume of the thin layer cell was about 1.5 μL. ECL experiments were carried out with a flow-injection chemiluminescence analyzer (Xi'an Remax Electronic Science Tech. Co. Ltd, Xi'an, China), an EC 2000 workstation (Dalian Elite Analytical Instruments Co. Ltd, Dalian, China) and CHI 830. TEM images were obtained using a Tecnai F30 300KV (Philips-FEI Co. Holland). Fluorescence experiments were performed on an F-4500 fluorescence spectrofluorimeter (Hitachi, Japan). A GCMS-QP2010 system (Shimatsu Co. Ltd, Japan) was used for the result comparison of METH analysis. The pH values were measured using a pH510 meter (EUTECH, Singapore).

Preparation of a modified electrode for ECL observation

RuSiNPs were synthesized according to the water-in-oil microemulsion method.^[24] The RuSiNPs was prepared by mixing 7.5 mL of cyclohexane, 1.76 mL of TX-100, 1.6 mL of 1-hexanol, and 400 μL of 20 mmol L⁻¹ M Ru(bpy)₃²⁺ aqueous solution under magnetic stirring. Five minutes later, 100 μL of TEOS and 60 μL of ammonia (25%) were added in order. The reaction was allowed to stir for 24 h. Then, the RuSiNPs were isolated by acetone, and washed by acetone and ethanol several times, then dispersed in ethanol and stored in a refrigerator. One milliliter of RuSiNPs ethanol suspension was dried at 30°C, and the residue was weighed to calculate the concentration of RuSiNPs. The RuSiNP suspen-

sion was then mixed with Nafion thoroughly under ultrasonic waves, so that finally the hybrid suspension contained 0.2% Nafion and 1 mg mL⁻¹ RuSiNPs.

A GCE (diameter 5 mm) was polished with 0.3 and 0.05 μm α-Al₂O₃, rinsed with water and sonicated successively after each polishing step and finally dried in a nitrogen flow. Three microliters of the suspension prepared above was dropped onto the surface of the GCE. When not in use, the modified electrode was kept in the dry state at room temperature.

METH sample collection and preparation

A 0.1000 g METH sample from each test case was dissolved in a 50 mL PBS solution, and then filtered through a Millex Filter Unit with a pore size of 0.45 μm (Millipore, USA). A 0.010 mL aliquot of the above sample solution was diluted to 100.0 mL.

ECL measurement

The PBS solution was pumped into the thin-layer electrolysis flow cell using a flow-injection chemiluminescence analyzer, and continuous cyclic voltammetry was added to the flow cell, then the ECL peaks were obtained. After the ECL signals were stable, cyclic voltammetry was paused and the PBS solution was changed to the sample solution. Two minutes later, the sample solution was fulfilled the flow cell. Then cyclic voltammetry was carried out again. The sample ECL signal was obtained by subtracting PBS signal from sample signal.

Results and discussion

Characteristics of RuSiNPs

The features of RuSiNPs were studied and, as shown in the TEM image of RuSiNPs, RuSiNPs were dispersed well and with a diameter of about 50 nm (Fig. 1). The fluorescence spectra of the RuSiNPs suspension and the RuSiNPs immobilized in the Nafion film revealed that their maximum emission wavelengths were 594 and 589 nm, respectively. There was only 6 nm difference in emission wavelength comparing the fluorescence spectra of Ru(bpy)₃²⁺ in aqueous solution. This result confirmed that Ru(bpy)₃²⁺ was successfully doped in SiO₂ nanoparticles and held its photochemical characteristic well in Nafion film.

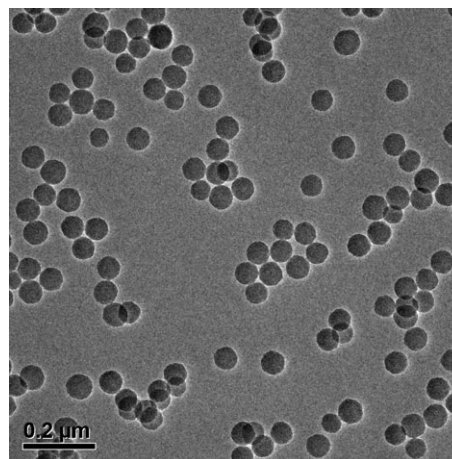


Figure 1. TEM image of RuSiNPs.

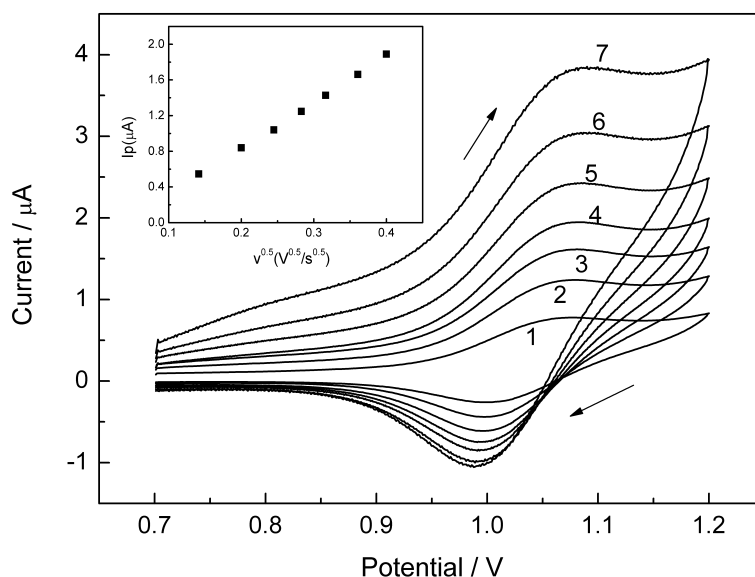


Figure 2. Cyclic voltammograms of the glassy carbon electrode modified with RuSiNPs at various scan rates (the rates of 1–7 are 20, 40, 60, 80, 100, 130 and 160 mV s^{-1}) in 0.1 mol L^{-1} PBS (pH 9.0). Insert: linearity of the oxidation peak current and the square root of scan rate.

Electrochemical characteristics of the RuSiNPs modified electrode

CV was used to investigate the electrochemical property of the RuSiNPs modified electrode. The cyclic voltammograms (CVMs) of RuSiNPs immobilized in Nafion film on a GCE in 0.1 mol L^{-1} PBS (pH 9.0) at various scan rates are shown in Fig. 2. Similar to the CVM of $\text{Ru}(\text{bpy})_3^{2+}$ in aqueous solution, an oxidation peak of $\text{Ru}(\text{bpy})_3^{2+}$ at 1.07 V and a corresponding reduction peak at 1.00 V could be found. The interval between the two peaks was about 70 mV, which was attributed to the one-electron redox reaction of $\text{Ru}(\text{bpy})_3^{2+}$ and shows good electrochemical reversibility. The interval between redox waves increases slightly with increasing scan rate because the peak potential is a function of the applied potential scan rate.^[37] The reversibility of $\text{Ru}(\text{bpy})_3^{2+}$ redox reaction became a little lower when the applied potential scan rate was higher than 100 mV s^{-1} , but the deviation could be ignored at a lower scan rate. In the experiments, the potential scan rate was kept at 60 mV s^{-1} . In addition, the experimental result shown in the Fig. 2 insert indicated that the value of the oxidation peak was proportional to the square root of the scan rate in the range 20–160 mV s^{-1} , indicating that the electrode process was controlled by a diffusion process.

CVMs of the RuSiNPs–Nafion film in PBS (pH = 9.0) with and without $1.0 \times 10^{-5} \text{ mol L}^{-1}$ METH at a scan rate of 60 mV s^{-1} are presented in Fig. 3(a). METH increased the oxidation current dramatically and decreased the reduction current slightly. This is because the METH is oxidized to generate intermediates which can further react with $\text{Ru}(\text{bpy})_3^{3+}$.^[38] Meanwhile, the ECL intensity increased in the presence of METH [Fig. 3(b)]. The mechanism of $\text{Ru}(\text{bpy})_3^{2+}$ –METH, which is similar to the electrocatalytic reaction mechanism of *n*-propylamine/ $\text{Ru}(\text{bpy})_3^{2+}$,^[1] has been proposed in a previous study.^[38]

Optimal condition for RuSiNPs ECL observation

The amount of RuSiNPs in the modifying film affected the ECL intensity. With the concentration of RuSiNPs increasing, the ECL intensity increased to a maximum at 1.0 mg mL^{-1} and then

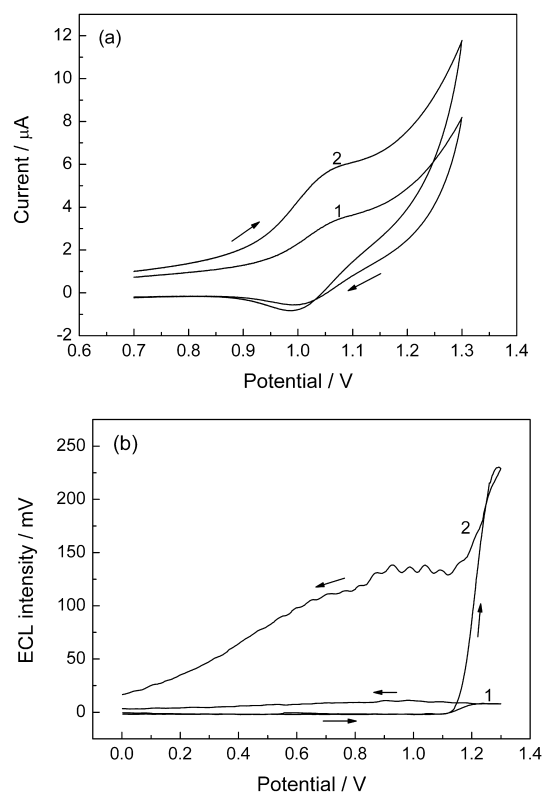


Figure 3. (a) Cyclic voltammograms of the modified glassy carbon electrode: (1) 0.1 mol L^{-1} PBS (pH 9.0); (2) 0.1 mol L^{-1} PBS (pH 9.0) + $1.0 \times 10^{-5} \text{ mol L}^{-1}$ METH. (b) ECL-potential curves for the modified electrode in (1) 0.1 mol L^{-1} PBS (pH 9.0); (2) $1.0 \times 10^{-5} \text{ mol L}^{-1}$ METH. Scan rate 60 mV s^{-1} .

decreased [Fig. 4(a)]. This was attributed to more RuSiNPs being able to increase more active sites, but the thickness was also increased, which resulted in more scatter and inner filter effects and prevented METH from reacting on the electrode surface.^[39] In addition, Nafion was selected to immobilize RuSiNPs to the electrode surface and the effect of Nafion was considered [Fig. 4(b)].

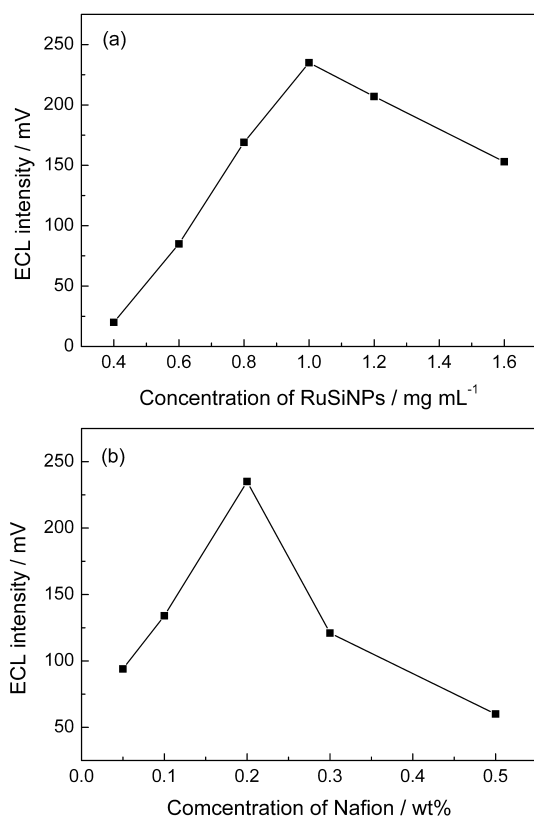


Figure 4. Effect of RuSiNPs concentration (a) and Nafion concentration (b) on the ECL intensity in the presence of $1.0 \times 10^{-5} \text{ mol L}^{-1}$ METH with the scan rate of 60 mV s^{-1} .

With the concentration of Nafion increasing, the ECL intensity increased. This is because less Nafion resulted in the leakage of RuSiNPs. When the concentration of Nafion was larger than 0.2% (wt), the ECL intensity decreased due to inhibition of METH transferring from solution to inner film.^[39] Therefore 1.0 mg mL^{-1} of RuSiNPs and 0.2% (wt) of Nafion were selected.

The medium pH takes a key role in ECL measurements of amines.^[1] Taking this into consideration, the effect of pH on RuSiNPs ECL emission was investigated in the range 7.0–11.0. The ECL intensity increased significantly from 7.0 up to 9.0 and then decreased at higher pH. The pH dependence of the ECL is due to the deprotonation of an intermediate, which is similar to the ECL reaction of aliphatic amines.^[1,40]

The effect of scan rate on the ECL intensity was also studied. ECL intensity decreased with increasing scan rates from 20 to 140 mV s^{-1} , and such an influence is complicated. It is related to the ECL intermediate reaction kinetics of the ECL system and diffusion of METH in the film. The scan rate of 60 mV s^{-1} was selected taking into consideration the analysis time.

Evaluation of the modified electrode

The stability of the Nafion-RuSiNPs modified GCE was tested by means of a repetitive measurement ECL response. Since $\text{Ru}(\text{bpy})_3^{2+}$ is a very stable ECL reagent, its photochemical characters maintain the stability of the ECL reagent for a long time. In addition, the environment of SiNPs provided a suitable polarity for the enrichment of $\text{Ru}(\text{bpy})_3^{2+}$, which obviously increased $\text{Ru}(\text{bpy})_3^{2+}$ concentration, and the strong interaction between

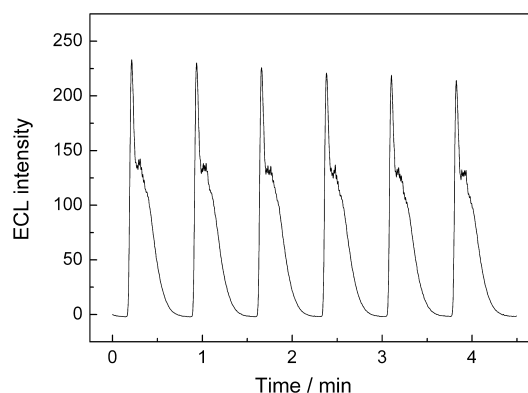


Figure 5. ECL intensity of the modified electrode in PBS (pH 9.0) containing $1.0 \times 10^{-5} \text{ mol L}^{-1}$ METH under continuous cyclic voltammetry for six cycles with scan rate of 60 mV s^{-1} .

$\text{Ru}(\text{bpy})_3^{2+}$ and SiNPs. Lastly, Nafion is a type of polyelectrolyte, which enables the Nafion–RuSiNPs film to be strongly adsorbed onto the surface of the GCE. After one week of continuous testing, only a 2.8% decrease was observed in the ECL response of 0.01 mmol L^{-1} METH. The result suggested that the modified electrode had good stability.

Under the selected conditions, a calibration curve for METH was constructed. The linear range was from 1.0×10^{-7} to $1.0 \times 10^{-5} \text{ mol L}^{-1}$ and the detection limit was $2.6 \times 10^{-8} \text{ mol L}^{-1}$, compared with $8.0 \times 10^{-9} \text{ mol L}^{-1}$ ^[41], $3.3 \times 10^{-8} \text{ mol L}^{-1}$ ^[35] and $2.0 \times 10^{-7} \text{ mol L}^{-1}$.^[38] The reproducibility of the modified electrode was tested. Under continuous cyclic potential scanning for six cycles in 0.1 mol L^{-1} PBS (pH 9.0) containing $1.0 \times 10^{-5} \text{ mol L}^{-1}$ METH, a stable ECL emission was obtained (Fig. 5). The relative standard deviation was 3.2%, suggesting the good reproducibility of the METH detection.

Analysis of METH

METH samples from different test cases were tested using the proposed ECL approach. The detection and comparison results are listed in Table 1. The METH content ranging from 87.5 to 94.3% indicated that the purities of the captured METH samples were all quite high. The recovery of the ECL method, measured as the percentage difference between the mean concentrations found and the amounts added, ranged from 95.3 to 106.0%. According to the recovery results, the coexisting substances in the sample, including synthetic materials or their by-products, did not obviously affect the ECL determination. In addition, the relative standard deviation (RSD) for the quality control samples ranged from 3.1 to 3.8%. The ECL method reliability has been validated by GC-MS. There is only at most a 2% error between the ECL and the GC-MS methods compared with their analytical results. Finally, the total of 5 min analytical time showed that the ECL method could be applied as an adjunct to a quick analysis in some cases.

Conclusion

A sensitive, reproducible ECL sensor was prepared for determining METH. $\text{Ru}(\text{bpy})_3^{2+}$ was enriched in silica matrix preventing $\text{Ru}(\text{bpy})_3^{2+}$ leaching out and the large surface of the nanoparticles was good for generating an ECL signal. The electrode modified

Table 1. ECL determination results and recoveries of METH samples using a Ru-SiNPs modified GCE ($n = 6$)

Sample*	Found, 10^{-6} (mol L $^{-1}$)		Content (%)		RSD (%)	Added, 10^{-6} (mol L $^{-1}$)	Found, 10^{-6} (mol L $^{-1}$)	Recovery (%)
	ECL	GC-MS	ECL	GC-MS				
1	1.26	1.27	94.3 ± 2.3	94.8 ± 1.5	3.8	1.0	2.34	103.6 ± 2.7
2	1.23	1.21	91.6 ± 3.2	90.3 ± 1.2	3.1	1.0	2.13	95.6 ± 3.3
3	1.17	1.18	87.5 ± 3.6	88.2 ± 1.9	3.2	1.0	2.30	106.0 ± 2.5

*Samples were provided by the Institute of Criminal Science and Technology, Xiamen.

with a RuSiNPs/Nafion composite film showed good photochemical and electrochemical activity. The modified electrode was used for ECL determination of METH and a good result was obtained. This therefore provides a feasible method for the rapid determination of METH in many drug investigation cases.

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References

- [1] Richter MM. Electrochemiluminescence (ECL). *Chem Rev* 2004;104:3003.
- [2] Li M, Lee SH. Determination of trimethylamine in fish by capillary electrophoresis with electrogenerated tris(2,2'-bipyridyl) ruthenium(II) chemiluminescence detection. *Luminescence* 2007;22:588.
- [3] Lin MS, Wang JS, Lai CH. Electrochemiluminescent determination of Nicotine based on tri (2,2'-bipyridyl) ruthenium (II) complex through flow injection analysis. *Electrochim Acta* 2008;53:7775.
- [4] Yi CQ, Li PW, Tao Y, Chen X. High-performance liquid chromatographic determination of quinolizidine alkaloids in radix sophora flavescens using tris(2,2'-Bipyridyl)ruthenium(II) electrochemiluminescence. *Microchim Acta* 2004;147:237.
- [5] Li JG, Yan QY, Gao YL, Ju HX. *Anal Chem* 2006;78:2694.
- [6] Rubinsteln I, Martin CR, Bard AJ. Electrogenerated chemiluminescence determination of oxalate. *Anal Chem* 1983;55:1580.
- [7] Rubinsteln I, Bard AJ. Electrogenerated chemiluminescence. 37. Aqueous ecl systems based on tris(2,2'-bipyridyl)ruthenium $^{2+}$ and oxalate or organic acids. *J Am Chem Soc* 1981;103:512.
- [8] Martin AF, Nieman TA. Chemiluminescence biosensors using tris(2,2'-bipyridyl) ruthenium(II) and dehydrogenases immobilized in cation exchange polymers. *Biosens Bioelectron* 1997;12:479.
- [9] Miao WJ, Bard AJ. Electrogenerated chemiluminescence. 77. DNA hybridization detection at high amplification with [Ru(bpy) $_3$] $^{2+}$ -containing microspheres. *Anal Chem* 2004;76:5379.
- [10] Tokel NE, Bard AJ. Electrogenerated chemiluminescence. IX. Electrochemistry and emission from systems containing tris(2,2'-bipyridyl)ruthenium(II) dichloride. *J Am Chem Soc* 1972;94:2862.
- [11] Zhang X, Bard AJ. *J Phys Chem* 1988;92:5566.
- [12] Greenway GM, Greenwood A, Watts P, Wiles C. Solid-supported chemiluminescence and electrogenerated chemiluminescence based on a tris(2,2'-bipyridyl)ruthenium(II) derivative. *Chem Commun* 2006;1:85.
- [13] Guo ZH, Shen Y, Wang MK, Zhao F, Dong SJ. Electrochemistry and electrogenerated chemiluminescence of SiO $_2$ nanoparticles/Tris(2,2'-bipyridyl)ruthenium multilayer films on indium Tin oxide electrodes. *Anal Chem* 2004;76:184.
- [14] Collinson MM, Novak B, Martin SA, Taussig JS. *Anal Chem* 2000;72:2914.
- [15] Choi HN, Cho SH, Lee WY. Electrogenerated Chemiluminescence from Tris(2,2'-bipyridyl) ruthenium(II) Immobilized in Titania-Perfluorosulfonated Ionomer Composite Films. *Anal Chem* 2003;75:4250.
- [16] Qiu B, Chen X, Chen HL, Chen GN. Electrochemiluminescence determination of codeine or morphine with an organically modified silicate film immobilizing Ru(bpy) $_3^{2+}$. *Luminescence* 2007;22:189.
- [17] Shi LH, Liu XQ, Li HJ, Xu GB. *Anal Chem* 2006;78:7330.
- [18] Shen LH, Li XX, Qi HL, Zhang CX. Electrogenerated chemiluminescence of ruthenium complex immobilized in a highly cross-linked polymer and its analytical applications. *Luminescence* 2008;23:370.
- [19] Oyama N, Anson FC. Catalysis of electrode processes by multiply-charged metal complexes electrostatically bound to polyelectrolyte coatings on graphite electrodes, and the use of polymer-coated rotating disk electrodes in diagnosing kinetic and conduction mechanisms. *Anal Chem* 1980;52:1192.
- [20] Khramov AN, Collinson MM. Electrogenerated chemiluminescence of tris(2,2'-bipyridyl)ruthenium(II) ion-exchanged in nafion-silica composite films. *Anal Chem* 2000;72:2943.
- [21] Klostranec JM, Chan WCW. Quantum Dots in Biological and Biomedical Research: Recent Progress and Present Challenges. *Adv Mater* 2006;18:1953.
- [22] Zhang JH, Liu HY, Wang ZL, Ming NB. Au-Induced Polyvinylpyrrolidone Aggregates with Bound Water for the Highly Shape-Selective Synthesis of Silica Nanostructures. *Chem Eur J* 2008;14:4374.
- [23] Zou H, Wu SS, Shen J. Polymer/silica nanocomposites: preparation, characterization, properties, and applications. *Chem Rev* 2008;108:3893.
- [24] Zhang LH, Dong SJ. Electrogenerated chemiluminescence sensors using Ru(bpy) $_3^{2+}$ doped in silica nanoparticles. *Anal Chem* 2006;78:5119.
- [25] Chang Z, Zhou JM, Zhao K, Zhu NN, He PG, Fang YZ. Ru(bpy) $_3^{2+}$ -doped silica nanoparticle DNA probe for the electrogenerated chemiluminescence detection of DNA hybridization. *Electrochim Acta* 2006;52:575.
- [26] Wang XY, Zhou JM, Yun W, Xiao SS, Chang Z, He PE, Fang YZ. Detection of thrombin using electrogenerated chemiluminescence based on Ru(bpy) $_3^{2+}$ -doped silica nanoparticle aptasensor via target protein-induced strand displacement. *Anal Chim Acta* 2007;598:242.
- [27] Hun X, Zhang ZJ. Electrogenerated chemiluminescence sensor for itopride with Ru(bpy) $_3^{2+}$ -doped silica nanoparticles/chitosan composite films modified electrode. *Sens Actuators B* 2008;131:403.
- [28] Hun X, Zhang ZJ. Electrogenerated chemiluminescence sensor for metoclopramide determination based on Ru(bpy) $_3^{2+}$ -doped silica nanoparticles dispersed in Nafion on glassy carbon electrode. *J Pharm Biomed Anal* 2008;47:670.
- [29] Wei H, Zhou LL, Li J, Liu JF, Wang EK. Electrochemical and electrochemiluminescence study of Ru(bpy) $_3^{2+}$ -doped silica nanoparticles with covalently grafted biomacromolecules. *J Colloid Interface Sci* 2008;321:310.
- [30] Inoue H, Kuwayama K, Iwata YT, Kanamori T, Tsujikawa K, Miyaguchi H. Simple and simultaneous detection of methamphetamine and dimethyl sulfone in crystalline methamphetamine seizures by fast gas chromatography. *Forensic Toxicol* 2008;26:19.
- [31] Nakashima K, Kaddoumi A, Ishida Y, Itoh T, Taki K. Determination of methamphetamine and amphetamine in abusers' plasma and hair samples with HPLC-FL. *Biomed Chromatogr* 2003;17:471.

- [32] Wu YH, Lin KL, Chen SC, Chang YZ. Simultaneous quantitative determination of amphetamines, ketamine, opiates and metabolites in human hair by gas chromatography/mass spectrometry. *Rapid Commun Mass Spectrom* 2008;22:887.
- [33] Cheng W, Mok VK, Chan K, Li AF. A rapid and convenient LC/MS method for routine identification of methamphetamine/dimethylamphetamine and their metabolites in urine. *Forensic Science International* 2007;166:1.
- [34] Wei F, Fan Y, Zhang M, Feng YQ. Poly(methacrylic acid-ethylene glycol dimethacrylate) monolith in-tube solid-phase microextraction applied to simultaneous analysis of some amphetamine derivatives in urine by capillary zone electrophoresis. *Electrophoresis* 2005;26:3141.
- [35] Sun JY, Xu XY, Wang CY, You TY. Analysis of amphetamines in urine with liquid-liquid extraction by capillary electrophoresis with simultaneous electrochemical and electrochemiluminescence detection. *Electrophoresis* 2008;29:3999.
- [36] Andersson M, Gustavsson E, Stephanson N, Beck O. Direct injection LC-MS/MS method for identification and quantification of amphetamine, methamphetamine, 3,4-methylenedioxyamphetamine and 3,4-methylenedioxymethamphetamine in urine drug testing. *J Chromatogr B* 2008;861:22.
- [37] Nicholson RS, Shain I. Theory of stationary electrode polarography: single scan and cyclic methods applied to reversible, irreversible, and kinetic systems. *Anal Chem* 1964;36:706.
- [38] Yi CQ, Tao Y, Wang B, Chen X. Electrochemiluminescent determination of metamphetamine based on tris(2,2'-bipyridine)ruthenium(II) ion-association in organically modified silicate films. *Anal Chim Acta* 2005;541:75.
- [39] Hun X, Zhang ZJ. *Electroanalysis* 2008;20:874.
- [40] Noffsinger JB, Danielson ND. Generation of chemiluminescence upon reaction of aliphatic amines with tris(2,2'-bipyridine)ruthenium(III). *Anal Chem* 1987;59:865.
- [41] Dai H, Wang YM, Wu XP, Zhang L, Chen GN. An electrochemiluminescent sensor for methamphetamine hydrochloride based on multiwall carbon nanotube/ionic liquid composite electrode. *Biosens Bioelectron* 2009;24:1230.