

Supporting information

Stable Benzyl Cation is the Key Intermediate for the Chiral Inversion of Denopamine by Heat

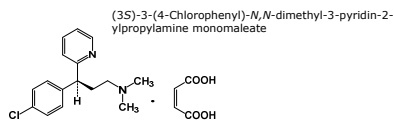
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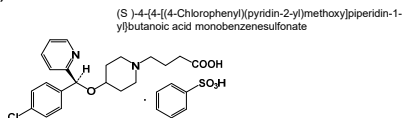
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(a) d-CPM $C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ 390.86



(b) BB $C_{21}H_{25}ClN_2O_3 \cdot C_6H_6O_3S$ 547.06



(c) LCTZ $C_{21}H_{25}ClN_2O_3 \cdot 2HCl$ 461.81

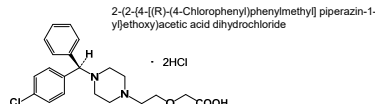


Fig. S1. Chemical structures and chemical names of three antihistamines. (a) *d*-chlorpheniramine maleate (*d*-CPM), (b) bepotastine besilate (BB) and (c) levocetirizine dihydrochloride (LCTZ).

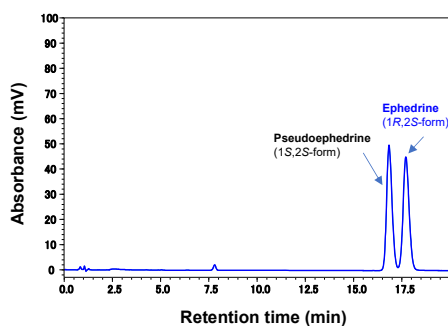


Fig. S2. Separation of a mixed solution of ephedrine and pseudoephedrine by a CS type ODS column with C_8SO_3Na as an ion-pairing reagent. Column; Shim-pack Velox C18 (2.7 μm , 4.6 mm i.d. \times 100 mm), mobile phase; a mixture of water and ACN (80:20, v/v) containing 0.1 % (v/v) phosphoric acid and 0.5 % (w/v) C_8SO_3Na , column temp.; 40 $^{\circ}C$, flow rate; 1.0 mL/min, detection; 215 nm.

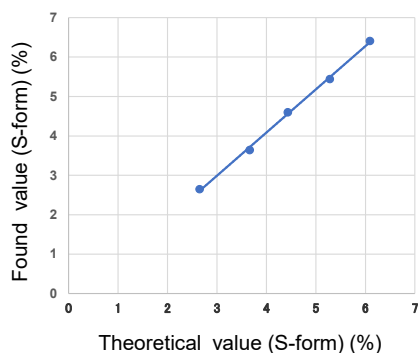
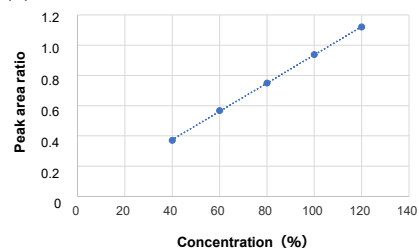


Fig. S3. Linearity of the minor S-form enantiomer in phenylephrine injections (from 1.0 % to 5.0 %).

(a) S-form



(b) R-form

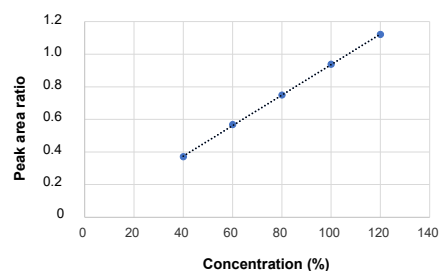


Fig. S4. Linearity of (a) S-form of phenylephrine and (b) R-form of phenylephrine near the concentration (from 40 % to 120 %) of the sample solution (0.01%, w/v).

Table S1. Recovery, linearity, limit of detection and limit of quantitation of the minor S-form enantiomer in phenylephrine injections (from 1.0 % to 5.0 %)

Recovery	Added S-form	Recovery(%)
1	1.0 %	100.0
2	2.0 %	99.5
3	3.0 %	103.8
4	4.0 %	103.0
5	5.0 %	103.6
Correlation Coef.	0.9994	
Limit of detection	0.32 %	
Limit of quantitation	0.98 %	