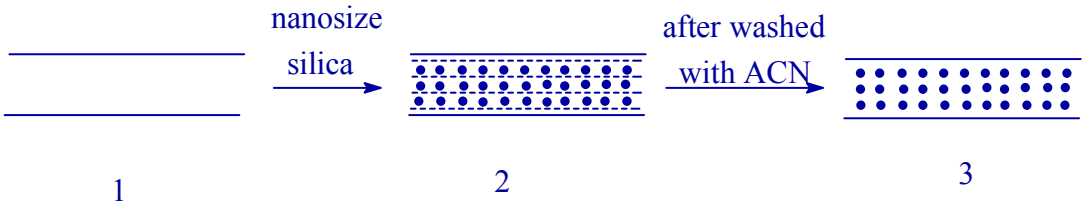
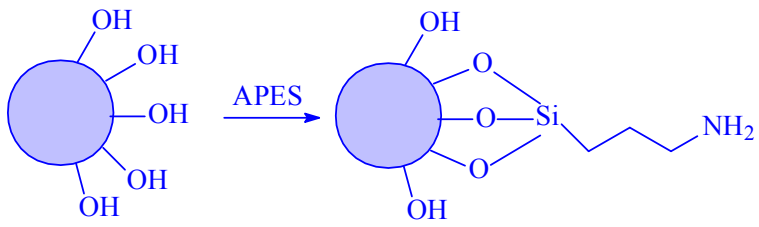
Electronic supplementary materials *Mendeleev Commun.*, 2016, **26**, 166–168

Chiral separation and quantitative analysis of citalopram by modified capillary electrophoresis

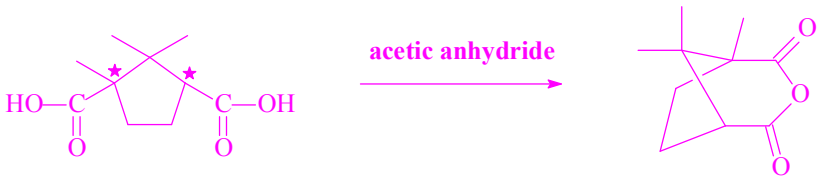
Yanjie Dong, Qianqian Li, Junwei Wang, Lu Lu, Yufang Wang, Linghong Bao, Zhongling Wang and Yuanguang Zhang



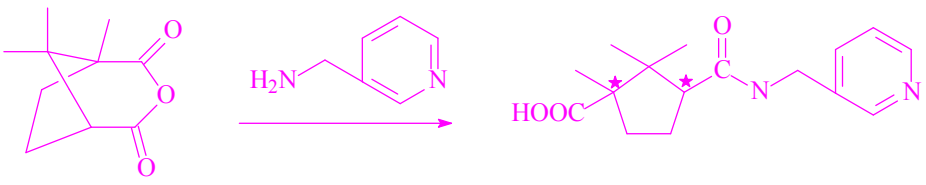
1 2 3



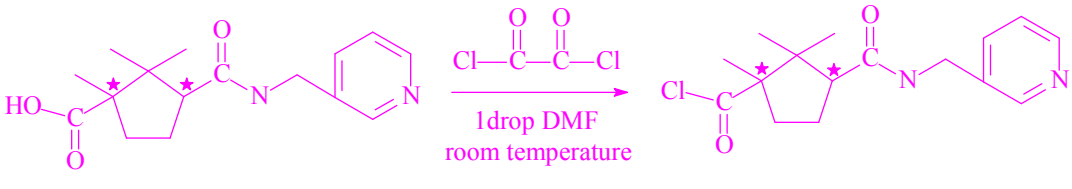
4 **5**



6 **7**



8 **9**



10 **11**

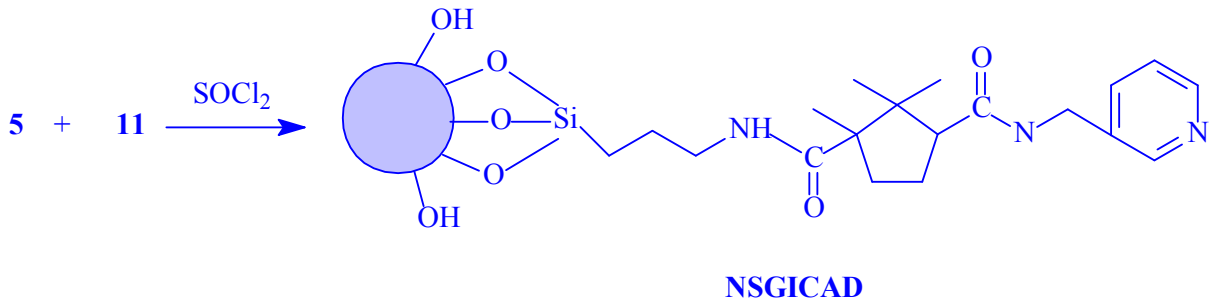


Figure S1 Schematic of preparation procedures of derivatized silica capillary.
1 Open-tubular capillary; 2 capillary loaded nanosize silica and methanol; 3 washed nanosize silica in capillary; 4 silanols of nanosize silica surface; 5 silanization of nanosize silica; 6 (1*R*,3*S*)-camphoric acid; 7,8 (1*R*,3*S*)-camphoric anhydride; 9,10 (1*R*,3*S*)-camphoric acid-derivative; 11 acylchloriration of (1*R*,3*S*)-camphoric acid-derivative; 12 NSGICAD-nanosize silica-immobilized (1*R*,3*S*)-camphoric acid derivative.

The commercial analytical grade materials were used as purchased. The nanosize silica (60-100 nm), hydrazine hydrate (85%), DMF, dichloromethane, 3-aminomethylpyridine, oxalyl chloride, acetic anhydride, hydrochloric acid and acetic acid were purchased from Shanghai Chemical Reagent Co. HPLC-grade methanol was purchased from Shanghai Chemical Plant. Citalopram and (3-aminopropyl)triethoxysilane (APES) were obtained from Acros Organics, while 0.10 M hexamine-HCl pH 5.40; 0.10 M 3-cyclohexylaminopropane-1-sulfonic acid (CAPS) pH 8.70 (Sigma, USA); 0.10 M phosphate pH 9.10 were obtained from Shanghai Chemical Plant, Deionized water was obtained using a Waters Milli-Q water-purification system (Millipore, Germany).

The (1*R*,3*S*)-camphoric acid-derived reagent was prepared as follows. The mixture of (1*R*,3S)-camphoric acid (5.0 g) and acetic anhydride (3.0 ml) was refluxed for 2 h and then cooled to 0 ^{o}C. A white solid was isolated by filtration. The crude (1*R*,3*S*)-camphoric anhydride was recrystallized from ethanol and dried *in vacuo*, yield 86%, mp 221-222 ^{o}C. (1*R*,3*S*)-Camphoric anhydride (2.73 g, 0.015 mol) was dissolved in 25.0 ml of dry dichloromethane and this was dropped to the solution of

3-aminomethylpyridine (1.62 g, 0.015 mol) in 20.0 ml of dry dichloromethane. The mixture was refluxed for 8 h, then cooled. The white solid was isolated by vacuum filtration. The pure 1,2,2-trimethyl-3-[*N*-(3pyridylmethyl)lcarbamoyl]-cyclopentanecarboxylic acid was obtained after rinsing with deionized water and dried *in vacuo*, yield 76%, mp 212-215 ^{o}C. A mixture of 1.0 g of this acid and 3.0 ml of oxalyl chloride in the presence of one drop of DMF was refluxed for 2 h and then cooled to 0 ^{o}C. A white solid was isolated by filtration. The pure 1,2,2-trimethyl-3-[*N*-(3-pyridylmethyl)carbamoyl]cyclopentanecarbonyl chloride was obtained after rinsing with water and drying *in vacuo*. To prepare the target NSGICAD, the latter compound (0.32 mmol, 0.10 g) in methanol (16.0 ml) was heated at 90 °C in the presence of one drop of glacial acetic acid (~0.02 ml). The obtained solution was injected into the capillary and kept at 60 ^{o}C overnight after both ends are sealed with rubber. Finally, the capillary was rinsed with methanol and deionized water successively to flush out the residual reagents and dried again.

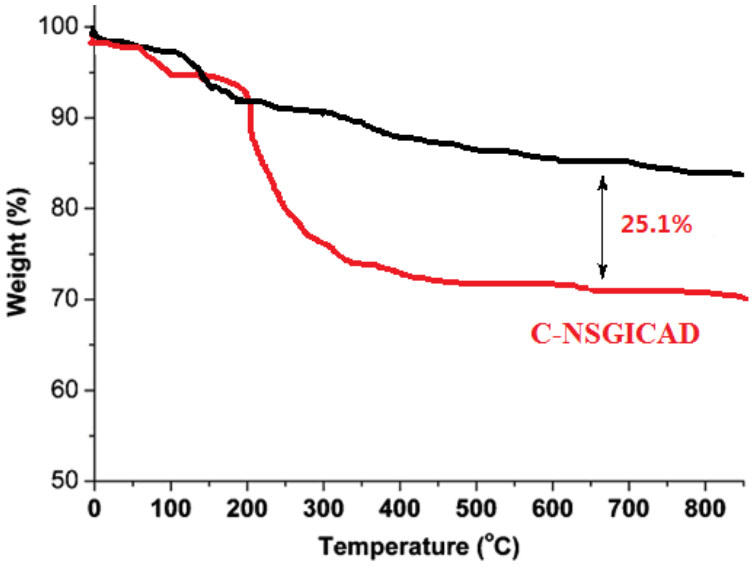


Figure S2 Thermogravimetric analysis of free SiO_2, NSGIR(red).

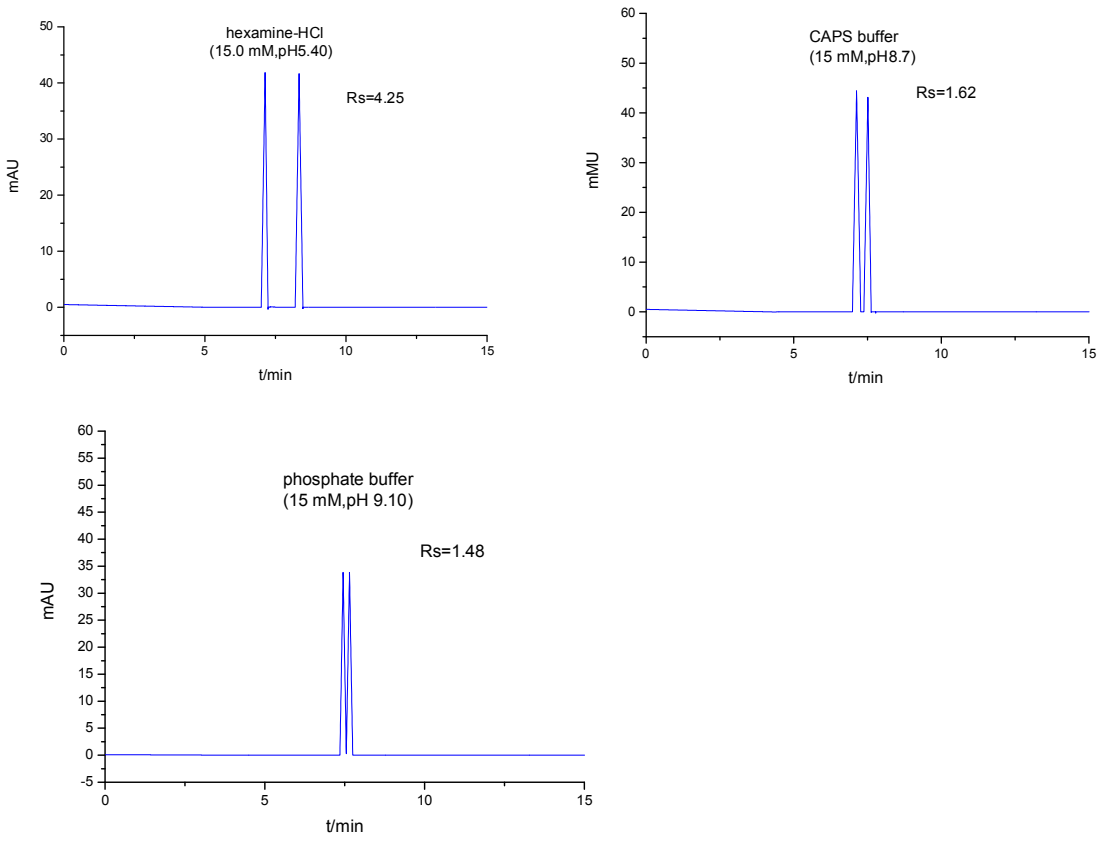


Figure S3 Electrophoretic manifestation of CE in different media.
Separation conditions: separation voltage 30 kV, separation temperature 25 ^{o}C, sample injection pressure 3.43×10^{3} Pa, duration 10 s, citalopram 0.10 mmol L^{-1}.

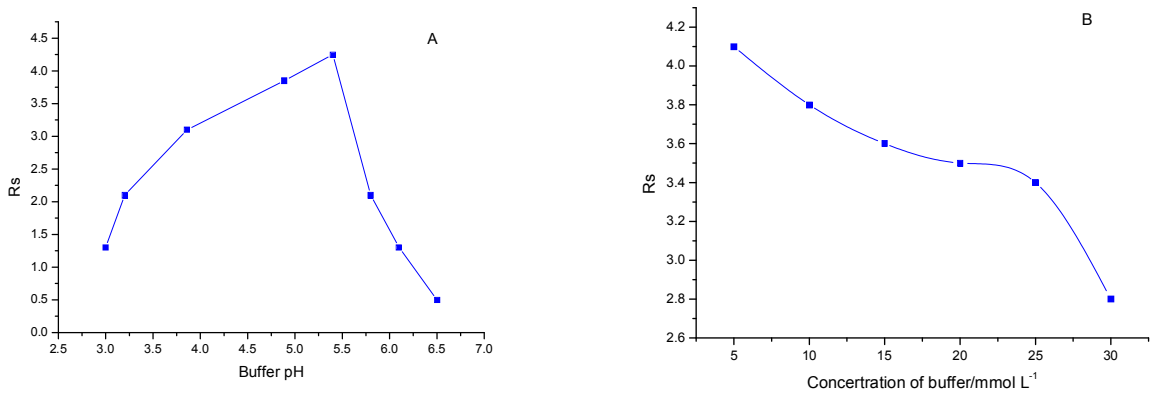


Figure S4 The resolution of citalopram at different hexamine-HCl buffer pH value (A) and concentration (B). Separation conditions: separation voltage 30 kV, separation temperature 25 ^{o}C, sample injection pressure 3.43×10^{3} Pa, duration 10 s, citalopram 0.10 mmol L^{-1}, detection wavelength 240.0 nm.

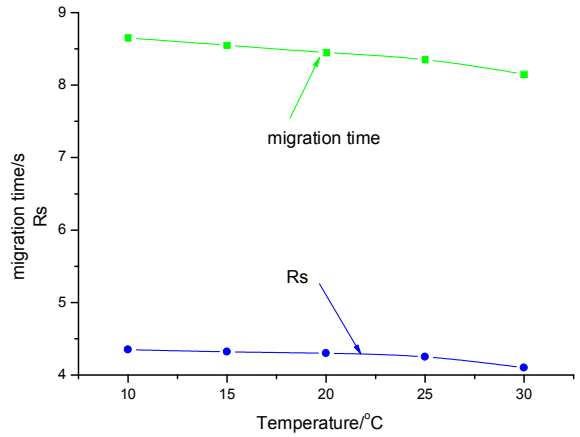


Figure S5 The effect of temperature on migration time and resolution. Separation conditions: separation voltage 30 kV, sample injection pressure 3.43×10^{3} Pa, duration10 s, citalopram 0.10 mmol L^{-1}, detection wavelength 240.0 nm, pH 5.40.

Table S1 Precision of the citalopram analysis by CE.

	Reproducibility in one day	Reproducibility in five day
AMT/min	12.18,12.62	12.17,12.64
S	0.034,0.035	0.033,0.035
RSD/%	0.28,0.28	0.27,0.28
Concentration/mmol L^{-1}	3.52×10^{-2}	3.51×10^{-2}

AMT is the average migration time; S is the standard deviation of migration time; and RSD is the relative standard deviation of migration time.

The same sample was divided into three parts, among which two parts were added an amount of citalopram standard solution respectively. All of the three samples were measured and the results are given in Table S2. The recovery ratio of samples was 99.5-101.0%.

Table S2 Determination results of citalopram (n = 5).

No.	Added concentration	Found concentration	Recovery ratio	RSD
	mmol L^{-1}	mmol L^{-1}	%	%
1	0	3.500×10^{-2}	-	0.36
2	1.000×10^{-2}	4.510×10^{-2}	101.0	0.35
3	2.000×10^{-2}	5.495×10^{-2}	99.75	0.36