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Supporting information

Sensing of Enantiomeric Excess in Chiral Carboxylic Acids

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Contents

General

All the synthesis was performed using standard laboratory techniques. All starting materials were purchased and used as received. Compounds **S1-S4** was prepared according to the literature procedures.[1] ^{1}H- and ^{13}C-NMR (APT) spectra were recorded using a Bruker® Avance II™ 500 MHz UltraShield™ (Bruker Corporation, Mass., USA) Spectrometer at 25 °C.
Solutions for optical measurements were prepared using freshly distilled propionitrile. Optically dilute solutions (0.1 A) were used for all photophysical experiments. Fluorescence emission spectra were acquired using an Edinburgh single photon counting spectrofluorometer (FLSP 920). Fluorescence emission spectra were recorded between 380 nm and 500 nm. The band passes of both excitation and emission monochromators were set to 1.0 nm. The emission from probes was scanned in 2 nm steps. The dwell time was adjusted to 0.30 sec. Scans were taken under ambient room conditions. Guest titrations were performed in propionitrile. Titration isotherms were constructed from changes in the fluorescence maximum at 424 nm. Data analysis and curve fitting was performed according to previously published methods.[2] Absorption spectra were recorded using a Hitachi U-3010 spectrophotometer. Fluorescence titrations were performed at room temperature using a quartz cuvette with a path length of 1 cm at right angle detection and titrations were carried out in propionitrile solutions of sensors by adding propionitrile solutions of carboxylates as tetrabutylammonium salts. EI DIP mass spectra were recorded using a Shimadzu QP5050A. The absolute quantum yields were measured using a Hamamatsu Quantaurus absolute quantum yield spectrometer QY-C11347.

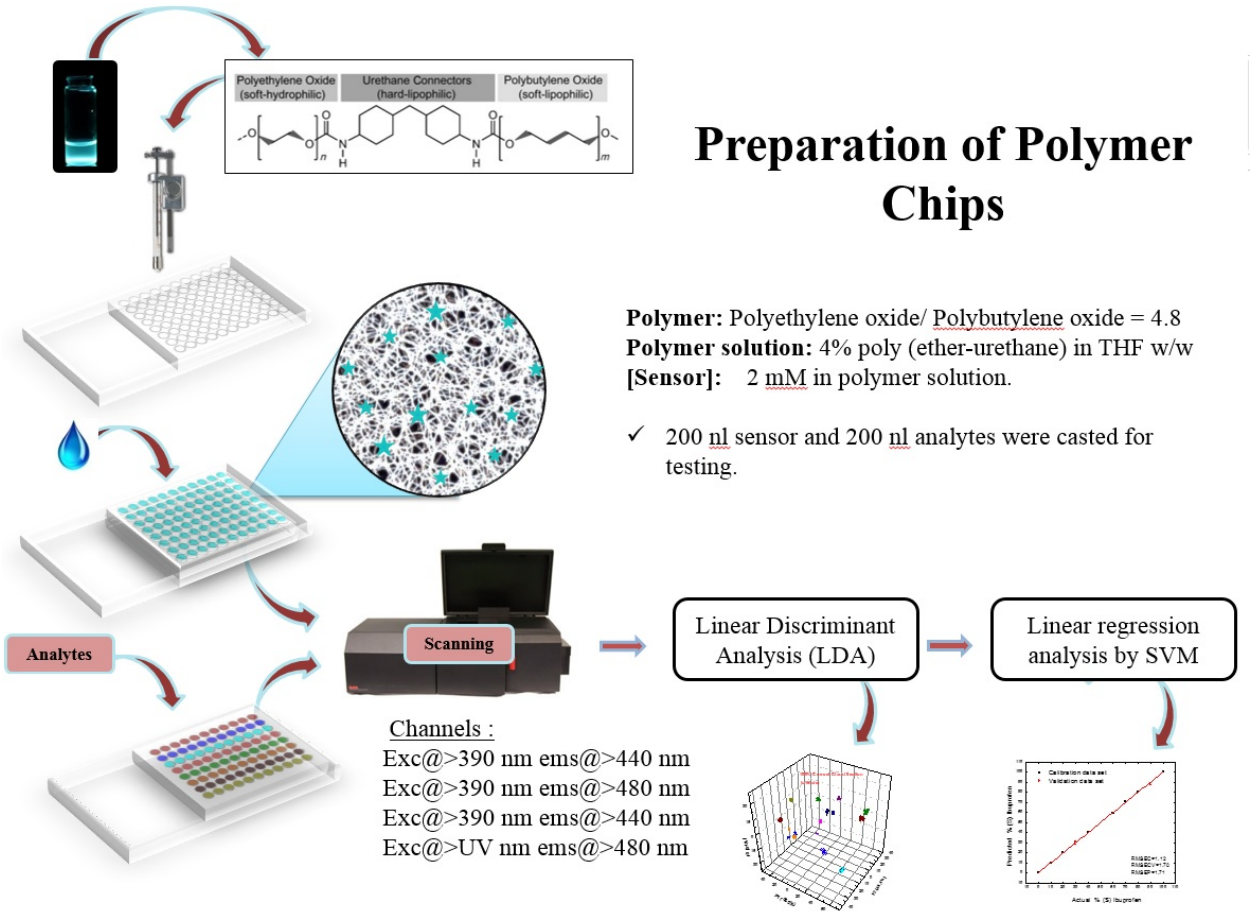


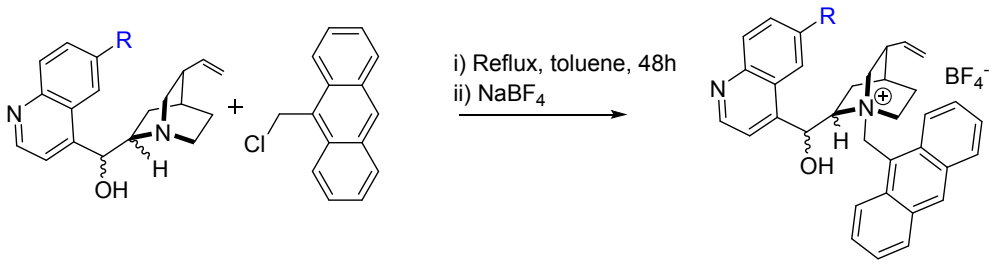
Figure 1. Procedure of preparation of polymer chips

The multi-well 10 x 21 (submicroliter) glass slides were fabricated by ultrasonic drilling of microscope slides (well diameter: 1000 ± 10 µm, depth: 250 ± 10 µm). Sensor solutions (2.0 mM) in polymer solution (4% poly(ether-urethane) in THF w/w) were prepared. In a typical array, 200 nL of sensor-polymer solutions were pipetted into each well of the multi-well glass slides and dried. Then, water (400 nL) was pipetted into each well and dried to form hydrated gel matrix. Finally, analytes (200 nL, 5 mM, 1 nmol) were added as aqueous solutions into each well and the chip was dried at room temperature for 1 hr.[3] Images from the sensor array were recorded using a Kodak Image Station 440CF (for preliminary experiments) and a Kodak Image Station 4000MM PRO (for qualitative and quantitative experiments). After acquiring the images, the integrated (nonzero) gray pixel value (n) is calculated for each well in each channel. Images of the sensor chip were recorded before (b) and after (a) the addition of an analyte. The final responses (R) were evaluated as indicated in the following equation:

$$R = \sum_{n} \frac{a_n}{b_n} - 1$$

Thus obtained data for qualitative analysis were then analyzed using Linear Discriminant Analysis (LDA). Support Vector Machine (SVM) was used for quantitative assays.

General Procedure of Synthesis



The sensors S1-S4 were prepared previously.[4] We have adopted the conditions published previously.[1] The cinchona alkaloid (1.6 mmols) and 9-(chloromethyl)anthracene (0.30 gram, 1.32 mmol) were dissolved in toluene (20 ml) in a 100 ml flask. The reaction mixture was refluxed for 48 hours. After cooling down to room temperature, diethyl ether (50 ml) was added. The resulting slurry was stirred at room temperature for 3 hours. The solid was collected by filtration. After chromatography (Silica/$CHCl_3$-MeOH-Et_3N 9:0.9:0.1 v/v), pure products were obtained as pale yellow solids. Counter anion exchange was performed as follows: The sensors were dissolved in methanol-water solution (0.8/0.2 v/v) and added into saturated solution of $NaBF_4$ in water. The precipitate final product were filtered and dried in vacuum.

S1 (*N-(9-Anthracenylmethyl) quininium tetrafluoroborate*): (302 mg, 32%). m.p. : 186 °C (dec.). ^{1}H NMR (500 MHz, DMSO) δ 8.99 (s, 1H), 8.90 – 8.86 (m, 1H), 8.81 (d, J = 9.0 Hz, 1H), 8.64 (d, J = 8.9 Hz, 1H), 8.28 (d, J = 8.2 Hz, 2H), 8.07 (dd, J = 9.2, 1.3 Hz, 1H), 7.88 (d, J = 3.3 Hz, 1H), 7.83 – 7.72 (m, 2H), 7.71 – 7.61 (m, 3H), 7.54 (d, J = 9.2 Hz, 1H), 7.05 (d, J = 6.5 Hz, 2H), 6.61 (d, J = 14.1 Hz, 1H), 5.75 – 5.65 (m, 1H), 5.61 (d, J = 14.0 Hz, 1H), 4.95 (dd, J = 17.8, 14.3 Hz, 2H), 4.52 (d, J = 6.2 Hz, 1H), 4.42 (t, J = 10.7 Hz, 1H), 4.03 (s, 3H), 3.82 (s, 1H), 3.05 (t, J = 11.3 Hz, 1H), 2.89 – 2.77 (m, 1H), 2.39 (d, J = 7.3 Hz, 1H), 2.27 (d, J = 12.4 Hz, 1H), 2.12 (d, J = 6.0 Hz, 1H), 1.89 (s, 1H), 1.60 (d, J = 10.4 Hz, 1H), 1.45 (t, J = 11.7 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO) δ 157.26, 147.59, 144.22, 143.79, 137.96, 133.16, 132.82, 132.15, 131.39, 131.19, 131.08, 129.80, 129.68, 127.83, 127.65, 125.54, 125.50, 125.36, 124.71, 124.51, 121.81, 120.45, 118.78, 116.68, 102.58, 68.72, 64.20, 59.76, 55.79, 55.31, 51.81, 37.44, 25.32, 24.70, 20.47 ppm. ESI-MS: m/z 515 ($[M-BF_4]^+$), calculated for $C_{35}H_{35}N_2O_2^+$ 515.27. Φ = 0.21 %. τ = 3.61 ns.

S2 (*N-(9-Anthracenylmethyl)cinchonidinium tetrafluoroborate***)**: **(**211 mg**,** 21.6%). m.p. : 130 °C (dec.). ^{1}H NMR (500 MHz, DMSO) δ 9.05 (d, J = 4.4 Hz, 1H), 8.99 (s, 1H), 8.90 (d, J = 9.1 Hz, 1H), 8.73 (d, J = 9.1 Hz, 1H), 8.60 (t, J = 7.5 Hz, 1H), 8.29 (d, J = 8.5 Hz, 2H), 8.17 (dd, J = 8.3, 0.9 Hz, 1H), 7.95 – 7.88 (m, 2H), 7.85 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.82 – 7.75 (m, 2H), 7.67 (ddd, J = 8.3, 6.4, 4.4 Hz, 2H), 7.29 (d, J = 4.0 Hz, 1H), 7.04 (s, 1H), 6.48 (d, J = 14.2 Hz, 1H), 5.85 (d, J = 14.1 Hz, 1H), 5.70 (ddd, J = 17.4, 10.5, 7.1 Hz, 1H), 4.99 (dd, J = 26.5, 13.9 Hz, 2H), 4.51 (dt, J = 22.3, 9.7 Hz, 2H), 3.92 – 3.84 (m, 1H), 3.13 – 3.06 (m, 2H), 2.76 (td, J = 11.2, 5.1 Hz, 1H), 2.45 – 2.37 (m, 1H), 2.25 – 2.18 (m, 1H), 2.05 – 2.01 (m, 1H), 1.88 (d, J = 2.7 Hz, 1H), 1.54 (t, J = 9.8 Hz, 1H), 1.38 (dd, J = 13.1, 10.4 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO) δ 150.72, 148.22, 146.19, 138.57, 133.61, 133.51, 132.49, 131.61, 131.58, 130.32, 130.11, 130.00, 128.15, 128.06, 127.61, 125.94, 125.93, 125.59, 125.20, 125.00, 124.63, 120.76, 119.58, 117.05, 68.57, 65.17, 60.77, 55.76, 51.76, 37.92, 31.17, 25.71, 25.11, 21.62. Φ = 0.20 %. τ = 4.19 ns.

S3 (*N-(9-Anthracenylmethyl) cinchoninium tetrafluoroborate***): (**465 mg**,** 48%). m.p. : 176 °C (dec.). ^{1}H NMR (500 MHz, DMSO) δ 9.06 (d, J = 4.2 Hz, 1H), 8.99 (s, 1H), 8.93 (d, J = 9.0 Hz, 1H), 8.64 (d, J = 8.1 Hz, 1H), 8.54 (d, J = 8.9 Hz, 1H), 8.29 (d, J = 8.4 Hz, 2H), 8.16 (d, J = 8.2 Hz, 1H), 8.00 – 7.78 (m, 5H), 7.73 – 7.61 (m, 2H), 7.32 (d, J = 25.4 Hz, 1H), 6.95 (d, J = 11.6 Hz,

1H), 6.25 (d, J = 14.2 Hz, 1H), 6.01 (d, J = 14.0 Hz, 1H), 5.98 – 5.83 (m, 1H), 5.15 (d, J = 10.4 Hz, 1H), 5.02 (d, J = 17.2 Hz, 1H), 4.41 (dt, J = 19.5, 9.5 Hz, 2H), 4.24 (t, J = 10.6 Hz, 1H), 3.01 (t, J = 11.1 Hz, 1H), 2.73 (dt, J = 23.9, 9.9 Hz, 1H), 2.39 – 2.21 (m, 2H), 1.81 – 1.66 (m, 2H), 1.58 (s, 1H), 1.01 (d, J = 13.3 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO) δ 150.30, 147.73, 145.16, 137.14, 133.21, 132.97, 132.09, 131.24, 131.12, 129.91, 129.83, 129.62, 129.58, 127.85, 127.58, 127.23, 125.56, 125.46, 125.21, 124.54, 124.16, 124.05, 120.25, 119.02, 116.94, 66.75, 65.87, 56.71, 54.64, 54.24, 36.98, 25.48, 23.49, 21.27 ppm. ESI-MS: m/z 485 ($[M\text{-}BF_4]^+$), calculated for $C_{34}H_{33}N_2O^+$ 485.26. Φ = 0.25 %. τ = 4.89 ns.

S4 (*N-(9-Anthracenylmethyl) quinidinium tetrafluoroborate*): (546 mg, 59%). m.p. : 170 °C (dec.). ^{1}H NMR (500 MHz, DMSO) δ 8.99 (s, 1H), 8.88 (d, J = 4.4 Hz, 1H), 8.75 (d, J = 9.0 Hz, 1H), 8.50 (d, J = 9.1 Hz, 1H), 8.29 (d, J = 8.5 Hz, 2H), 8.06 (d, J = 9.2 Hz, 1H), 7.88 (d, J = 4.4 Hz, 1H), 7.84 (dd, J = 11.1, 4.3 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.71 (d, J = 2.6 Hz, 1H), 7.67 (ddd, J = 8.4, 6.5, 4.7 Hz, 2H), 7.56 (d, J = 2.6 Hz, 1H), 7.54 (d, J = 2.6 Hz, 1H), 7.26 (d, J = 3.0 Hz, 1H), 6.97 (s, 1H), 6.20 (d, J = 14.3 Hz, 1H), 6.01 (ddd, J = 17.5, 10.4, 7.3 Hz, 1H), 5.83 (d, J = 14.2 Hz, 1H), 5.18 (d, J = 10.4 Hz, 1H), 5.07 (d, J = 17.3 Hz, 1H), 4.41 (dd, J = 17.2, 8.2 Hz, 2H), 4.18 (s, 3H), 3.17 (t, J = 11.0 Hz, 1H), 2.68 – 2.59 (m, 1H), 2.39 (ddd, J = 17.4, 16.8, 10.2 Hz, 2H), 1.82 – 1.62 (m, 2H), 1.62 – 1.41 (m, 1H), 1.13 – 1.01 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO) δ 157.88, 147.98, 144.24, 144.02, 137.78, 133.36, 133.26, 132.56, 131.81, 131.61, 130.37, 130.20, 128.42, 128.12, 126.00, 125.96, 125.89, 125.10, 124.36, 122.17, 120.93, 120.84, 119.10, 117.52, 103.05, 67.66, 65.89, 56.47, 55.96, 55.74, 55.42, 37.58, 26.00, 24.10, 21.43 ppm. ESI-MS: m/z 515 ($[M\text{-}BF_4]^+$), calculated for $C_{35}H_{35}N_2O_2^+$ 515.27. Φ = 0.28 %. τ = 6.59 ns.

Preparation of TBA salts of Guests

Chiral carboxylate analytes were dispersed in water and aqueous solution of tetrabutylammonium hydroxide (0.5M) was added slowly until pH 7 was reached. While adding TBA-OH, carboxylate mixture started to dissolve as TBA salts formed. Then, the water was removed by lyophilization.

Sensor-Guest complex study by Mass spectrometry

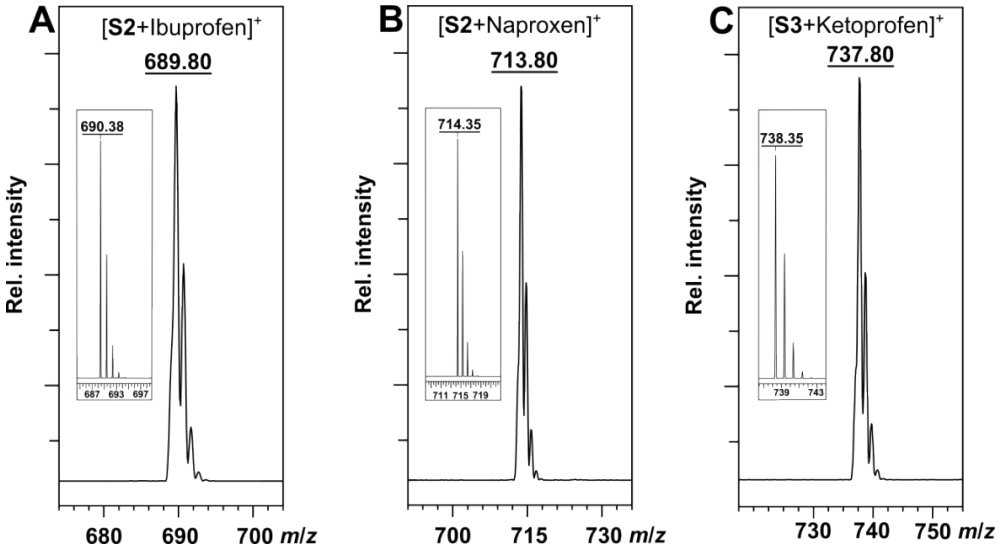
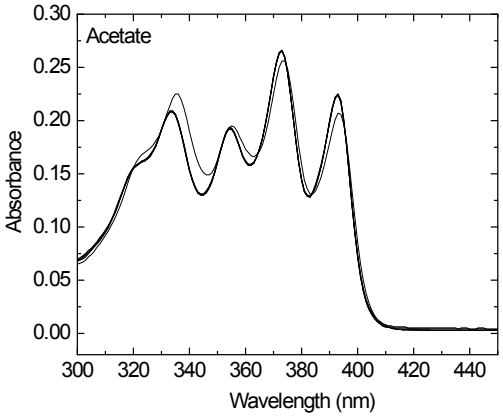


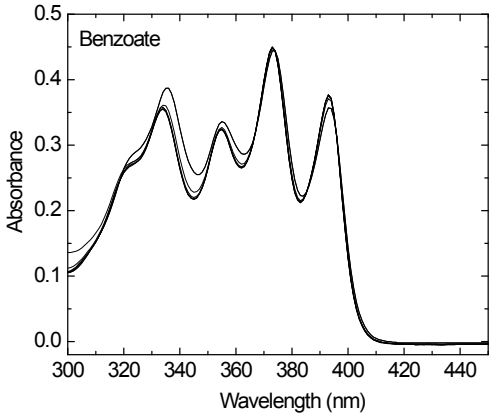
Figure 2. (A) ESI mass spectrum of the complex of **S2** and ibuprofen. Inset: Calculated isotope pattern for $C_{47}H_{50}N_2O_3^+$. (B) ESI mass spectrum of the complex of **S2** and naproxen. Inset: Calculated isotope pattern for $C_{48}H_{46}N_2O_4^+$. (C) ESI mass spectrum of the complex of **S3** and ketoprofen. Inset: Calculated isotope pattern for $C_{50}H_{46}N_2O_4^+$.

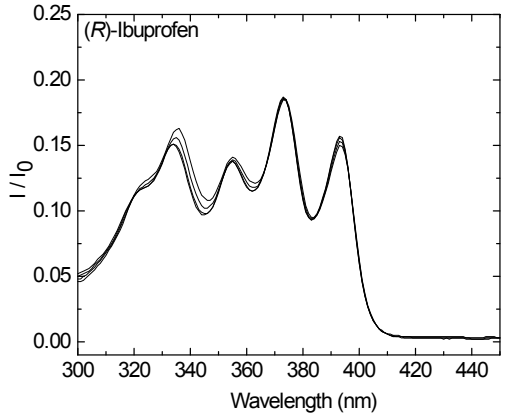
Examples of UV-Vis absorption titration experiments

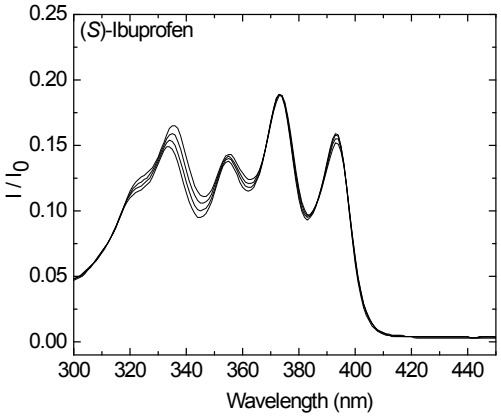
UV-Vis titrations were performed by addition of tetrabutylammonium salts of analytes into sensor solution in propionitrile. The absorption spectra were collected at 1:0.5, 1:1, and 1:4 (hosts:guest) ratios.

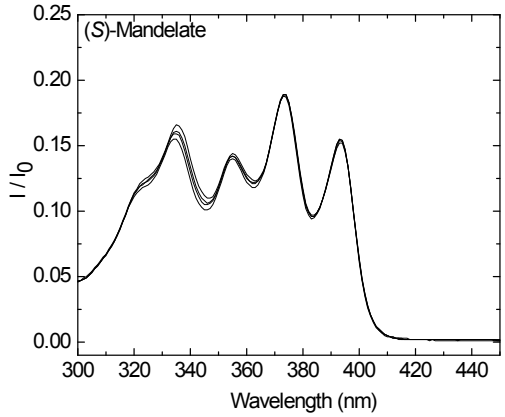
UV-Vis titration of S1

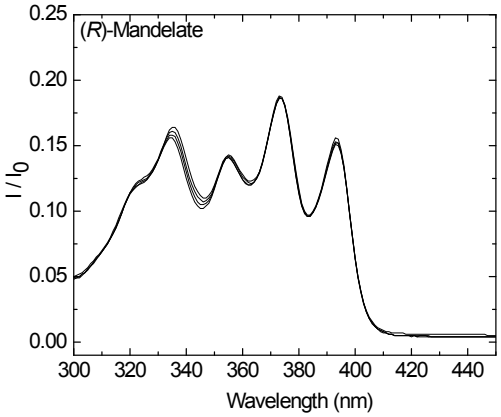


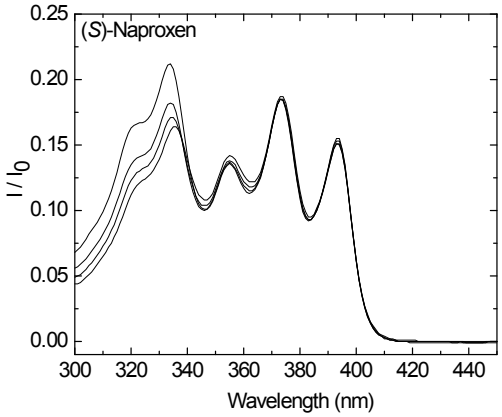








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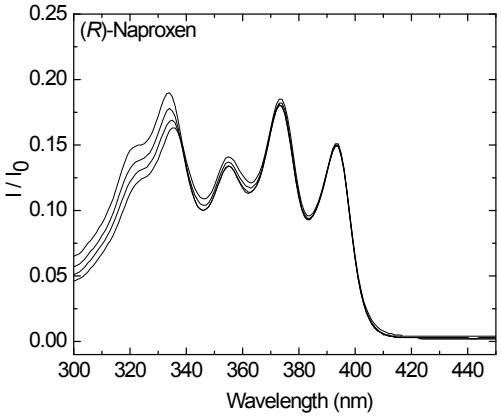
I / I0
Wavelength (nm)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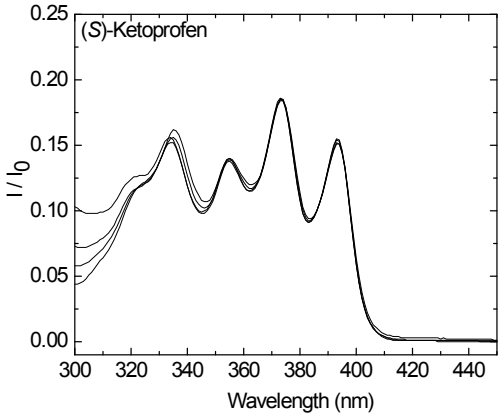
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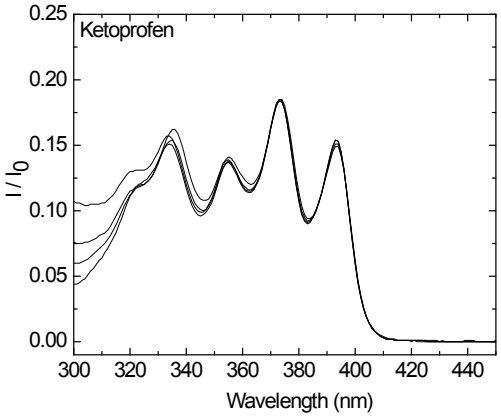
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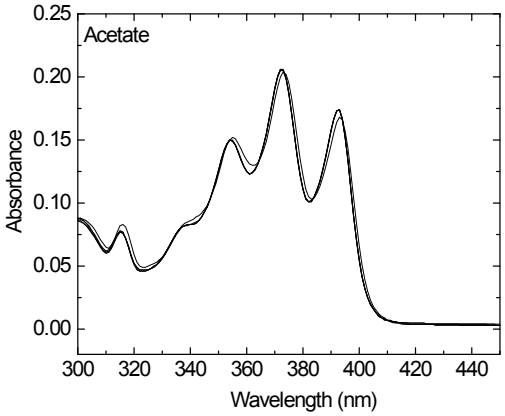
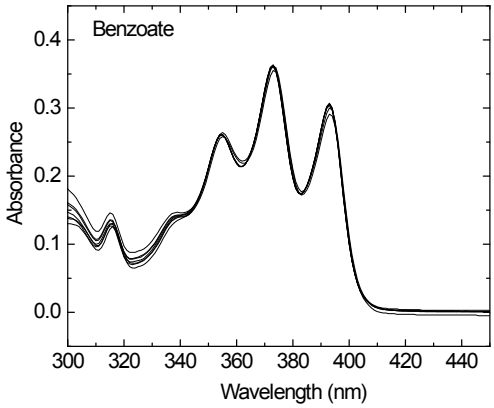
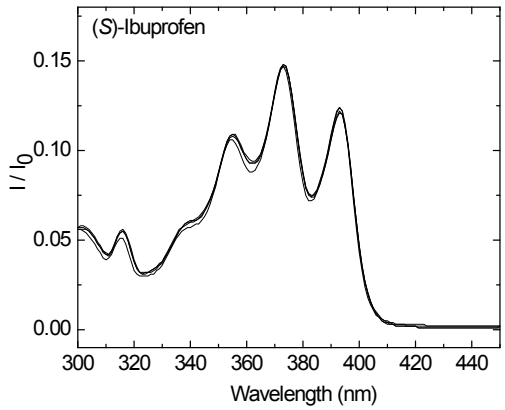
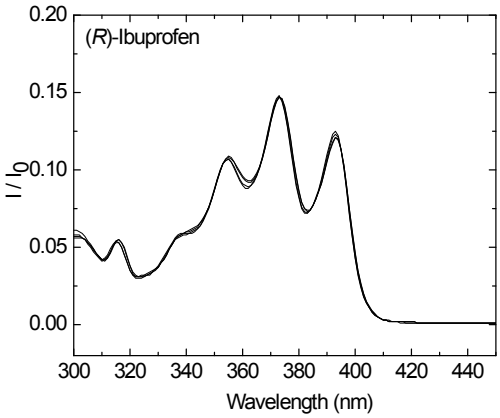
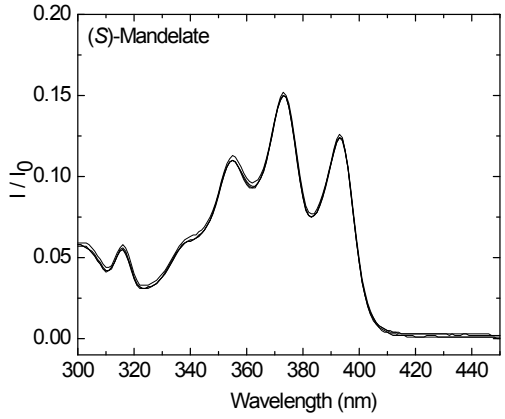
UV-Vis titration of S2

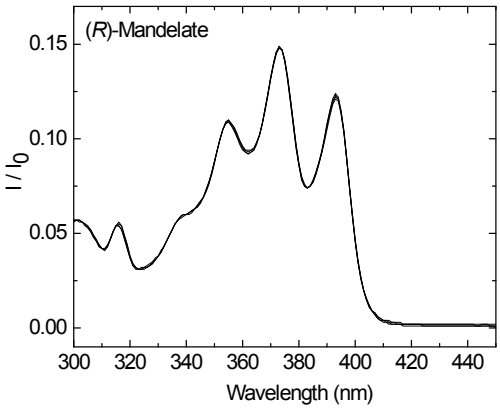


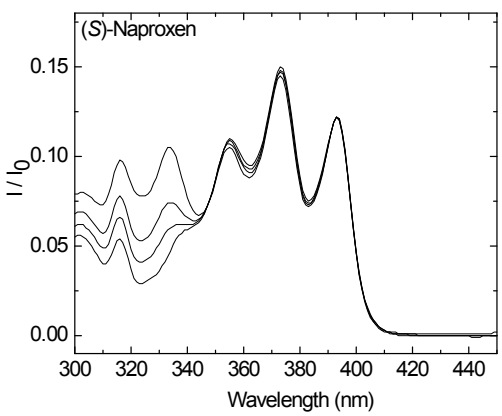








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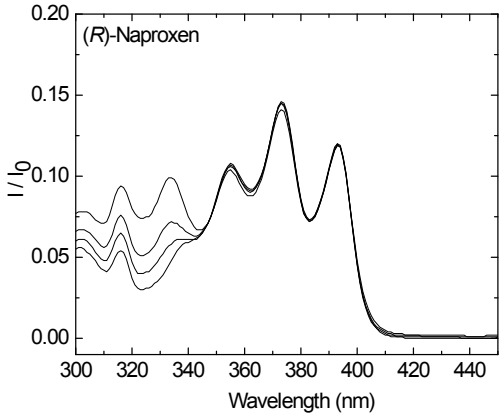
Wavelength (nm)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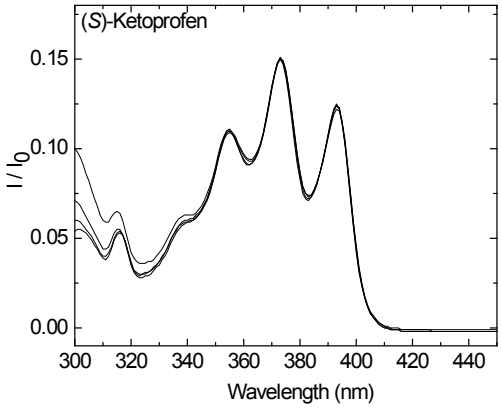
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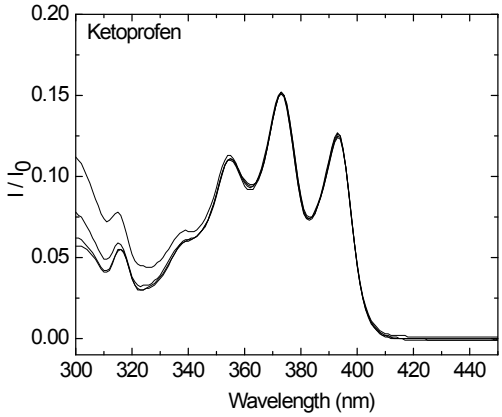
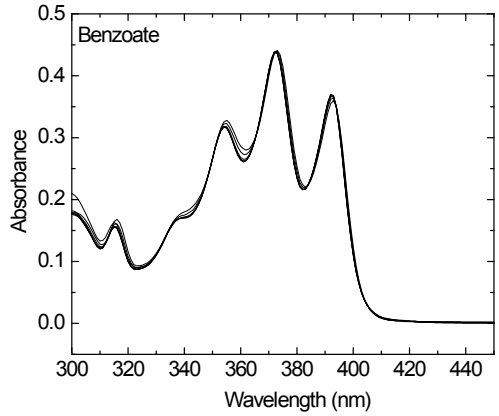
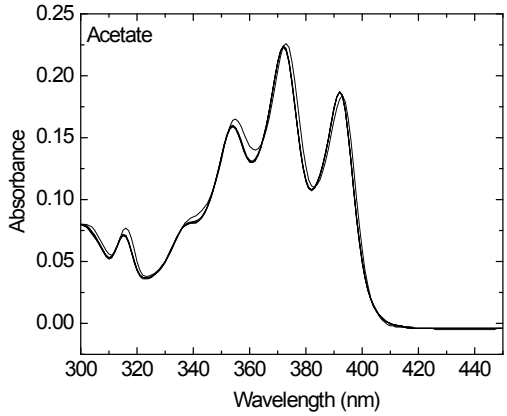
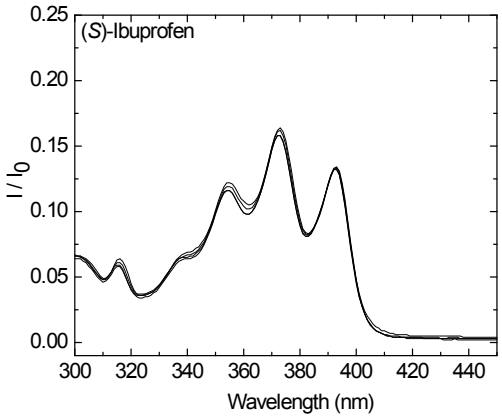
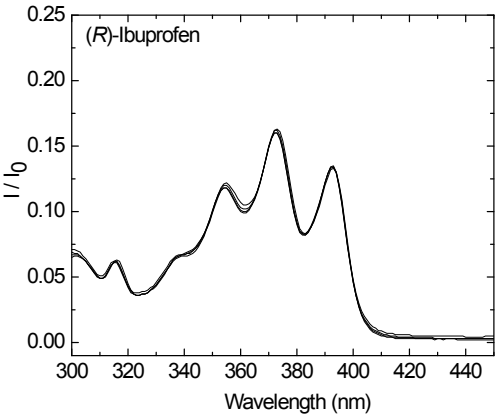

Ketoprofen
I / I0
Wavelength (nm)

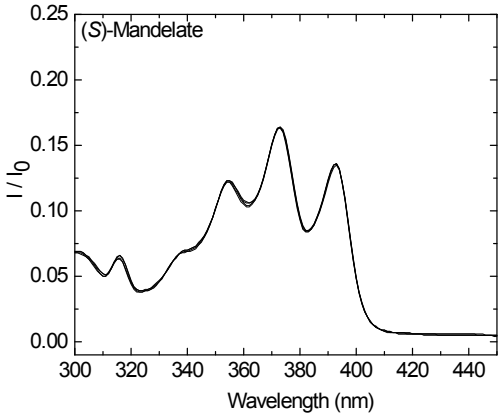
UV-Vis titration of S3

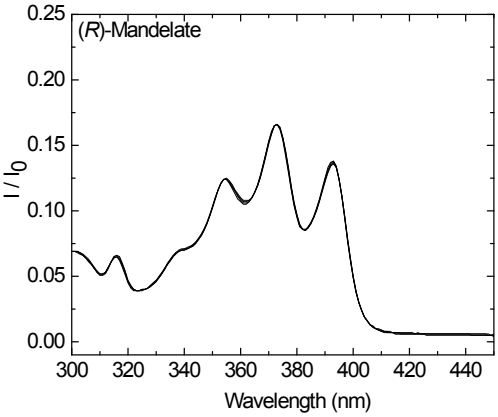


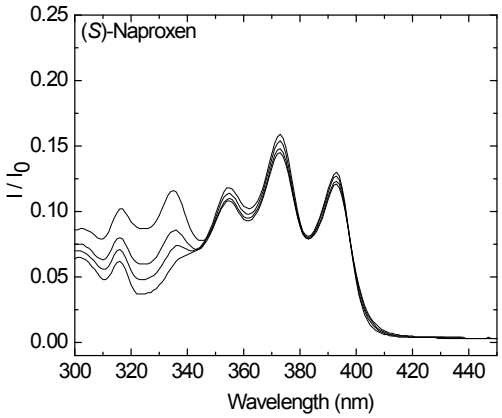


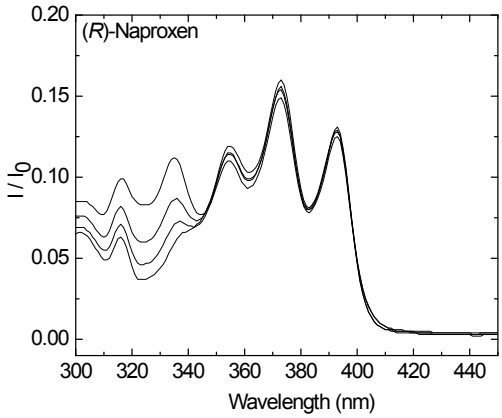


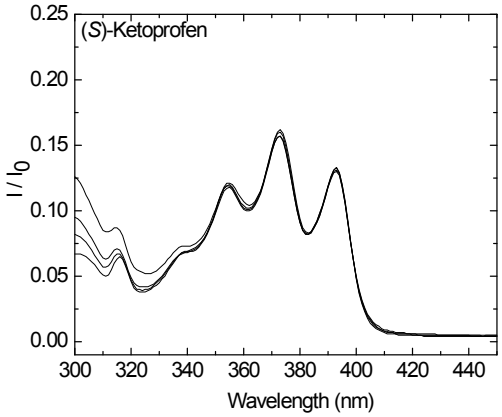


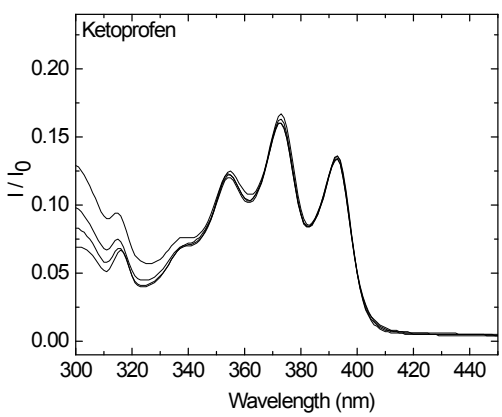




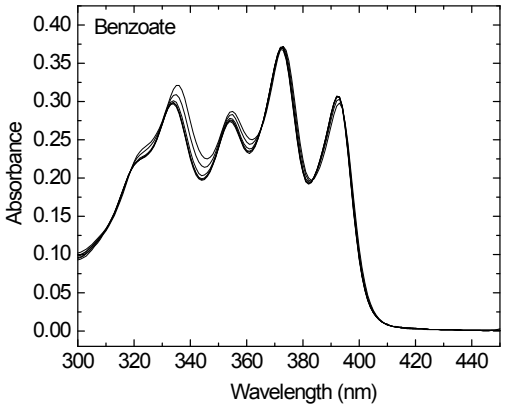

(S)-Naproxen
I / I0
Wavelength (nm)

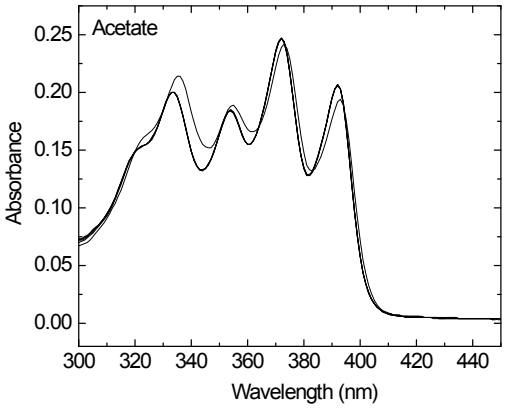

(R)-Naproxen
I / I0
Wavelength (nm)

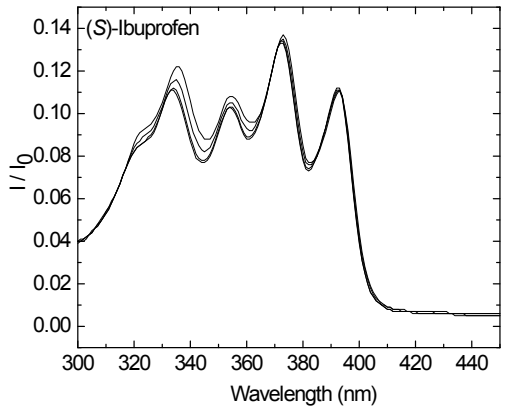

(S)-Ketoprofen
I / I0
Wavelength (nm)

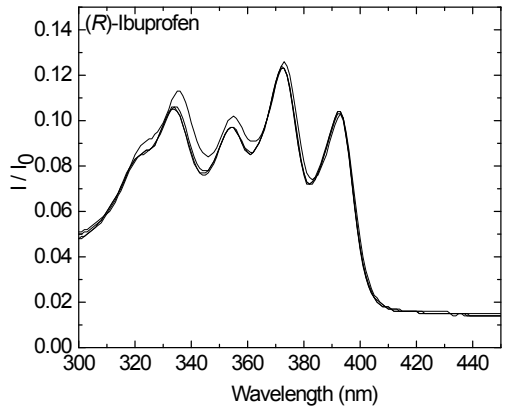

Ketoprofen
I / I0
Wavelength (nm)

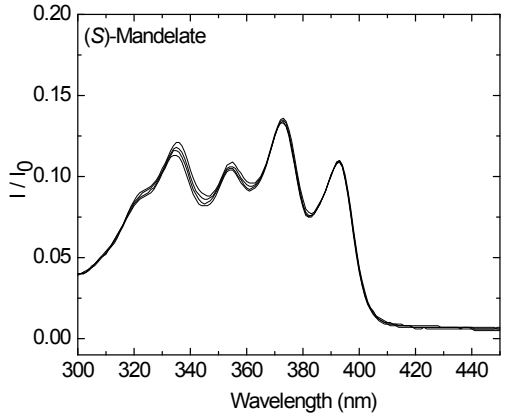
UV-Vis titration of S4

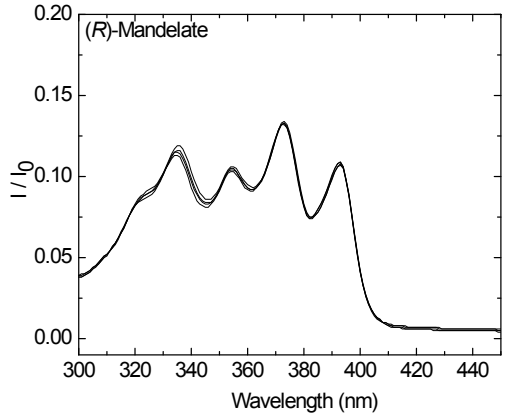


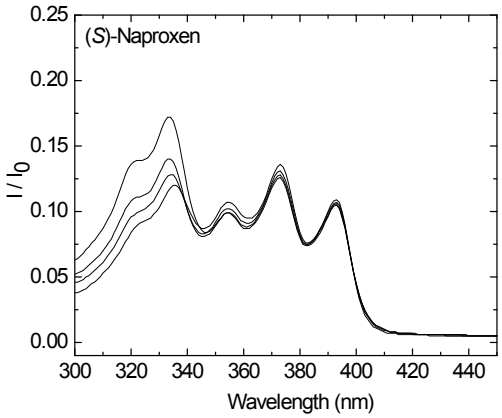


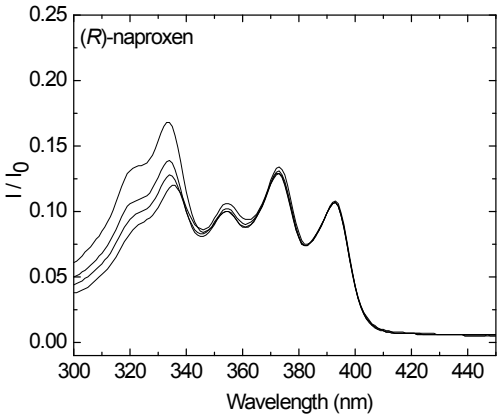


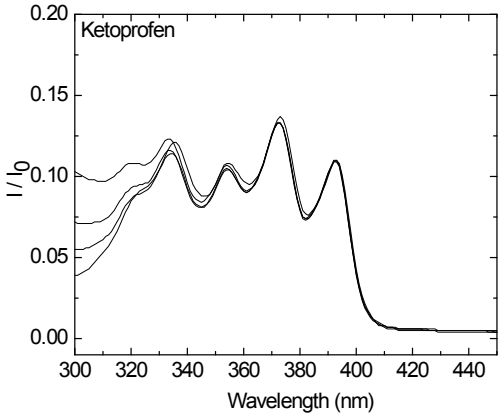


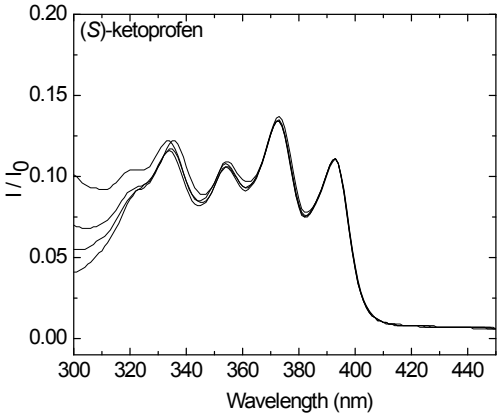





(S)-Naproxen
I / I0
Wavelength (nm)


(R)-naproxen
I / I0
Wavelength (nm)


Ketoprofen
I / I0
Wavelength (nm)


(S)-ketoprofen
I / I0
Wavelength (nm)

Fluorescence Titrations

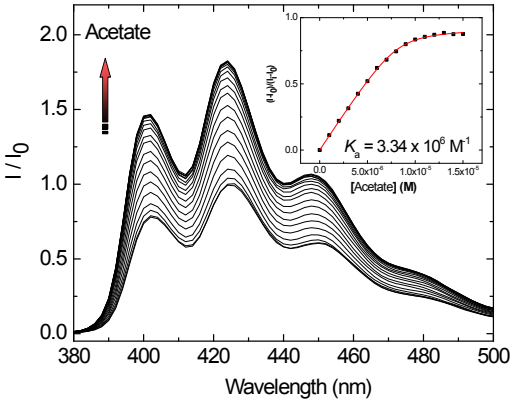
Fluorescence titrations were recorded upon addition of tetrabutylammonium salt of analytes into sensor solution in propionitrile.

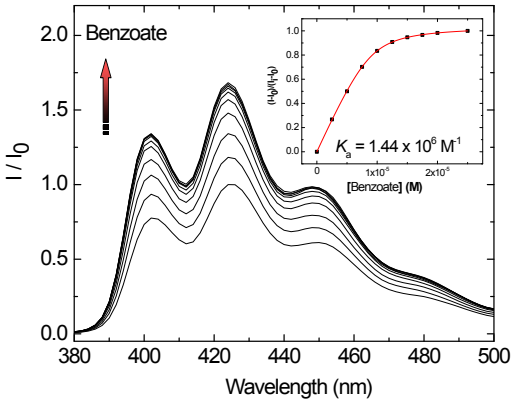
Table S1. The affinity constants (K_a, M^{-1})[a] obtained from fluorescence titration.

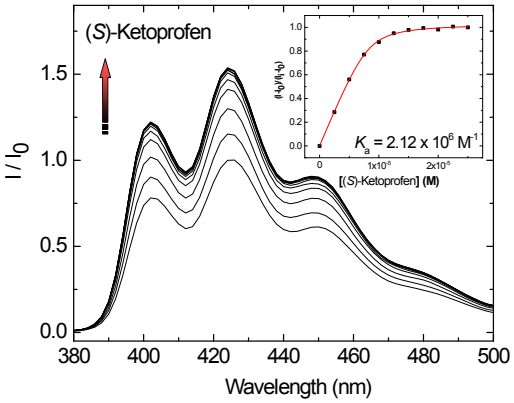
	S1	Error %	**S2**	Error %	**S3**	Error %	**S4**	Error %
Acetate	3.34×10^6	16.4	5.31×10^5	10.9	7.53×10^5	13.3	$> 10^7$	NA
Benzoate	1.44×10^6	4.7	7.65×10^5	7.71	2.17×10^6	14.7	1.08×10^6	12.5
(*S*)-Mandelate	2.33×10^5	16.3	4.51×10^4	16.5	8.53×10^4	9.8	1.13×10^6	19.0
(*R*)-Mandelate	1.40×10^5	5.6	3.23×10^4	10.3	6.87×10^4	7.2	3.17×10^5	2.4
(*S*)-Ibuprofen	2.22×10^6	16.6	1.17×10^6	16.6	3.41×10^6	16.6	$> 10^7$	NA
(*R*)-Ibuprofen	3.29×10^6	18.4	3.91×10^6	17.1	2.58×10^6	15.2	$> 10^7$	NA
(*S*)-Ketoprofen	2.12×10^6	9.7	3.00×10^5	8.5	ND[b]	ND	ND[b]	ND
(*R*)-Ketoprofen	1.37×10^6	16.9	1.42×10^5	14.5	2.92×10^5	8.7	2.08×10^5	6.5
(*S*)-Naproxen	3.00×10^6	7.5	3.85×10^6	14.4	2.31×10^6	11.2	1.54×10^6	9.7
(*R*)-Naproxen	9.10×10^6	16.1	3.41×10^6	18.9	2.70×10^6	16.9	1.67×10^6	16.8

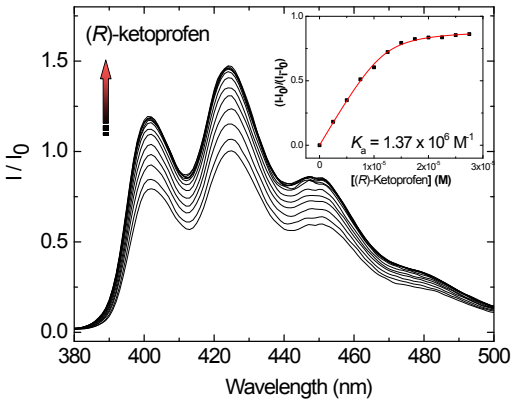
[a] The titrations are recorded in propionitrile and K_as were calculated based on the change in fluorescence intensity change at λ_{Em}= 424 nm. The errors of the curve fitting were < 20%. [b] K_a could not be calculated due to the low magnitude of response.

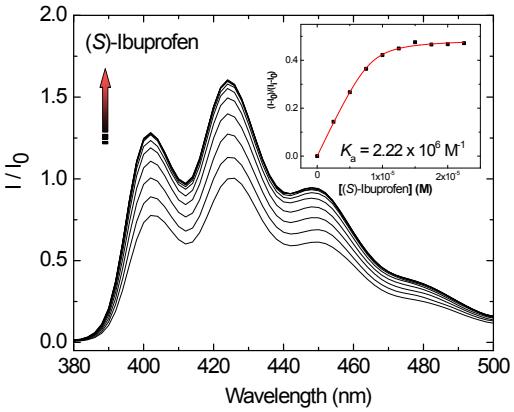
S1 Titrations

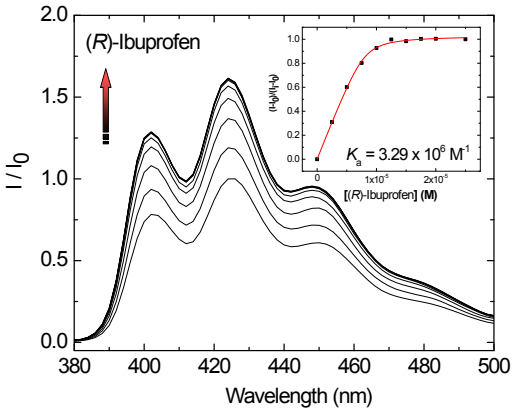


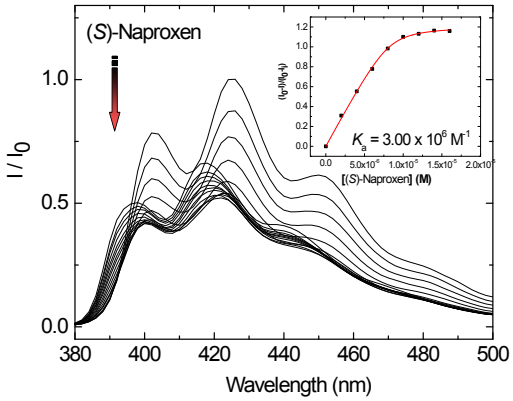


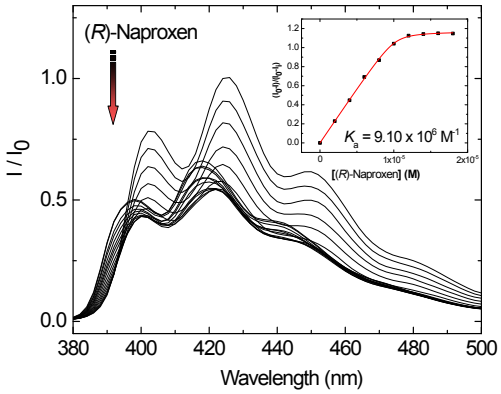


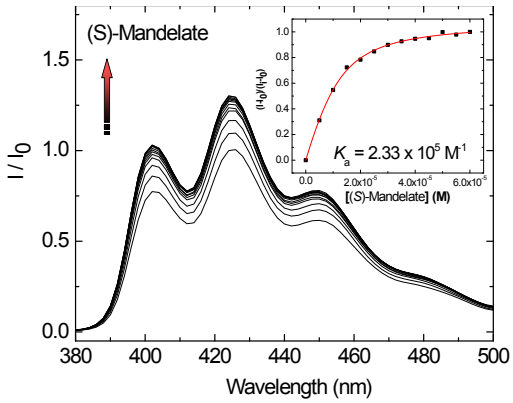


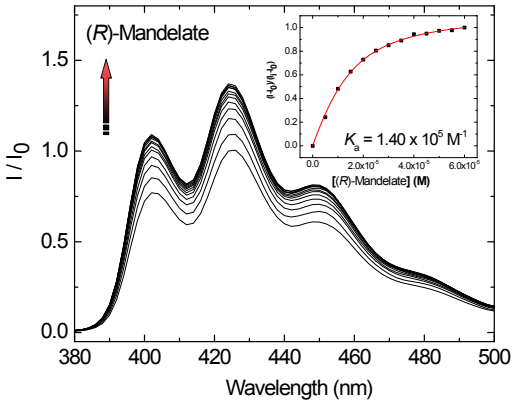




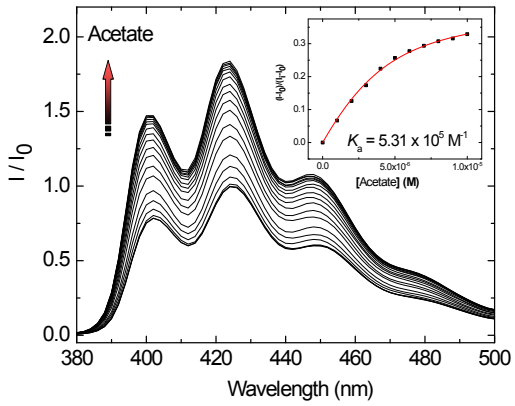

(S)-Naproxen
K_a = 3.00 x 10^6 M^{-1}
[(S)-Naproxen] (M)
I / I$_0$
Wavelength (nm)

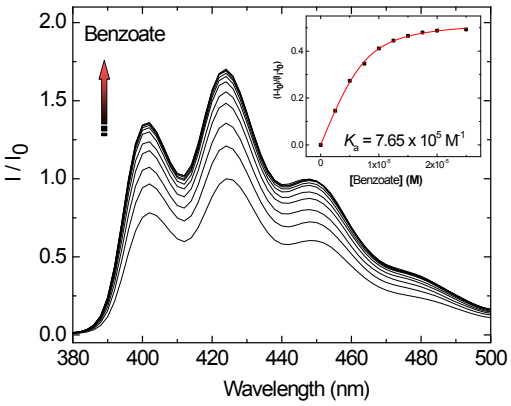

(R)-Naproxen
K_a = 9.10 x 10^6 M^{-1}
[(R)-Naproxen] (M)
I / I$_0$
Wavelength (nm)

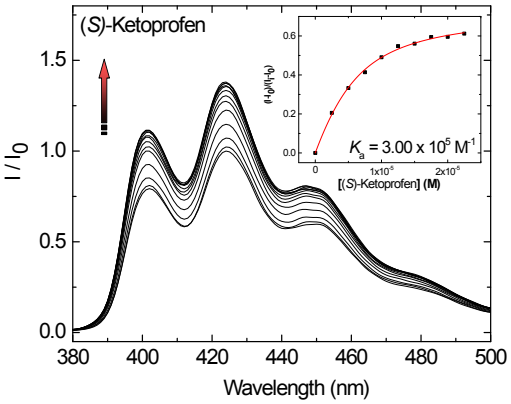

(S)-Mandelate
K_a = 2.33 x 10^5 M^{-1}
[(S)-Mandelate] (M)
I / I$_0$
Wavelength (nm)

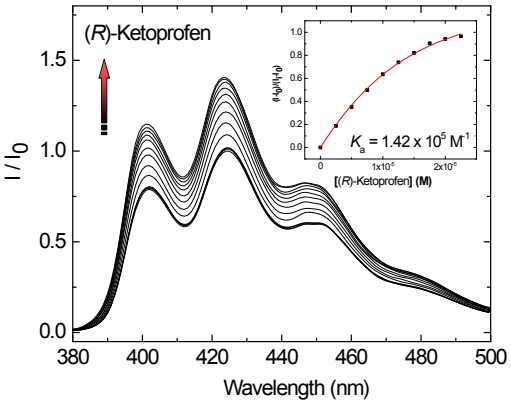

(R)-Mandelate
K_a = 1.40 x 10^5 M^{-1}
[(R)-Mandelate] (M)
I / I$_0$
Wavelength (nm)

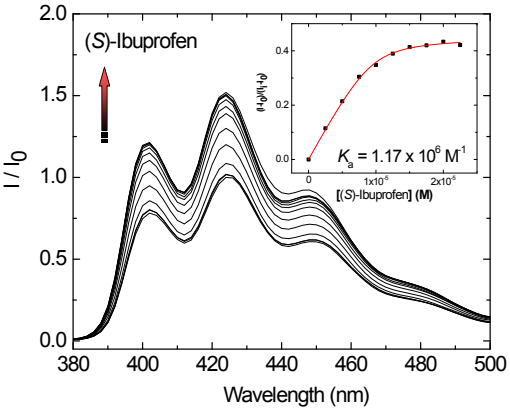
S2 Titrations

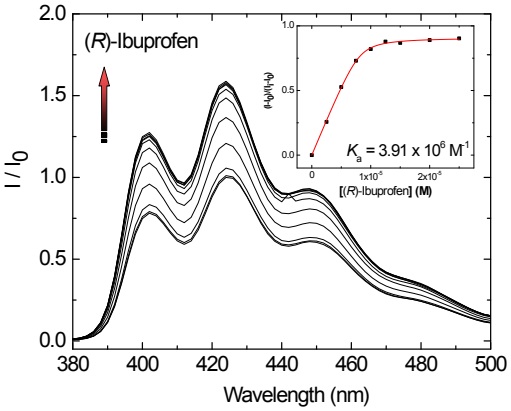


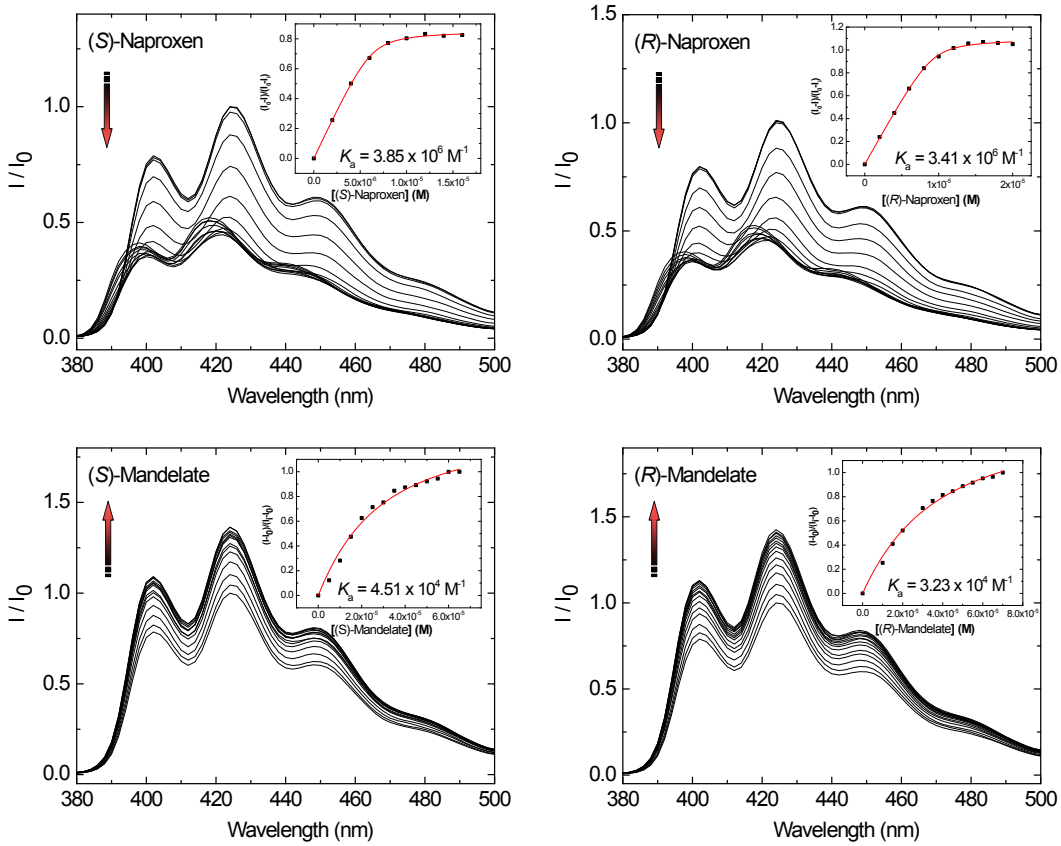




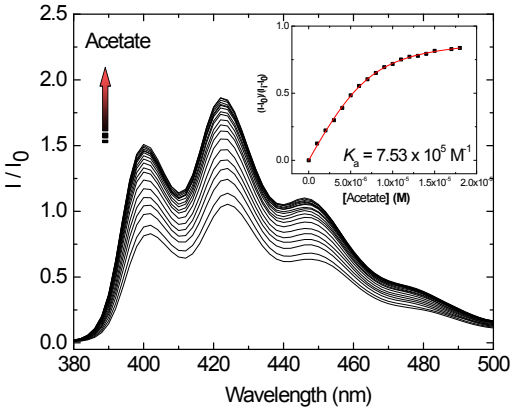


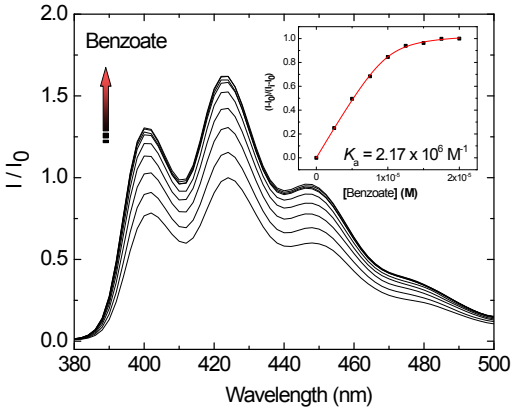


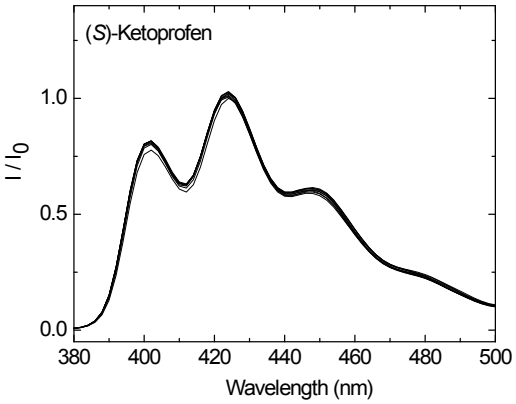


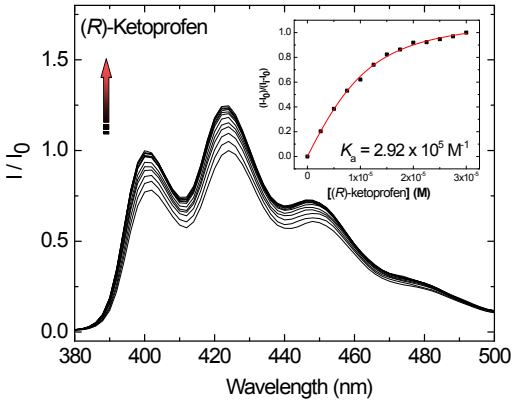

(S)-Naproxen
K_a = 3.85 x 10^6 M^{-1}
[(S)-Naproxen] (M)
(R)-Naproxen
K_a = 3.41 x 10^6 M^{-1}
[(R)-Naproxen] (M)
(S)-Mandelate
K_a = 4.51 x 10^4 M^{-1}
[(S)-Mandelate] (M)
(R)-Mandelate
K_a = 3.23 x 10^4 M^{-1}
[(R)-Mandelate] (M)
I / I$_0$
Wavelength (nm)

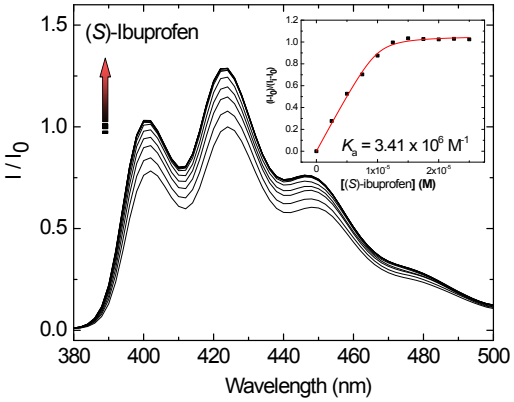
S3 Titrations

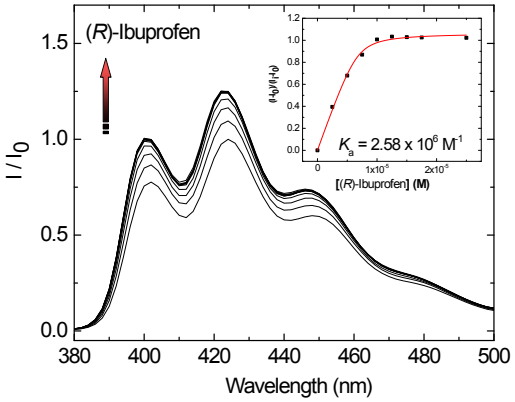


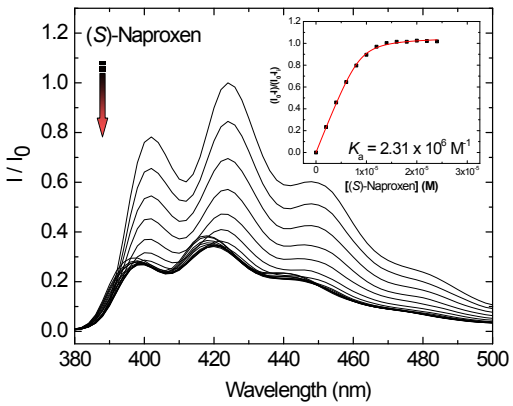


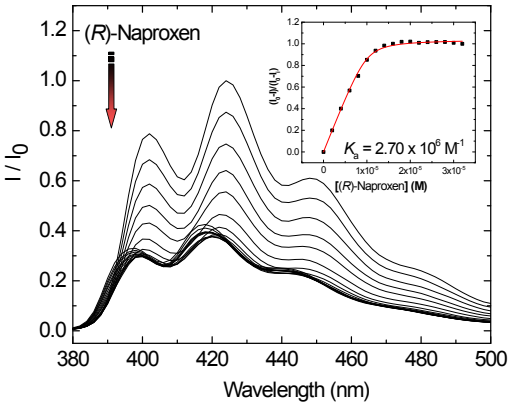


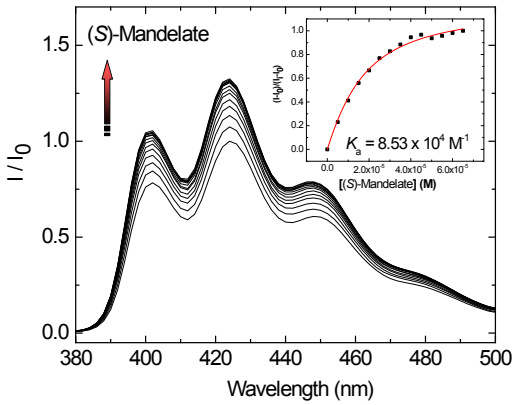


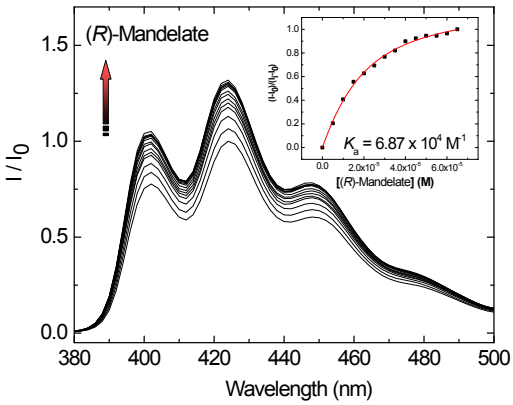




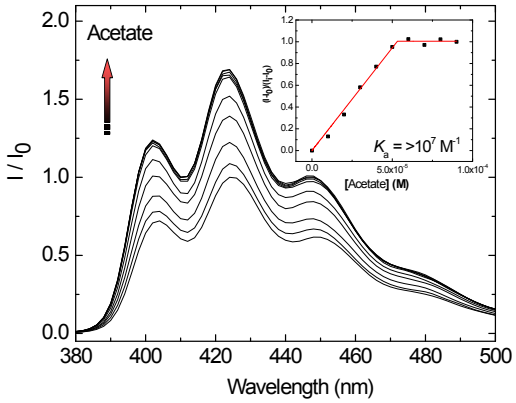

(S)-Naproxen
I / I0
Wavelength (nm)
Ka = 2.31 x 10^6 M^-1
[(S)-Naproxen] (M)

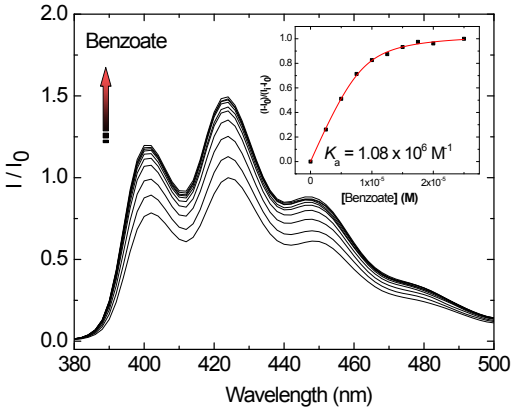

(R)-Naproxen
I / I0
Wavelength (nm)
Ka = 2.70 x 10^6 M^-1
[(R)-Naproxen] (M)

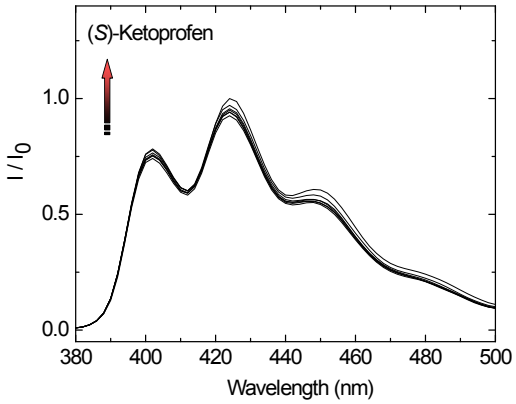

(S)-Mandelate
I / I0
Wavelength (nm)
Ka = 8.53 x 10^4 M^-1
[(S)-Mandelate] (M)

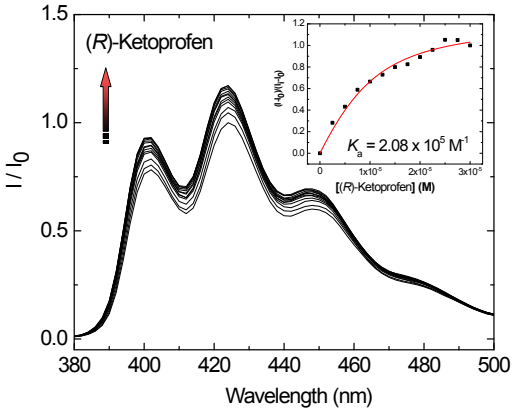

(R)-Mandelate
I / I0
Wavelength (nm)
Ka = 6.87 x 10^4 M^-1
[(R)-Mandelate] (M)

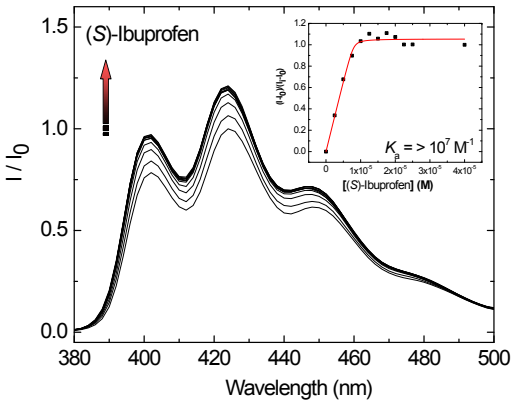
S4 Titrations

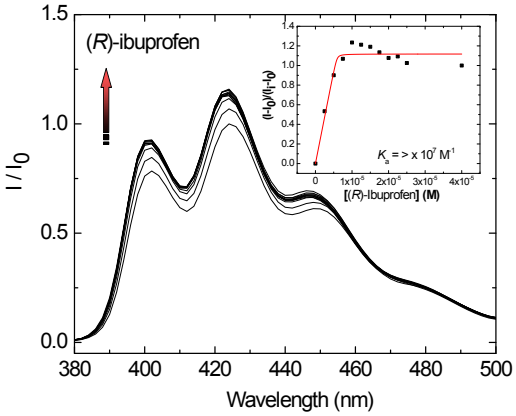


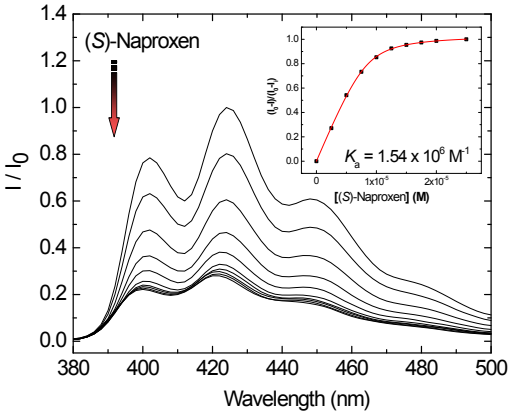


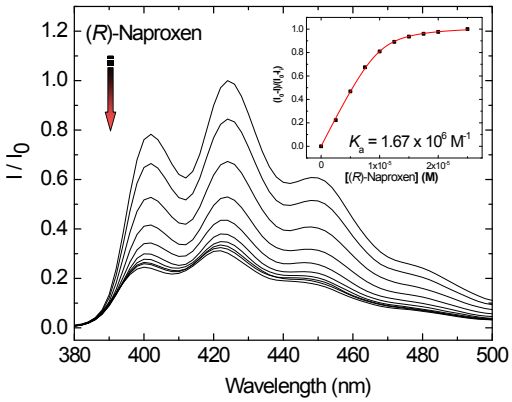


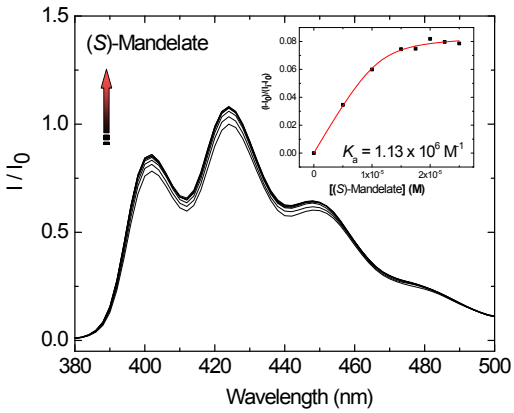


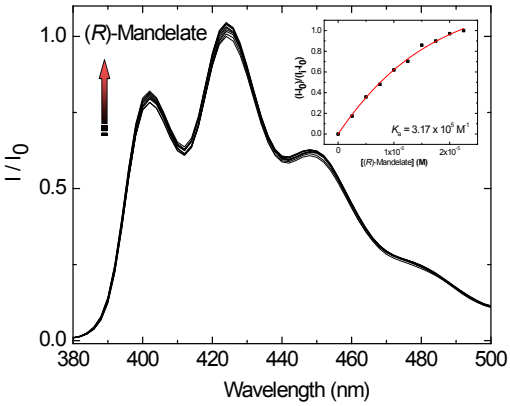





(S)-Naproxen
K_a = 1.54 x 10^6 M^{-1}
[(S)-Naproxen] (M)
I / I$_0$
Wavelength (nm)


(R)-Naproxen
K_a = 1.67 x 10^6 M^{-1}
[(R)-Naproxen] (M)
I / I$_0$
Wavelength (nm)


(S)-Mandelate
K_a = 1.13 x 10^6 M^{-1}
[(S)-Mandelate] (M)
I / I$_0$
Wavelength (nm)


(R)-Mandelate
K_a = 3.17 x 10^5 M^{-1}
[(R)-Mandelate] (M)
I / I$_0$
Wavelength (nm)

X-ray structural analysis

The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromatized Mo-K_α radiation using an Oxford Cryostream low temperature device. Data reduction was performed using DENZO-SMN.[5] The structure was solved by direct methods using SIR97[6] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[7] Crystals of S3 with (*S*)-ibuprofen and S3 with (*R*)-ibuprofen grew as colorless crystals by diffusion of hexanes into propionitrile solution of the complexes.

Table S2. Crystal data and structure refinement for S3 with (*S*)-ibuprofen.

Bond precision: C-C = 0.0062 A Wavelength=1.54180

Cell: a=12.9055(4) b=25.5214(7) c=27.4203(10)
α=90° β=90° γ=90°

Temperature: 100 K

	Calculated	*Reported*
Volume	9031.3(5)	9031.3(5)
Space group	$P2_12_12_1$	$P2_12_12_1$
Moiety formula	$2(C_{34}\ H_{33}\ N_2\ O)$, $2(C_{13}\ H_{17}\ O_2)$, 0.5(C6 H14), C3 H5 N	$2(C_{34}\ H_{33}\ N_2\ O)$, $2(C_{17}\ H_{13}\ O_2)$, $C_3\ H_5\ N$, 1/2 $C_6\ H_{14}$
Sum formula	$C_{100}\ H_{112}\ N_5\ O_6$	$C_{100}\ H_{112}\ N_5\ O_6$
Mr	1479.95	1479.94
D,g cm^{-3}	1.089	1.088
Z	4	4
μ (mm^{-1})	0.521	0.521
F000	3180.0	3180.0
F000'	3188.58	
h,k,l_{max}	15, 31, 33	15, 31, 33
Nref	17126 [9348]	16758
T_{min},T_{max}	0.957, 0.969	0.809, 1.000
$T_{min'}$	0.732	

Correction method= MULTI-SCAN

Data completeness= 1.79 / 0.98 Theta(max)= 69.992

R(reflections)= 0.0624 (14677) wR2(reflections)= 0.1903 (16758)

S = 1.040 N_{par}= 1003

Table S3. Crystal data and structure refinement for S3 with (*R*)-ibuprofen.

Bond precision: C-C = 0.0067 A Wavelength=1.54180
Cell: a=26.3802(8) b=13.2726(4) c=48.5657(15)
α=90° β=102.432(4)° γ=90°
Temperature: 133 K

	Calculated	*Reported*
Volume	16605.8(9)	16605.8(9)
Space group	I 2	I 2
Moiety formula	8(C_{34} H_{33} N_2 O), 8(C_{13} H_{17} O_2), 2(C_6 H_{14}), 5(C_3 H_5 N)	8(C_{34} H_{33} N_2 O), 8(C_{13} H_{17} O_2), 5(C_3 H_5 N), 2(C_6 H_{14})
Sum formula	C_{403} H_{453} N_{21} O_{24}	C_{403} H_{453} N_{21} O_{24}
Mr	5974.86	5974.86
Dx,g cm^{-3}	1.195	1.195
Z	2	2
Mu (mm^{-1})	0.572	0.572
F000	6420.0	6420.0
F000'	6437.32	
h,k,l_{max}	32, 16, 60	32, 16, 60
N_{ref}	33457 [17487]	27629
T_{min},T_{max}	0.921, 0.972	0.844, 1.000
$T_{min'}$	0.814	

Correction method= MULTI-SCAN
Data completeness= 1.58 / 0.83 Theta(max)= 73.373
R(reflections)= 0.0566 (24714) wR2(reflections)= 0.1663 (27629)
S = 1.024 N_{par}= 2053

Qualitative analysis

Linear discriminant analysis (LDA)

Table S4. The jackknifed classification matrix of qualitative analysis of 9 analytes and a control by using S1-S4 in hydrogel matrix.

Jackknifed classification matrix

	Acetate	Benzoate	Control	Ketoprofen	*R*-Ibuprofen	*R*-Mandelate	*R*-Naproxen	*S*-Ibuprofen	*S*-Ketoprofen	*S*-Mandelate	*S*-Naproxen	**% correct**
Acetate	8	0	0	0	0	0	0	0	0	0	0	**100**
Benzoate	0	8	0	0	0	0	0	0	0	0	0	**100**
Control	0	0	8	0	0	0	0	0	0	0	0	**100**
Ketoprofen	0	0	0	8	0	0	0	0	0	0	0	**100**
R-Ibuprofen	0	0	0	0	8	0	0	0	0	0	0	**100**
R-Mandelate	0	0	0	0	0	8	0	0	0	0	0	**100**
R-Naproxen	0	0	0	0	0	0	8	0	0	0	0	**100**
S-Ibuprofen	0	0	0	0	0	0	0	8	0	0	0	**100**
S-Ketoprofen	0	0	0	0	0	0	0	0	8	0	0	**100**
S-Mandelate	0	0	0	0	0	0	0	0	0	8	0	**100**
S-Naproxen	0	0	0	0	0	0	0	0	0	0	8	**100**
Total	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**100**

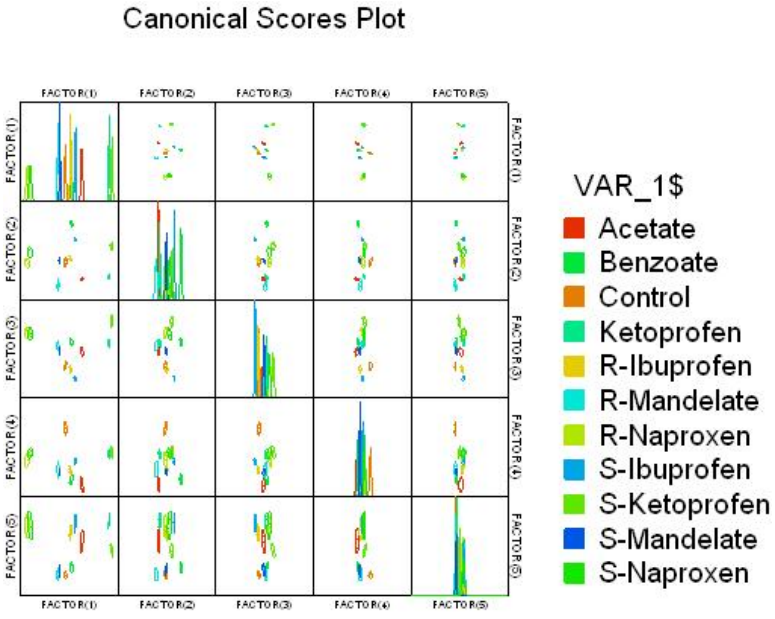


Figure 3. The canonical scores plot of qualitative analysis of of 9 analytes and a control by using S1-S4 in hydrogel matrix.

Semi-quantitative assay for Naproxen

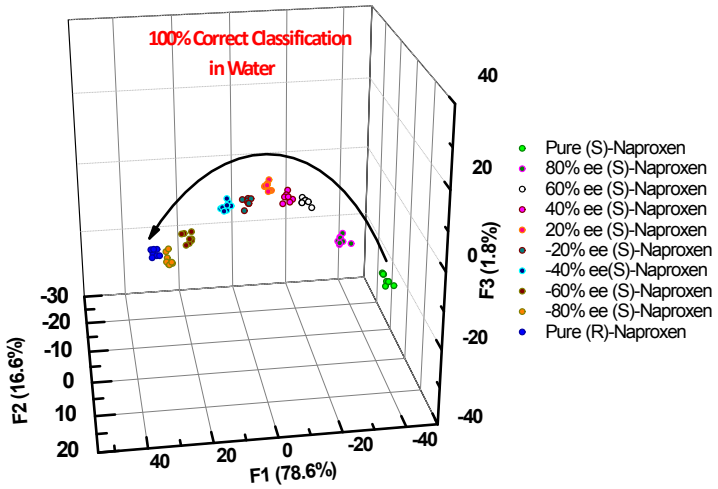


Figure 4. Linear discriminant analysis (LDA) of enantiomeric excess of (*S*)-Naproxen in hydrogel matrix. LDA shows the trend depending on the enantiomeric composition of Naproxen.

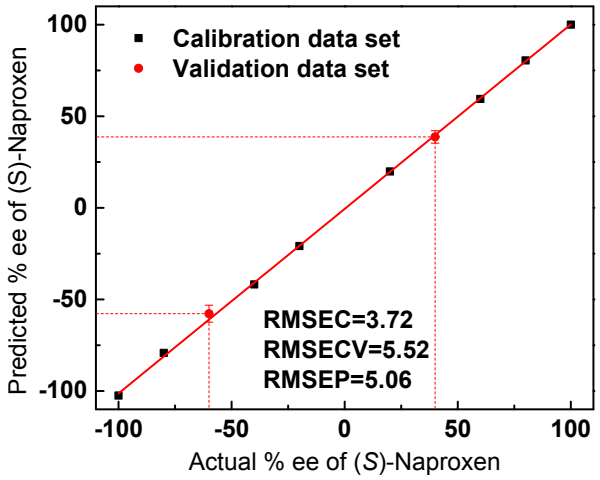


Figure 5. The result of the linear regression using support vector machine (SVM) affords quantitative analysis of enantiomeric excess in the mixtures. The plots of actual vs. predicted concentration show high accuracy of prediction for multiple guest concentrations. Two unknown samples (red squares ■) were simultaneously correctly analyzed.

Table S5. The jackknifed classification matrix of Semi-quantitative analysis of (*S*)-Naproxen by using S1-S4 in hydrogel matrix.

Jackknifed classification matrix

	(*S*)-10% Naproxen	(*S*)-20% Naproxen	(*S*)-30% Naproxen	(*S*)-40% Naproxen	(*S*)-60% Naproxen	(*S*)-70% Naproxen	(*S*)-80% Naproxen	(*S*)-90% Naproxen	(*R*)-Pure Naproxen	(*S*)-Pure Naproxen	**% correct**
10 % (*S*)-Naproxen	8	0	0	0	0	0	0	0	0	0	**100**
20 % (*S*)-Naproxen	0	8	0	0	0	0	0	0	0	0	**100**
30 % (*S*)-Naproxen	0	0	8	0	0	0	0	0	0	0	**100**
40 % (*S*)-Naproxen	0	0	0	8	0	0	0	0	0	0	**100**
60 % (*S*)-Naproxen	0	0	0	0	8	0	0	0	0	0	**100**
70 % (*S*)-Naproxen	0	0	0	0	0	8	0	0	0	0	**100**
80 % (*S*)-Naproxen	0	0	0	0	0	0	8	0	0	0	**100**
90 % (*S*)-Naproxen	0	0	0	0	0	0	0	8	0	0	**100**
Pure (*R*)-Naproxen	0	0	0	0	0	0	0	0	8	0	**100**
Pure (*S*)-Naproxen	0	0	0	0	0	0	0	0	0	8	**100**
Total	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**100**

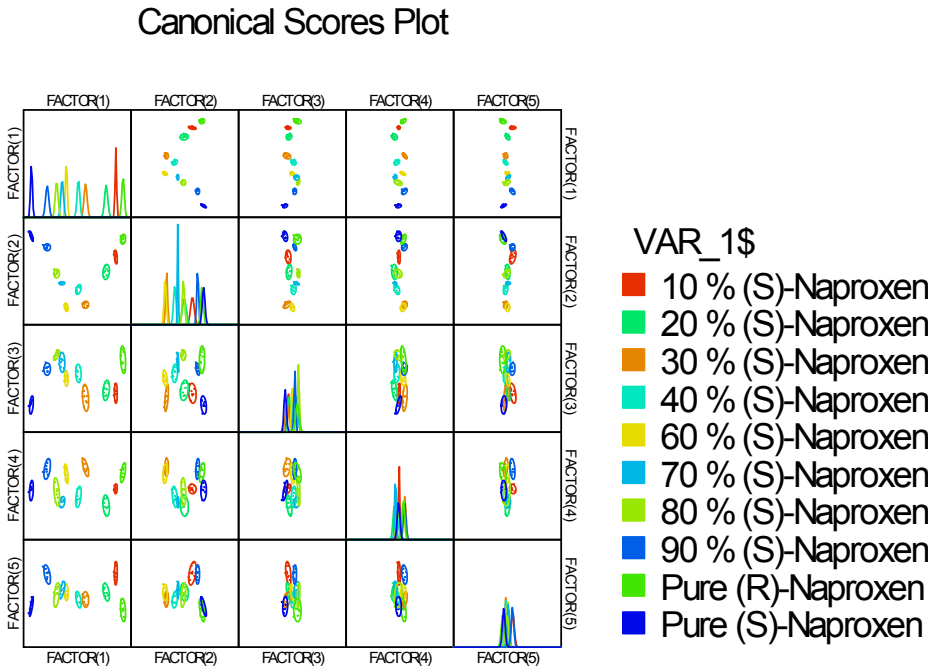


Figure 6. The canonical scores plot of Semi-quantitative analysis of (*S*)-Naproxen by using S1-S4 in hydrogel matrix.

Semi-quantitative assay for Ibuprofen

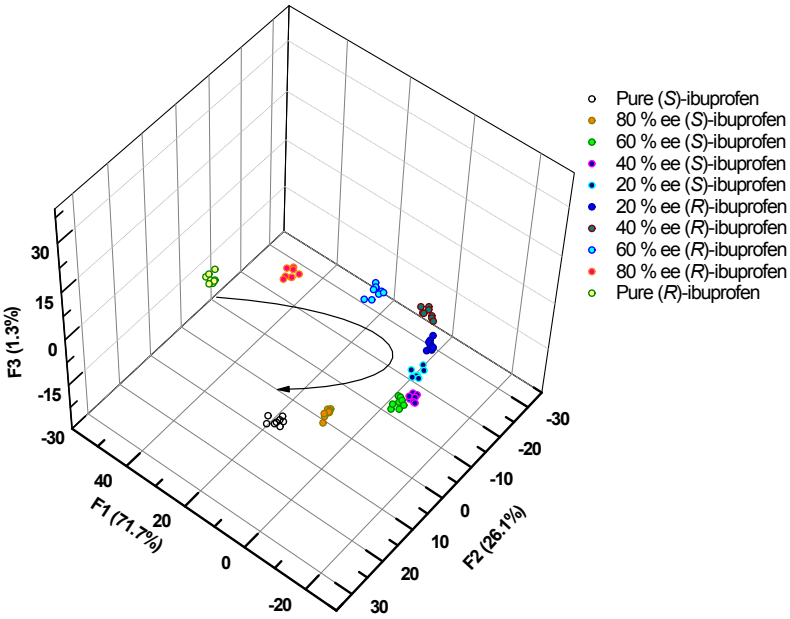


Figure 7. Linear discriminant analysis (LDA) of enantiomeric excess of (*S*)-Ibuprofen in hydrogel matrix. LDA shows the trend depending on the enantiomeric composition of ibuprofen.

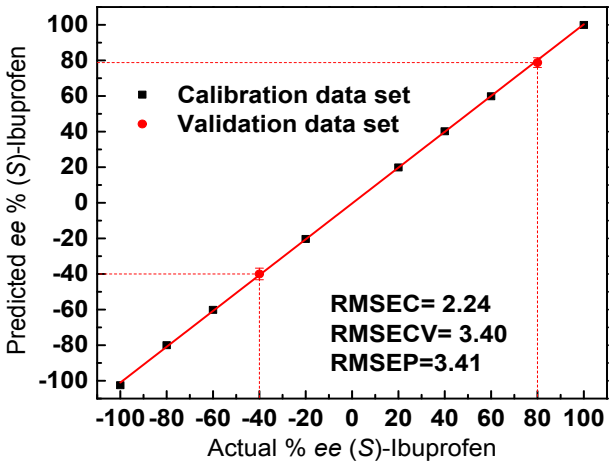


Figure 8. The result of the linear regression using support vector machine (SVM) affords quantitative analysis of enantiomeric excess in the mixtures. The plots of actual vs. predicted concentration show high accuracy of prediction for multiple guest concentrations. Two unknown samples (red squares ■) were simultaneously correctly analyzed.

Table S6. The jackknifed classification matrix of Semi-quantitative analysis of (*S*)-Ibuprofen by using S1-S4 in hydrogel matrix

Jackknifed classification matrix

	(*S*)-10% Ibuprofen	(*S*)-20% Ibuprofen	(*S*)-30% Ibuprofen	(*S*)-40% Ibuprofen	(*S*)-60% Ibuprofen	(*S*)-70% Ibuprofen	(*S*)-80% Ibuprofen	(*S*)-90% Ibuprofen	(*R*)-Pure Ibuprofen	(*S*)-Pure Ibuprofen	**% correct**
10 % (*S*)-Ibuprofen	8	0	0	0	0	0	0	0	0	0	**100**
20 % (*S*)-Ibuprofen	0	8	0	0	0	0	0	0	0	0	**100**
30 % (*S*)-Ibuprofen	0	0	8	0	0	0	0	0	0	0	**100**
40 % (*S*)-Ibuprofen	0	0	0	8	0	0	0	0	0	0	**100**
60 % (*S*)-Ibuprofen	0	0	0	0	8	0	0	0	0	0	**100**
70 % (*S*)-Ibuprofen	0	0	0	0	0	8	0	0	0	0	**100**
80 % (*S*)-Ibuprofen	0	0	0	0	0	0	8	0	0	0	**100**
90 % (*S*)-Ibuprofen	0	0	0	0	0	0	0	8	0	0	**100**
Pure (*R*)-Ibuprofen	0	0	0	0	0	0	0	0	8	0	**100**
Pure (*S*)-Ibuprofen	0	0	0	0	0	0	0	0	0	8	**100**
Total	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**100**

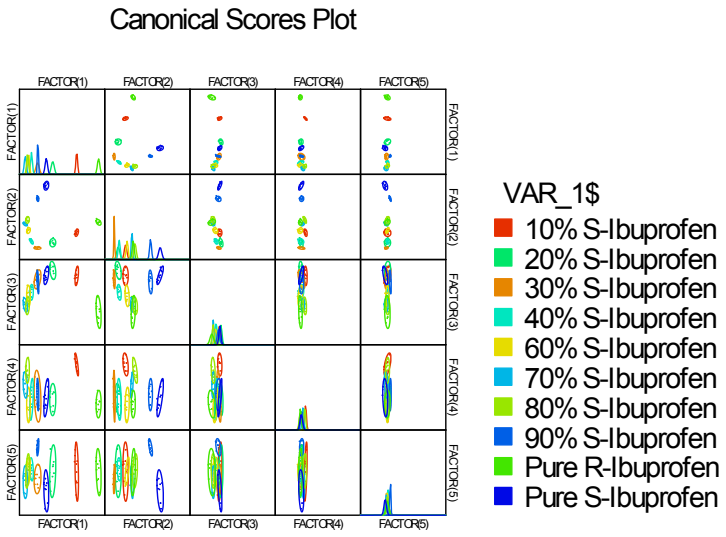


Figure 9. The canonical scores plot of Semi-quantitative analysis of (*S*)-Ibuprofen by using S1-S4 in hydrogel matrix.

Semi-quantitative assay for Ketoprofen

Table S7. The jackknifed classification matrix of Semi-quantitative analysis of (*S*)-Ketoprofen by using S1-S4 in hydrogel matrix.

Jackknifed classification matrix

	55% (*S*)-Ketoprofen	60% (*S*)-Ketoprofen	65% (*S*)-Ketoprofen	75% (*S*)-Ketoprofen	80% (*S*)-Ketoprofen	85% (*S*)-Ketoprofen	90% (*S*)-Ketoprofen	95% (*S*)-Ketoprofen	Pure (*S*)-Ketoprofen	*Rac*-Ketoprofen	**% correct**
55% (*S*)-Ketoprofen	8	0	0	0	0	0	0	0	0	0	**100**
60% (*S*)-Ketoprofen	0	8	0	0	0	0	0	0	0	0	**100**
65% (*S*)-Ketoprofen	0	0	8	0	0	0	0	0	0	0	**100**
70% (*S*)-Ketoprofen	0	0	0	8	0	0	0	0	0	0	**100**
80% (*S*)-Ketoprofen	0	0	0	0	8	0	0	0	0	0	**100**
85% (*S*)-Ketoprofen	0	0	0	0	0	8	0	0	0	0	**100**
90% (*S*)-Ketoprofen	0	0	0	0	0	0	8	0	0	0	**100**
95% (*S*)-Ketoprofen	0	0	0	0	0	0	0	8	0	0	**100**
Pure (*S*)-Ketoprofen	0	0	0	0	0	0	0	0	8	0	**100**
Rac-Ketoprofen	0	0	0	0	0	0	0	0	0	8	**100**
Total	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**100**

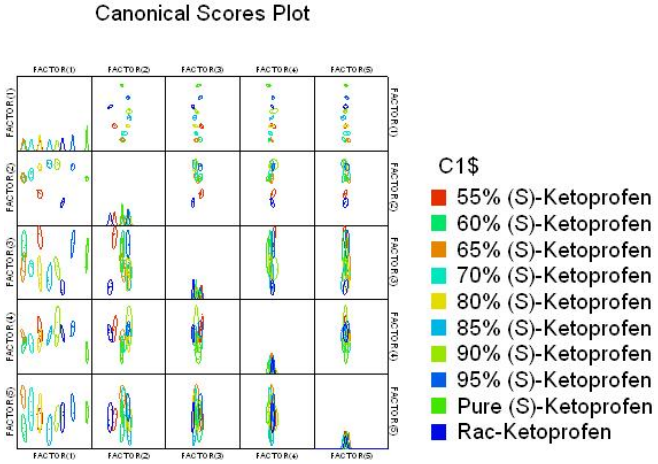


Figure 10. The canonical scores plot of Semi-quantitative analysis of (*S*)-Ketoprofen by using S1-S4 in hydrogel matrix.

References

[1] Perrard, T.; Plaquevent, J.; Desmurs, J.; Hébrault, D. *Org. Lett*. **2000**, *2*, 2959.

[2] Connors, A. K. *Binding Constants: the Measurement of Molecular Complex Stability*; Wiley: New York, 1987.

[3] Liu, Y.; Minami, T.; Nishiyabu, R.; Wang, Z.; Anzenbacher Jr., P. *J. Am. Chem. Soc*. **2013**, *135*, 7705.

[4] Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* ***1997****, 38*, 8595.

[5] Otwinowski, Z.; Minor, W. *Denzo-SMN.* In *Methods in Enzymology, Macromolecular Crystallography, part A*; Carter, Jr., C. W.; Sweets, R. M., Eds.; Academic Press: 1997; Vol. 276, pp 307–326.

[6] Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Cryst.* **1999**, *32*, 115.

[7] Sheldrick, G. M. *SHELXL97. Program for the Refinement of Crystal Structures*, University of Gottingen, Germany. 1994.