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Study of a new chiral selector: Sodium arsenyl-(L)-(+) tartrate for capillary electrophoresis

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ABSTRACT

Sodium arsenyl-(L)-(+) tartrate ($Na_2[As_2(+)\text{-}tart_2]\cdot 3H_2O$) was examined and evaluated as a chiral selector using capillary electrophoresis. This chiral selector showed enantioselective associations with many cationic analytes, including primary, secondary, and tertiary amines. Also, baseline separations of ruthenium(II) polypyridyl complexes were achieved within 10 min. The effect of buffer type, chiral selector concentration, voltage applied, buffer concentration, buffer pH and organic modifier concentration were examined and optimized.

1. Introduction

Capillary electrophoresis (CE) has been found to be an effective and efficient alternative to chromatography for analytical enantiomeric separations over the last few decades due to its several known advantages such as short analysis time, high efficiency, low sample consumption and simple instrumentation [1–7]. Unlike HPLC, the most common approach for enantiomeric separation in CE involves the addition of one or more chiral selectors into the run buffer. In spite of a vast number of chiral selectors reported in literature for enantiomeric separations, only a few classes have been successfully used in CE because of some inherent requirements for CE chiral selectors: high water solubility, high stability in aqueous medium and low UV absorptivity, etc. Indeed, the dominant chiral selectors in CE are cyclodextrins and their derivatives, many of which were originally developed for HPLC and thin layer chromatography [8–11]. The demand for and continuous exploration of new chiral selectors, however, is necessary due to the increase of structural complexity of new synthetic chiral molecules.

Several tartrate-based compounds have been employed as chiral selectors for enantiomeric separations with marginal success. For example, L-*n*-octyl tartrate was reported to separate propranolol enantiomers using an indirect chiral separation [12]. Enantiomeric separations of aminoalcohols, amines and alkyl tropate were reported using (2R,3R)-di-*n*-butyl tartrate and (2R,3R)-di-*n*-propyl tartrate in HPLC [13,14]. Sodium-(S)-(+)-tartrate was used as a run buffer additive in CE to separate several cobalt(III) ethylenediamine complexes [15]. Recently, potassium antimony-D-tartrate and dibenzoyl-L-tartrate have been reported to separate enantiomers of several metal complexes including Ru, Cr, Ni, Co and Fe [16]. However, the resolution and efficiency of these metal complex separations were not reported. In this work, we introduce sodium arsenyl-(L)-(+) tartrate as a new chiral selector for CE.

A member of tartrate-based transition metal complexes, sodium arsenyl-(L)-(+) tartrate ($Na_2[As_2(+)\text{-}tart_2]\cdot 3H_2O$) (subsequently referred to as arsenyl tartrate) is a tartrato (4-)-bridged binuclear, metal tartrate-based compound (Fig. 1). It was previously reported for diastereoselective precipitations of chiral ruthenium racemic complexes [17]. This metal tartrate-based compound has four stereogenic centers located at the only carbon atom that also have a hydrogen attached. In agreement with X-ray crystallographic analysis of the molecular structure of arsenyl tartrate,

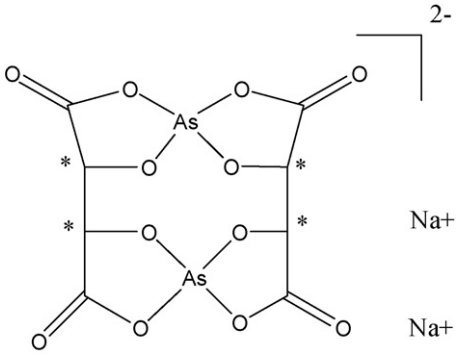

Fig. 1. Sodium arsenyl-(L)-(+) tartrate. Stereogenic centers are marked with an asterisk.

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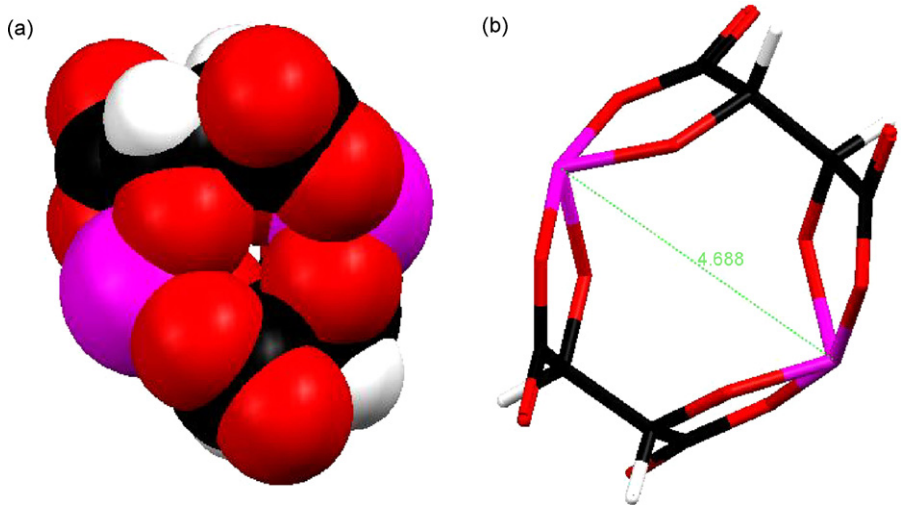


Fig. 2. Structure of sodium arsenyl-(L)-(+) tartrate. (a) Space-filling molecular model, (b) stick capped model. Color denotation: (red) oxygen; (pink) arsenic; (black) carbon; (white) hydrogen. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

the modeling study shows that the tartrate compound is highly hydrophilic with all oxygen atoms located on the outer surface of the molecule to form a rugby-ball-shaped complex with no readily accessible cavity (Fig. 2a). The mean distance between the arsenic atom and the oxygen (CO–) is typically about 1.8 Å, while the mean distance between the arsenic atom and the oxygen (COO–) is about 2.04 Å. The distance between the two arsenic atoms is about 4.6 Å (Fig. 2b). Also, only a trans-coordination geometry forming a pseudo-trigonal bipyramidal structure is possible for this molecule [18,19]. The arsenyl tartrate molecule is negatively charged and only stable at pHs 5 or above since this molecule slowly decomposes in an acidic environment [20]. A UV absorption spectrum of arsenyl tartrate in aqueous solution at pH 8.0 was obtained. (Fig. 3) It shows that no substantial UV absorption at wavelengths of 230 nm or above. To our knowledge, there has been no reported use of arsenyl tartrate as a chiral selector in capillary electrophoresis.

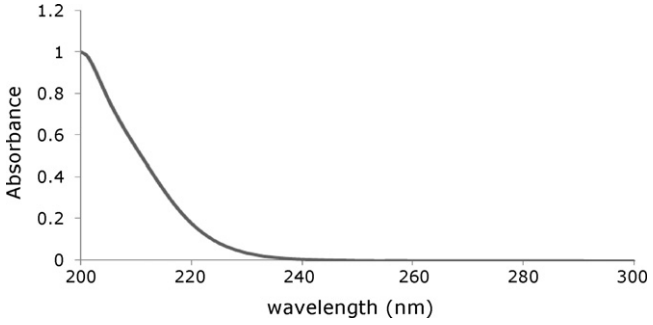


Fig. 3. UV spectrum of arsenyl tartrate at Tris buffer pH 8.0.

2. Materials and methods

2.1. Materials

Sodium arsenyl-(L)-(+) tartrate was synthesized as previously reported [21]. All ruthenium(II) polypyridyl complexes were synthesized as previously reported and their structures were confirmed by H NMR [22–26]. Phosphoric acid, sodium hydroxide, HPLC grade methanol, sodium phosphate and sodium carbonate were all purchased from Fisher Scientific (St. Louis, MO, USA). Tris(hydroxylmethyl)aminomethane was acquired from Aldrich (Milwaukee, WI, USA), The fused-silica capillaries were obtained from Polymicro Technologies (Phoenix, AZ, USA).

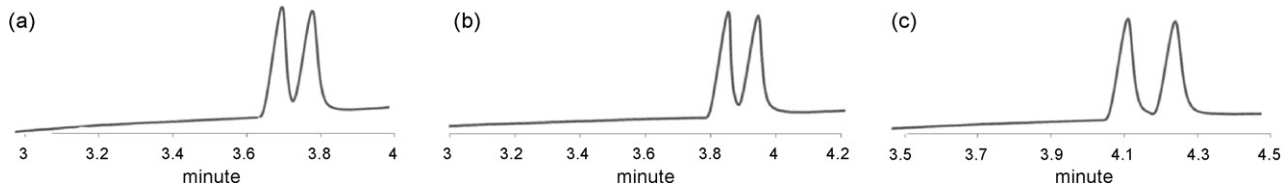


Fig. 4. The effect of different buffer types on enantioseparation of mianserin. Condition: arsenyl tartrate conc.: 30 mg/mL; 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +15 kV; detection at 214 nm; (a) 30 mM sodium phosphate buffer at pH 8.02; (b) 30 mM sodium carbonate buffer at pH 8.02; (c) 30 mM Tris buffer at pH 8.02.

Table 1
The effect of different buffer concentration on enantioseparation of pheniramine.

Tris buffer conc. (mM) at pH 8.02	Tm_1	Tm_2	W_1	W_2	R_s	N	α
5	12.53	12.95	0.32	0.3	1.4	24500	1.03
35	12.92	13.33	0.35	0.4	1.1	21800	1.03
55	13.09	13.42	0.35	0.35	0.9	22400	1.03
75	12.82	13.13	0.33	0.4	0.8	24100	1.02

Condition: arsenyl tartrate conc.: 40 mg/mL; 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +6 kV; detection at 214 nm; Tm_1 and Tm_2: migration time of peak 1 and peak 2 respectively; W_1 and W_2: peak width of peak 1 and peak 2 respectively; R_s: separation resolution; N: number of theoretical plates; α: selectivity.

Table 2
The effect of arsenyl tartrate concentration on enantioseparation of brompheniramine.

Arsenyl tartrate conc. (mg/mL)	T_1	T_2	W_1	W_2	R_s	N	α
10				(No separation)			
40	8.95	9.25	0.28	0.35	1.0	16300	1.034
70	13.50	14.30	0.47	0.50	1.6	13200	1.059
110	21.75	24.23	0.95	0.90	2.7	8400	1.114

Condition: buffer: 30 mM Tris at pH 8.02; 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +8 kV; detection at 214 nm; Tm_1 and Tm_2: migration time of peak 1 and peak 2 respectively; W_1 and W_2: peak width of peak 1 and peak 2 respectively; R_s: separation resolution; N: number of theoretical plates; α: selectivity.

Table 3
The effect of addition of methanol on enantioseparation of trimipramine.

Methanol % (v/v)	T_1	T_2	W_1	W_2	R_s	N	α
0	5.75	6.04	0.15	0.21	1.6	23500	1.05
10	7.15	7.55	0.2	0.2	2.0	20500	1.06
20	8.92	9.54	0.26	0.24	2.5	18800	1.07
30	10.72	11.74	0.32	0.3	3.3	18000	1.10
40	12.45	13.73	0.38	0.33	3.6	17200	1.10

Condition: buffer: 50 mM Tris at pH 8.02; 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +15 kV; detection at 214 nm; Tm_1 and Tm_2: migration time of peak 1 and peak 2 respectively; W_1 and W_2: peak width of peak 1 and peak 2 respectively; R_s: separation resolution; N: number of theoretical plates; α: selectivity.

2.2. Methods

All separations were performed on a Beckman Coulter P/ACE MDQ system capillary electrophoresis equipped with a photodiode array detector. The capillary used for all separations was 50 μm I.D. × 358 O.D. with a total length of 30 cm (20 cm from inlet to detection window). The capillary was maintained at a temperature of 25 °C. Tris(hydroxylmethyl)aminomethane was dissolved in denionized water and adjusted to desired pH with hydrochloric acid or sodium hydroxide as the background buffer. An organic modifier was added, based on volume percentage, prior to the addition of chiral selectors. Chiral selectors were then added into the buffer solution as running buffer. Racemic samples or artificial mixtures of enantiomers were dissolved in the background buffer to make sample solutions. All the electropherograms were obtained with detection at 214 nm in a normal polarity mode. All data were analyzed with Beckman System Gold Software.

New capillaries were initially conditioned with the following rinses: 1N sodium hydroxide and deionized water each for 5 min. Before each run, the capillaries were washed with 1 N sodium hydroxide, deionized water and running buffer each for 1 min. The sample solution was then injected hydrodynamically at 0.5 psi for 5 s.

2.3. Synthesis of sodium arsenyl-(L)-(+) tartrate

The procedure for the synthesis of arsenyl tartrate was previously reported [21]. In brief, L(+)-tartaric acid (20 g, 0.133 mol) and NaOH (5.33 g, 0.133 mol) were dissolved in water (150 mL), and the solution was heated to reflux. As_2O_3 (13.1 g, 0.066 mol) was added and the resulting slurry refluxed for 45 min until the solution became clear. The solution then was filtered and 300 mL ethanol was added to the filtrate, which resulted in some precipitation. The resulting mixture was then cooled to 4 °C for 12 h, upon which a large mass of white crystals formed. The crystals were isolated by filtration and washed with cold ethanol and air-dried. The product was identical to those reported by Marcovich and Tapscott in all respects [27].

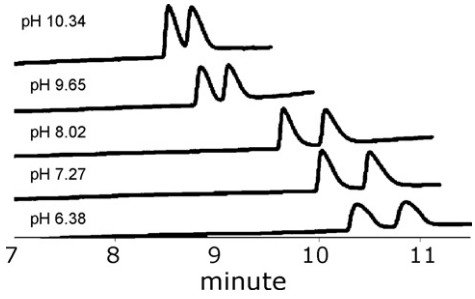


Fig. 5. The effect of buffer pHs on enantioseparation of mianserin. Condition: arsenyl tartrate conc.: 30 mg/mL; 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +8 kV; buffer: 50 mM Tris; detection at 214 nm.

3. Results and discussion

3.1. Factors affecting enantioseparation

Buffer type, buffer pHs and concentrations, chiral selector concentration addition of organic modifiers, variations of applied voltages are common factors that are varied to optimize the enantiomeric separations in capillary electrophoresis [28–32].

The buffer controls the ionic strength of the solution, stabilizes the current, controls pH, maintains the EOF and also modifies the interaction between chiral selectors and analytes [28,33]. Three different types of buffers were studied using racemic mianserin

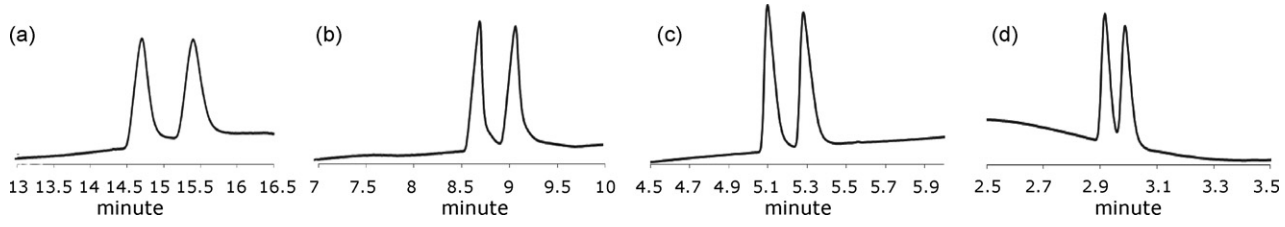


Fig. 6. The effect of applied voltages on enantioseparation of tetrahydrozoline. Condition: arsenyl tartrate conc.: 50 mg/mL; 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; buffer: 50 mM Tris at pH 8.02; detection at 214 nm; (a) +5 kV; (b) +8 kV; (c) +12 kV; (d) +17 kV.

as a test analyte and the electropherograms are shown in Fig. 4. Tris(hydroxylmethyl)aminomethane buffer, overall, provides the best enantiomeric separation with baseline resolution in a reasonable time. Therefore it was used for the rest of this study. High buffer concentrations might inhibit the electrostatic interactions that contribute to the association between the analytes and the chiral selectors. Table 1 summarizes the effect of different concentrations of Tris buffer. The results show that high buffer concentrations hurt the enantioresolution and produce longer migration times. This finding indicates the importance of electrostatic interactions for enantioseparation with arsenyl tartrate. Fig. 5 shows the electropherograms of the enantiomeric separations of mianserin at

Table 4
Experimental data for enantiomeric separations of amine-containing compounds using sodium arsenyl-(L)-(+) tartrate.

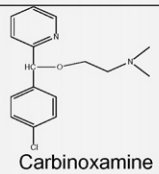
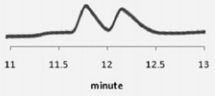
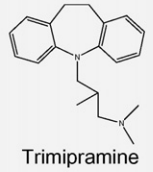
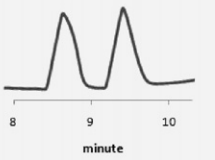
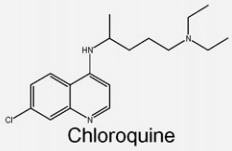
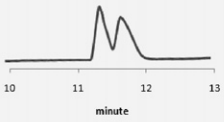
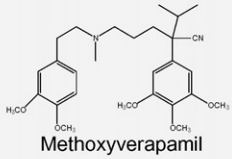
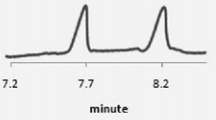
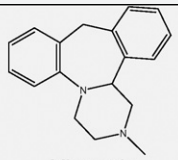
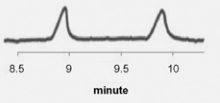
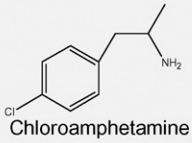
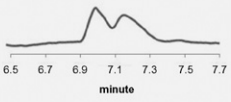
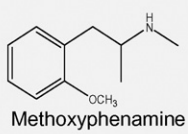
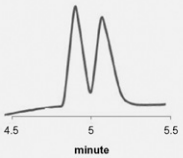
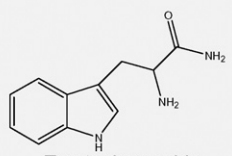
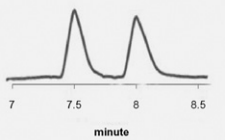
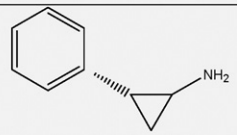
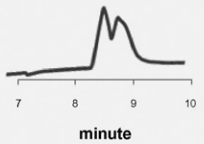
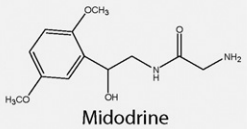
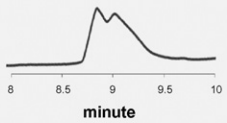
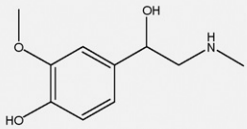
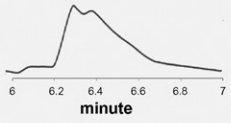
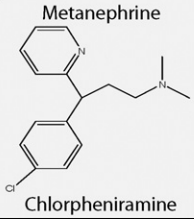
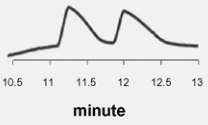
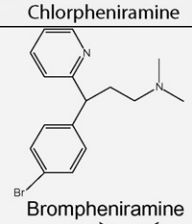
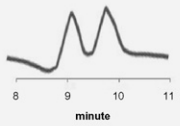
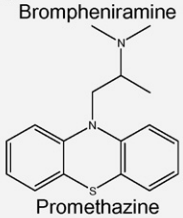
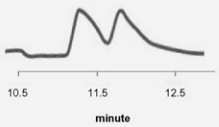
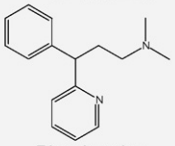
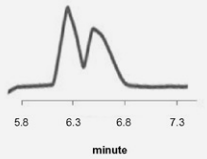
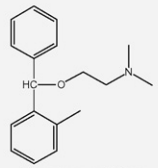
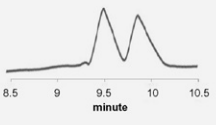
#	Structure and name of analyte	Arsensyl tartrate concentration (mg/mL)	Tm_1 (min)	Tm_2 (min)	R_s	N	α	Electropherogram
1	 Carbinoxamine	100	11.82	12.28	1.5	24800	1.04	
2	 Trimipramine	60	8.73	9.54	2.0	7600	1.10	
3	 Chloroquine	100	11.33	11.64	0.8	12800	1.03	
4	 Methoxyverapamil	60	7.64	8.23	4.0	41500	1.08	
5	 Mianserin	60	8.94	9.92	4.8	20500	1.11	
6	 Chloroamphetamine	120	6.97	7.16	0.6	12000	1.03	
7	 Methoxyphenamine	60	4.92	5.17	1.1	6200	1.05	
8	 Tryptophanamide	60	7.48	8.03	1.8	22400	1.07	

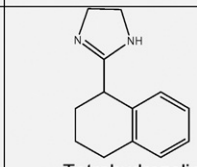
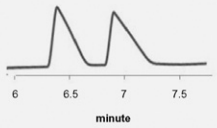
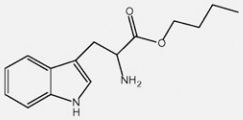
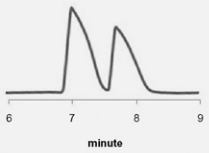
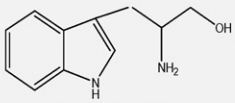
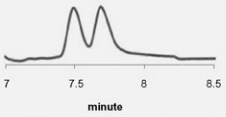
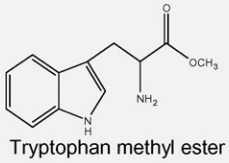
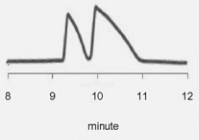
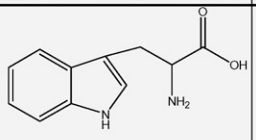
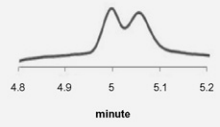
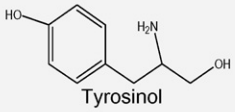
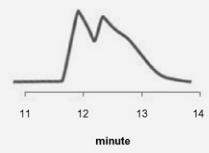
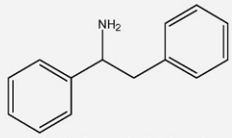
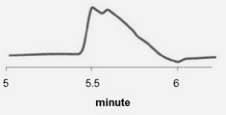
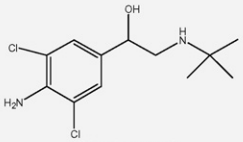
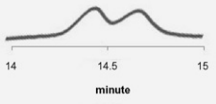
Table 4 (*Continued*)

#	Structure and name of analyte	Arsensyl tartrate concentration (mg/mL)	Tm_1 (min)	Tm_2 (min)	R_s	N	α	Electropherogram
9	 Tranylcypromine	100	8.62	8.84	0.5	13000	1.03	
10	 Midodrine	100	8.87	9.18	0.3	8300	1.03	
11	 Metanephrine	60	6.33	6.43	0.3	6400	1.02	
12	 Chlorpheniramine	50	11.38	12.23	1.6	13000	1.07	
13	 Brompheniramine	100	9.08	9.89	1.6	13000	1.09	
14	 Promethazine	100	11.32	11.84	1.0	12000	1.05	
15	 Pheniramine	100	6.23	6.62	0.9	6900	1.06	
16	 Orphenadrine	100	9.44	9.95	1.5	15000	1.04	

different pHs. Baseline separations were obtained at pHs 8.02 or below due to the fact that the lower the pHs slow the EOFs, which in turn improves selectivity and enhance enantioresolution.

Varying chiral selector concentrations have been reported to be an effective way to improve enantioresolution [34,35]. The separation of brompheniramine at four different arsenyl tartrate concentrations (while the other conditions were kept the same) is summarized in Table 2. Baseline separation was obtained at 70 mg/mL of arsenyl tartrate concentration. The enantioresolutions were improved and the migration times increased with an increase in arsenyl tartrate concentration. This is due to the fact that when the chiral selector is increased, the interaction between the analyte

Table 4 (*Continued*)

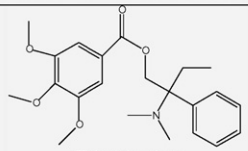
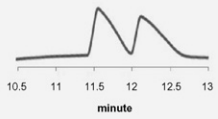
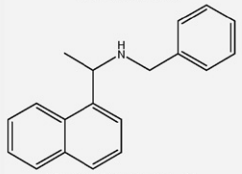
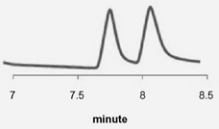
#	Structure and name of analyte	Arsensyl tartrate concentration (mg/mL)	Tm_1 (min)	Tm_2 (min)	R_s	N	α	Electropherogram
17	 Tetrahydrozoline	100	6.36	6.92	1.7	16200	1.09	
18	 Tryptophan butyl ester	60	7.05	7.76	1.6	3800	1.10	
19	 Tryptophanol	60	7.48	7.75	1.0	23300	1.04	
20	 Tryptophan methyl ester	60	9.47	10.08	1.5	9200	1.06	
21	 Tryptophan	60	4.97	5.08	0.7	34000	1.02	
22	 Tyrosinol	100	11.96	12.48	0.6	8500	1.04	
23	 1,2-diphenylethylamine	60	5.52	5.63	0.3	6500	1.02	
24	 Clenbuterol	100	14.47	14.74	1.0	22000	1.02	

and the chiral selectors was increased, thus improving enantioresolution. Furthermore, increasing the chiral selector concentration also increase the ionic strength and the viscosity of the run buffer which in turn contributes to longer migration times.

Addition of organic modifiers to the running buffer not only can increase the solubility of hydrophobic analytes but also slow the EOF and suppress the joule heating by lowering the current [31,36]. These factors can improve enantiomeric separation. Upon the addition of methanol, the EOF decreased causing the resolution to increase with longer migration times (see Table 3). In this study, 10% (v/v) of methanol was added into the run buffer in order to increase the solubility of the analytes.

The effect of applied voltage also was studied using racemic tetrahydrozoline as an example. Fig. 6 shows the electropherograms of the enantioseparations with varying applied voltages. As

Table 4 (*Continued*)

#	Structure and name of analyte	Arsensyl tartrate concentration (mg/mL)	Tm_1 (min)	Tm_2 (min)	R_s	N	α	Electropherogram
25	 Trimebutine	50	11.54	12.26	1.5	9000	1.06	
26	 (*S*)-*N*-Benzyl-1-(1-naphthyl)ethylamine	60	7.76	8.18	1.8	24100	1.05	

(a) Conditions: 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +10–15 kV; buffer: 5 mM Tris at pH 8.02 with 10% of methanol (v/v); detection at 214 nm.
(b) R_s: separation resolution.
(c) N: number of theoretical plates calculated from the first detected peak.
(d) α: selectivity.

Table 5
Experimental data for enantiomeric separations of ruthenium(II) polypyridyl complexes using sodium arsenyl-(L)-(+) tartrate.

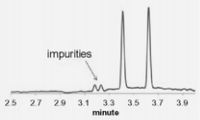
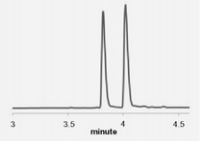
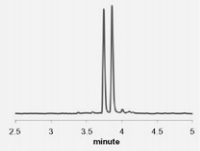
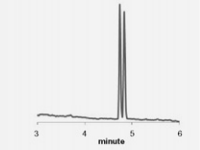
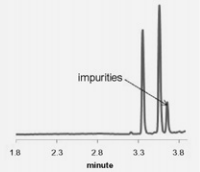
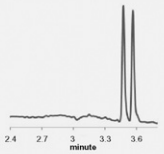
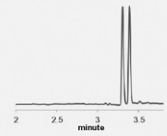
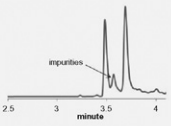
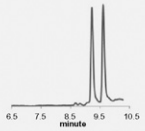
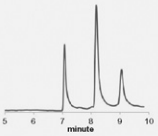
Name of structure	Arsenyl tartrate conc. (mg/mL)	Tm_1 (min)	Tm_2 (min)	R_s	N	α	Electropherogram
$[Ru(phen)_3](Cl)_2$	30	3.41	3.62	5.0	101000	1.06	
$[Ru(phen)_2nitrophen](Cl)_2$	30	3.82	4.02	3.3	69400	1.05	
$[Ru(phen)_2phendione](Cl)_2$	30	3.74	3.86	2.4	97100	1.03	
$[Ru(bpy)_3](Cl)_2$	60	4.74	4.83	1.4	90500	1.02	
$[Ru(phen)_2aminophen](Cl)_2$	30	3.35	3.55	4.5	88600	1.06	

Table 5 (*Continued*)

Name of structure	Arsenyl tartrate conc. (mg/mL)	Tm_1 (min)	Tm_2 (min)	R_s	N	α	Electropherogram
$[Ru(phen)_2tatpp](PF_6)_2$	30	3.47	3.56	2.0	95300	1.03	
$[Ru(phen)_2py_2](Cl)_2$	30	3.30	3.39	2.0	99000	1.03	
$[Ru(phen)_2phendiamine](PF_6)_2$	30	3.48	3.69	3.1	50400	1.06	
$[Ru(nitrophen)_2phendione](Cl)_2$	50	9.22	9.60	2.6	64600	1.04	
$[Ru_2(phen)_4tatpp](Cl)_4$[e]	60	7.07	8.18	6.7	38000	1.16	
		8.18	9.06	4.3	25200	1.11	

(a) Conditions: 30 cm capillary (20 cm to the detector) with 50 μm I.D. capillary; +6 kV; buffer : 5 mM Tris at pH 8.02 with 10% of methanol (v/v); detection at 214 nm.
(b) R_s: separation resolution.
(c) N: number of theoretical plates calculated from the first detected peak.
(d) α: selectivity.
(e) Top row for peak 1 and peak 2; bottom row for peak 2 and peak 3.

the voltage increased, the migration times and resolutions both decreased. Increases the applied voltages greatly increase the Joule heating in the capillary, which in turn causes faster EOF, hurting the enantioseparations.

3.2. Overview of enantioseparation results

Twenty-six amine-containing compounds showed enantioselectivity within reasonable time. 13 of them were baseline separated. All results are summarized in Table 4

. In this study, all separations were run at pH 8.02 where the arsenyl tartrate (the chiral selector) as negatively charged and where all amine-containing analytes were positively charged. This is based on the fact that charged chiral selectors often produce the best resolving power with analytes of the opposite charge due to strong electrostatic interactions between analyte–selector complexes, as well as their countercurrent migrations, thus enhancing the selectivity factor [37,38]. Compared to separations that use anionic cyclodextrin chiral selectors, the migration times were similar, while the charged cyclodextrins, overall, showed better enantioseparations for this specific group of analytes [39,40]. Also, the concentration of arsenyl tartrate required is higher than that of separations that use charged cyclodextrins. The possible reason is that enantioselective recognition mechanism of these two chiral selectors is different. Charged cyclodextrins involve electrostatic interactions between charged chiral selectors and oppositely charged analytes and inclusion or exclusion complexation [41]. However, electrostatic forces represent the only attractive interactions for arsenyl tartrate chiral selectors. Most of the separations were accomplished in 10 min. With a careful examination of data, we see that compound resolution increased as the size of the ester group increase. For example, compound #18 (Tryptophan butyl ester) was better separated than compound #20 (Tryptophan methyl ester). Another interesting phenomenon is that compounds with more benzyl or more fused rings gave better separations (i.e. compounds #2, #5, #8, #17 and #26).

Besides the amine-containing compounds, ten ruthenium(II) polypyridyl complexes were baseline separated within 10 min. All results are summarized in Table 5. Ruthenium(II) polypyridyl complexes have been reported to be useful in several applications such as catalysts for asymmetric synthesis, as DNA recognition probes or cleavage agents for DNA by generation of reactive oxygen species under a hypoxic environment [42–44]. The right- and left-handed configurations of these metal complexes are referred to as Δ and Λ enantiomers, respectively [17,43,44]. Several analytical techniques including chromatographic methods and diastereomeric formation using ion-pairing agent have been utilized to separate these metal complexes racemates [17,45,46]. Sodium L-(+)-arsenyl tartrate has

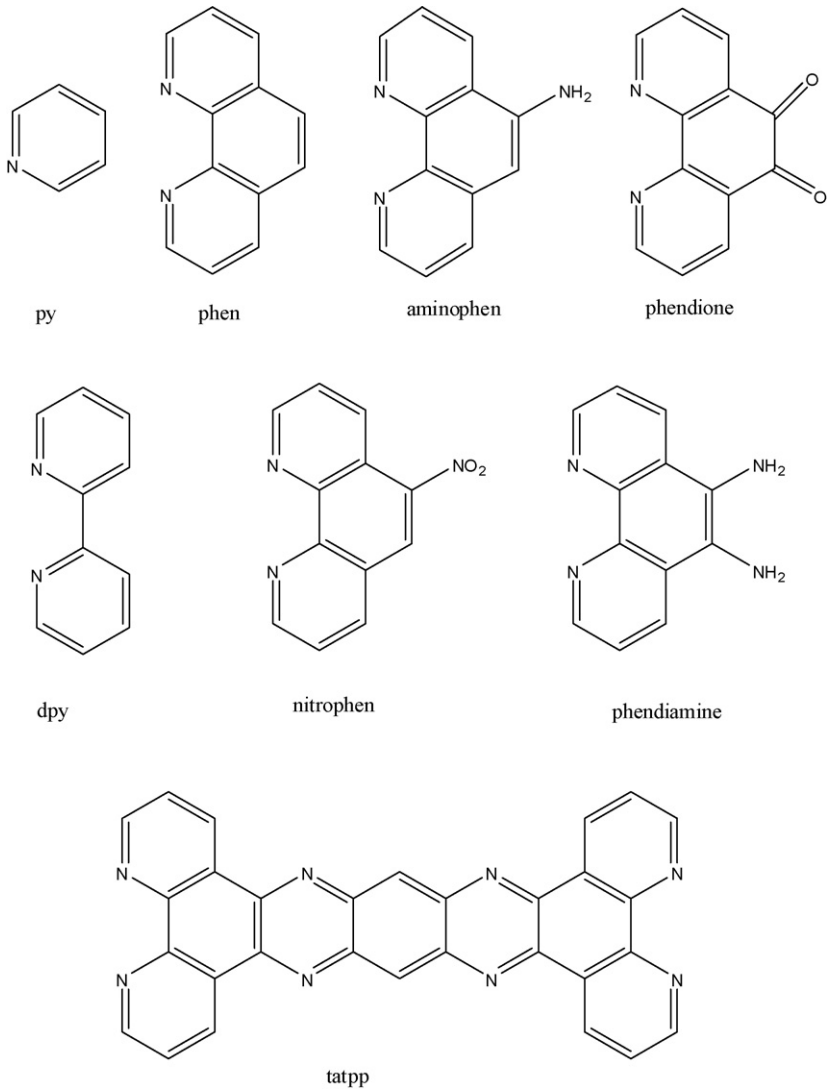


Fig. 7. Structures of polypyridyl ligands of ruthenium complexes. Py: pyridine; dpy: 2,2′-dipyridine; phen: 1,10-phenanthroline; nitrophen: 5-nitro-1,10-phenanthroline; Aminophen: 5-amino-1,10-phenanthroline; phendione: 1,10-phenanthroline-5,6-dione; phendiamine: 5,6-diamino-1,10-phenanthroline; tatpp: 9,10,20,22[3,2-a:2′3′-c:3″,2″-h,2‴,3‴-j]tetrapyrido-pentacene.

been previously reported for diastereoselective precipitations of ruthenium complexes by our group [17]. In this study, 10 ruthenium(II) polypyridyl complexes (nine monomers and one dimer) were all baseline separated within 10 min. The structures of these complexes are shown in Fig. 7. Compared to neutral or charged cyclodextrins, the arsenyl tartrate provided shorter analysis times, better efficiency and better resolutions, especially for the separation of dimer ($[Ru_2(phen)_4tatpp](Cl)_4$) [31].

In this study, the selectivity (α) is only estimated by dividing of the two migration times of the two enantiomeric peaks, i.e. Tm_2/Tm_1. Several EOF markers such as acetone, DMSO, benzyl alcohol and mesityl oxide were used in this study. However, none of them were detectable in any of the electropherograms.

3.3. Concluding remarks

Sodium arsenyl-(L)-(+) tartrate showed enantioselectivity towards amine-containing compounds. Most separations were achieved in 10 min. Electrostatic interactions play an important role in the enantioseparations. Compounds with more benzyl or fused rings showed better separations. Compared to charged cyclodextrins, arsenyl tartrate showed shorter analysis times for amine-containing compounds. Resolutions were improved and migration times were increased with increasing arsenyl tartrate concentrations. Lower buffer pH increased the enantioresolution by slowing the EOF. Increasing pH buffer concentration increased migration times and decreased resolutions. Addition of methanol in run buffer increased migration times as well as solubility of hydrophobic analytes. Ruthenium(II) polypyridyl complexes also showed enantioselectivity. Shorter analysis times and better resolutions were achieved using arsenyl tartrate than using neutral or charged cyclodextrins.

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