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Supporting Information

Modular Chiral Bidentate Phosphonites: Design, Synthesis and Application in Catalytic Asymmetric Hydroformylation Reactions

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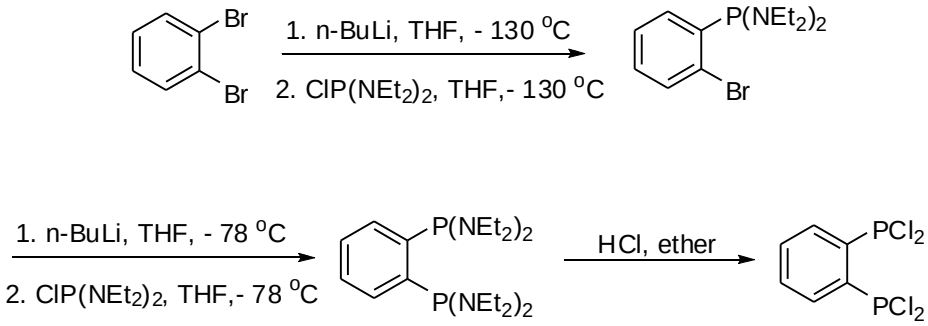


Scheme S1. Synthesis of 1,2-bis(dichlorophosphino)benzene.

Preparation of *N, N, N′, N*'- tetraethyl(2-bromophenyl)phosphonous acid diamide: The synthesis follows a protocol reported by Reetz et al.[1] To a 250-mL three-necked round-bottom flask equipped with a 100-mL dropping funnel were added a solution of *n*butyllithium (1.6 M, 31.7 mL, 50.7 mmol) in hexane and 150 mL of THF. The mixture was cooled down to -130°C (pentane/liq.N_2), to which a solution of 1,2-dibromobenzene (6 mL, 49.7 mmol) in THF (50 mL) was added dropwise within 30 min under vigorous stirring. The resulting solution was stirred for additional 30 min at -130°C before a solution of bis(diethylamino)chlorophosphine (11.0 g, 52.2 mmol) in 20 mL THF was added. The mixture was then allowed to warm to room temperature slowly, affording a pale yellow solution. This solution was then stirred overnight. After removal of the most of the solvent in vacuo, dry diethyl ether (30×3 mL) was added to the residue. The suspension was stirred for 30 min, and the resulting solids were removed by filtration under argon atmosphere. Removal of diethyl ether from the filtrate in vacuo yielded a yellow oily residue. Fractional distillation of the residue under high vacuum afforded the product as a colorless oil (150°C, 0.5 mmHg): 14.6 g, Yield = 86%; ^{1}H NMR (300 MHz, C_6D_6) δ = 7.49-7.53 (m, 1H), 7.43-7.47 (m, 1H), 7.04-7.10 (m, 1H), 6.72-6.78 (m, 1H), 2.90-3.08 (m, 8H), 0.97 (t, *J* = 8.1 Hz, 12H); ^{31}P NMR (C_6D_6, 121.46 M Hz) δ = 97.4 (s); IR (KBr pellet) ν = 2967, 1555, 1461, 1443, 1423, 1375, 1294, 1197,

1186, 1094, 1015, 921, 750 cm^{-1}; EI-MS: *m/z* = 330 (M^+, 20), 258 (100), 187 (36).

Preparation of 1,2-phenylenebis(*N,N,N′,N*'-tetraethylphosphinediamine): **To** a 250-mL three-necked round-bottom flask equipped with a 100-mL dropping funnel was added a solution of *N, N, N′, N′*-tetraethyl(2-bromophenyl)phosphonous acid diamide (20.51 g, 61.96 mmol) in dry THF (120 mL). The solution was cooled down to -78 °C, and then *n*-butyllithium solution in hexane (1.6 M, 38.7 mL, 61.96 mmol) was added dropwise in 1 h. The resulting yellow solution was stirred for additional 1 h at this temperature before a solution of bis(diethylamino)chlorophosphine (13.00 g, 61.96 mmol) in THF (40 mL) was added over a period of 30 min. The reaction mixture was then allowed to warm up to RT slowly and stirred overnight. After removal of the most of solvent in vacuo, dry diethyl ether (30×3 mL) was added to the residue. The suspension was stirred for 30 min, and the resulting solids were removed by filtration under argon atmosphere. Removal of diethyl ether from the filtrate in vacuo yields an organge oil of the product: 26.0 g, Yield = 99%; ^{1}H NMR (300 MHz, C_6D_6) δ = 7.70-7.80 (m, 2 H), 7.20-7.24 (m, 2 H), 3.02-3.11 (m, 16 H), 1.06 (t, *J* = 8.1 Hz, 24 H); ^{31}P NMR (C_6D_6, 121.46 MHz) δ = 98.5 (s); IR (KBr pellet) ν = 2967, 1460, 1375, 1185, 1102, 907, 755 cm^{-1}.

Preparation of 1,2-bis(dichlorophosphino)benzene: A 250-mL three-necked round-bottom flask equipped with a 100-mL dropping funnel was charged with a solution of hydrogen chloride in diethyl ether (4.8 M, 190 mL) at -78°C. To this solution was added 1,2-phenylenebis(*N,N,N′,N*'-tetraethylphosphinediamine) (15.0 g, 0.0352 mol) in diethyl ether (40 mL) over 1h. The reaction mixture was then allowed to warm up to RT slowly and stirred overnight, yielding a suspension containing a lot of white precipitate. The white solid was filtered off under argon and the solvent was removed from the filtrate under reduced pressure to give a pale yellow oily residue. Fractional distillation of the residue under high vacuum afforded the

pure product as a colorless oil (120°C, 0.5 mmHg): 8.0 g, Yield = 81%. It should be noted that this compound is very sensitive to moisture. All of the manipulations for its preparation and application must be carried out under moisture-free conditions.

Optimization of reaction conditions:

Table S1. The effect of substrate concentration on the AHF of styrene, vinyl acetate and allyl cyanide.

Entry	[Sub.]	Styrene[a]			Vinyl acetate[a]			Allyl cyanide[b]		
		conv.(%) [c]	b/l[c]	ee(%)[c]	conv.(%) [c]	b/l[c]	ee(%)[c]	conv.(%) [c]	ee(%)[c]	b/l[c]
1	4.3	88	3.1	52.4	98	33.2	86.0	55	3.2	56.3
2	3.0	95	3.0	53.2	99	31.7	86.6	70	3.3	57.0
3	1.8	84	2.9	52.4	94	29.6	87.0	55	3.3	67.0
4	1.0	73	2.9	51.9	86	32.6	87.1	54	3.6	67.6

[a] Reaction conditions: [Rh] / **10b** = 1:1.5, sub./cat. = 500, $P(H_2)$ = 10 bar, $P(CO)$ = 10 bar, toluene, 60°C, 6 h. [b] Reaction conditions: [Rh] / **10b** = 1:1.5, sub./cat. = 500, $P(H_2)$ = 10 bar, $P(CO)$ = 10 bar, toluene, 60°C, 6 h. [c] Conversions, branched/linear (b/l) ratios and *ee* values were determined by GC analysis. The absolute configuration for the products **16a**, **19** and **22** were assigned to be *R*, *S* and *R*, respectively, by comparing the signs of their optical rotations with those of literatures.[2,3]

Table S2. The effect of CO/H_2 pressure on the AHF of vinyl acetate and styrene.

Entry	PH_2 [bar]	PCO [bar]	Styrene[a]			Vinyl acetate[a]		
			conv.(%) [b]	b/l[b]	ee (%)[b]	conv.(%) [b]	b/l[b]	ee (%)[b]
1	10	5	99	2.2	43.7	99	28.7	85.5
2	10	10	95	3.0	53.2	99	31.7	86.6
3	10	20	65	4.0	51.2	88	28.4	85.5
4	5	10	44	2.6	39.4	73	30.8	85.4
5	20	10	99	4.1	58.7	99	29.6	86.3
6	30	10	96	4.6	60.7	98	31.2	86.7
7	40	10	99	5.0	64.1	99	32.6	86.9
8	60	10	99	5.4	65.0	99	31.3	86.8

[a] Reaction conditions: [Rh] / **10b** = 1:1.5, sub./cat. = 500, [substrate] = 3.0 M, toluene, 60°C, 6 h. [b] Conversions, branched/linear (b/l) ratios and *ee* values were determined by GC analysis. The absolute configuration for the products **16a** and **19** were assigned to be *R* and *S*, respectively by comparing the signs of their optical rotations with those of literatures.[2]

Table S3. The effect of CO/H_2 pressure on the AHF of allyl cyanide.

Entry	$P(H_2)$[bar]	$P(CO)$[bar]	Allyl cyanide[a]		
			conv.(%) [b]	ee(%)[b]	b/l[b]
1	10	10	55	67	3.3
2	20	10	76	71	3.2
3	30	10	99	71	3.2
4	40	10	99	71	3.3
5	50	10	99	65	3.3
6	30	5	99	68	3.1
7	30	20	65	67	3.3

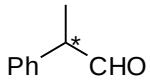
[a] Reaction conditions: [Rh] / **10b** = 1:1.5, sub./cat. = 500, [substrate] = 1.0 M, toluene, 60°C, 6 h. [c] Conversions, branched/linear (b/l) ratios and *ee* values were determined by GC analysis. The absolute configuration for the products **22** was assigned to be *R* by comparing its optical rotation with those of literatures.[3]

Table S4. Solvent effect on AHF.

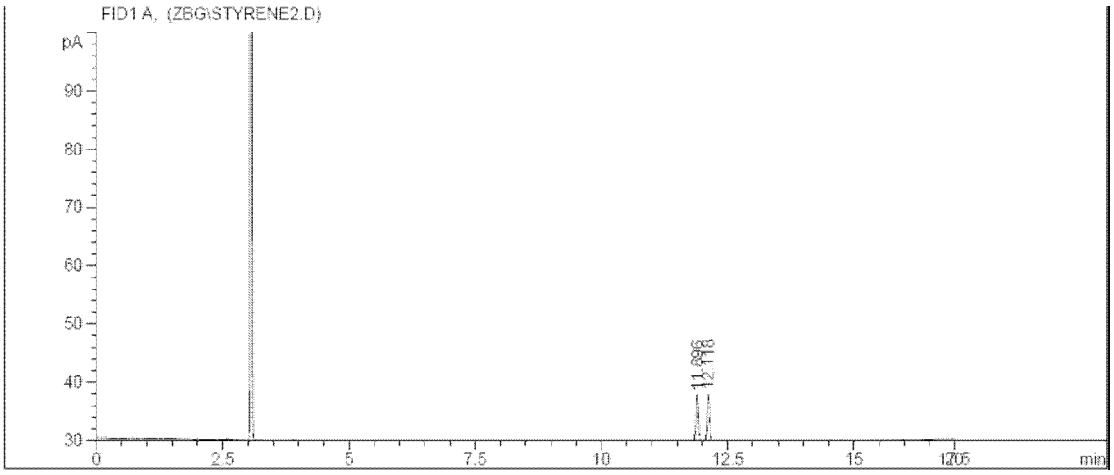
Entry	Solvent	Vinyl acetate [a]			Styrene [a]			Allyl cyanide [b]		
		conv.(%)[c]	b/l[c]	ee(%)[c]	conv.(%) [c]	b/l[c]	ee(%)[c]	conv.(%) [c]	b/l[c]	ee(%)[c]
1	Toluene	99	32.6	86.9	99	5.0	64.1	99	3.2	71.6
2	THF	92	27.9	86.9	87	5.2	65.9	99	2.9	63.8
3	Benzene	92	29.0	87.2	88	5.0	66.2	99	3.0	64.6
4	*t*-BuOMe	99	36.0	86.4	99	5.7	63.8	99	3.2	73.6
5	CH_2Cl_2	99	32.7	82.0	99	6.1	58.3	99	3.8	71.2
6[d]	Toluene	78	34.0	91.1	66	9.5	72.6	99	3.4	72.2
7[d]	*t*-BuOMe	99	40.7	91.2	99	12.2	79.1	80	3.2	76.8

[a] Reaction conditions: [Rh] / **10b** = 1:1.5, sub./cat. = 500, *P*(H_2) = 40 bar, *P*(CO) = 10 bar, [substrate] = 3.0 M, 60°C, 2 h. [b] Reaction conditions: [Rh] / **10b** = 1:1.5, sub./cat. = 500, *P*(H_2) = 30 bar, *P*(CO) = 10 bar, [substrate] = 1.0 M, 60°C, 4 h. [c] Conversions, branched/linear (b/l) ratios and *ee* values were determined by GC analysis. The absolute configuration for the products **16a**, **19** and **22** were assigned to be *R*, *S* and *R*, respectively, by comparing the signs of their optical rotations with those of literatures.[2,3] [d] Ligand **10c** is used instead of **10b**.

Chiral GC Determination of enantiomeric excess (ee) of the asymmetric hydroformylation of alkene



Supelco's Beta Dex 225 column, Temperature program: 100 ^{o}C for 5 min, then 4 ^{o}C/min to160 ^{o}C; Flow rate: 1.0 mL/min



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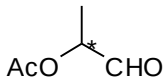
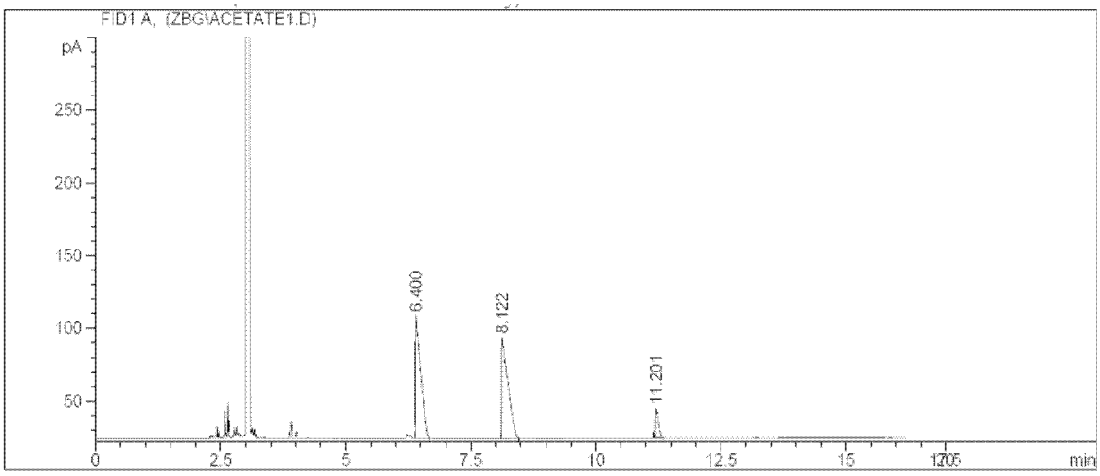
1	11.896	BB	0.0515	25.41172	7.89950	50.14239
2	12.118	BB	0.0502	25.26740	7.92249	49.85761





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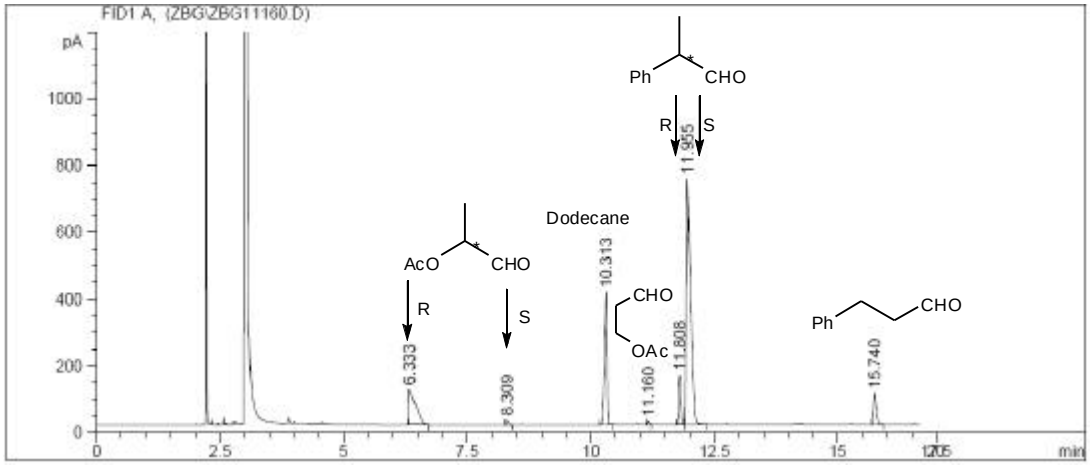
1	6.400	PB	0.0896	608.29590	83.84933	46.91278
2	8.122	PB	0.1088	610.17218	68.59573	47.05748
3	11.201	PB	0.0562	78.18480	19.76339	6.02974



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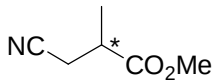
1	6.333	VB	0.1098	963.69067	106.46970	13.24250
2	8.309	BB	0.0429	44.96760	14.04241	0.61792
3	10.313	PB	0.0534	1467.92236	396.77274	20.17137
4	11.160	PV	0.0384	24.88945	9.63238	0.34202
5	11.808	BV	0.0481	462.26807	148.49254	6.35223
6	11.955	VB	0.0709	3952.01245	738.47760	54.30635
7	15.740	BB	0.0524	361.50546	92.44598	4.96761



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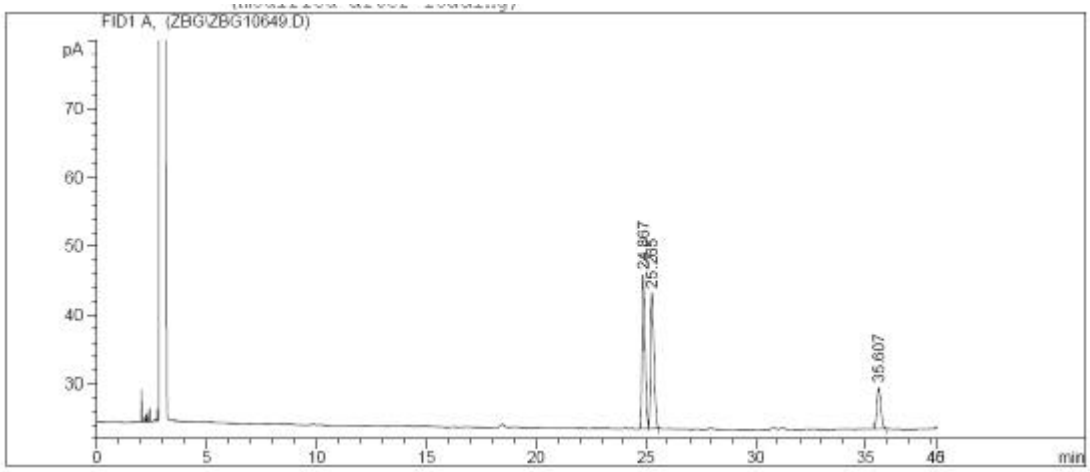

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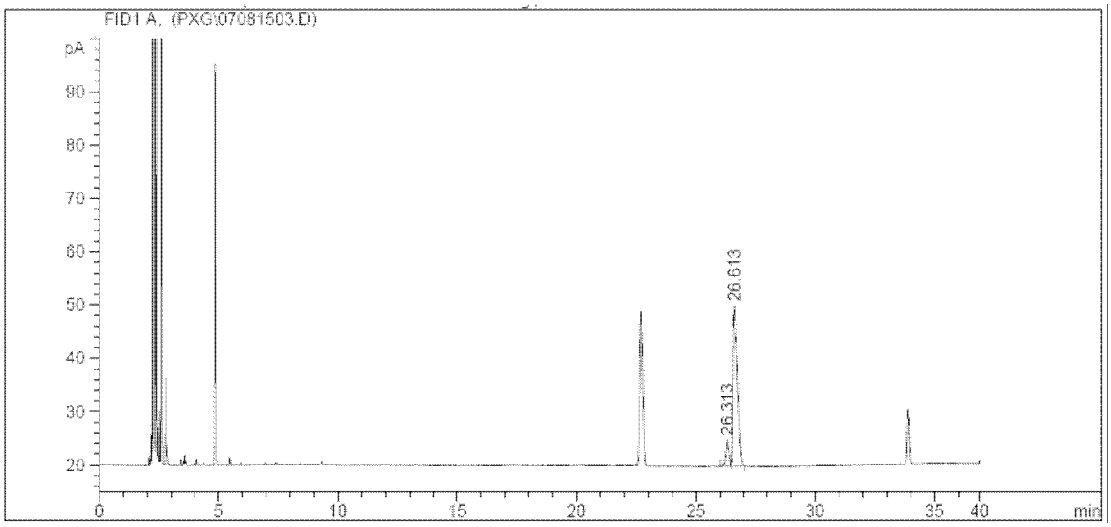
3	35.607	BB	0.1529	77.28188	5.97588	15.05649



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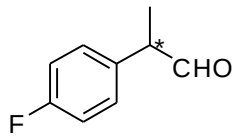
2	26.613	VB	0.1407	358.45407	29.93555	89.63362



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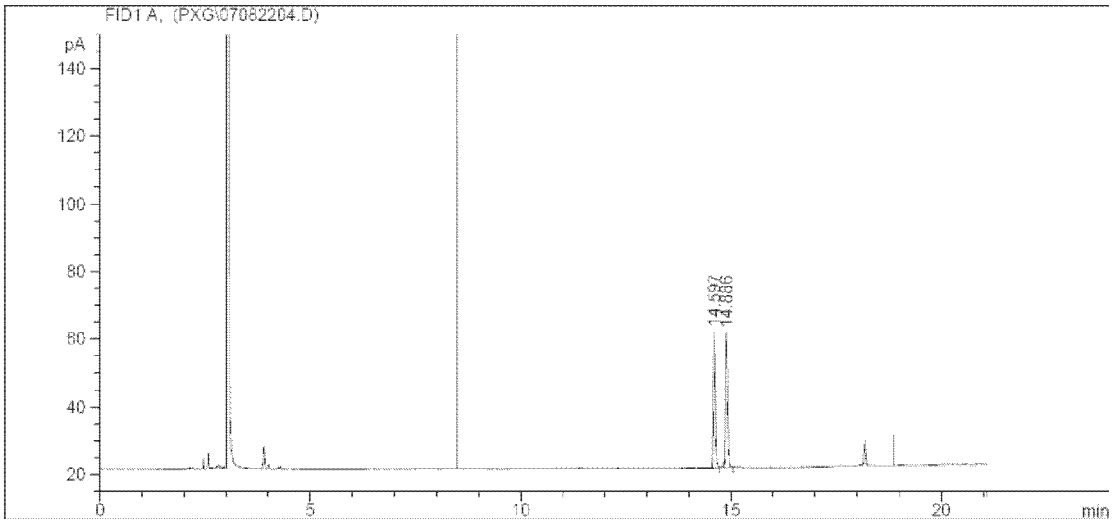

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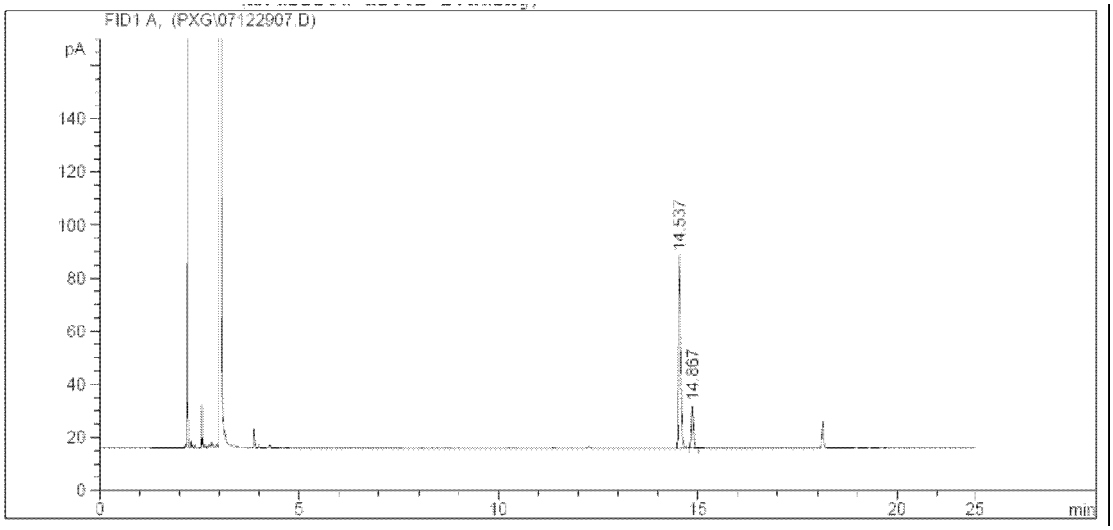
2	14.886	VB	0.0498	134.33340	39.92525	50.14578



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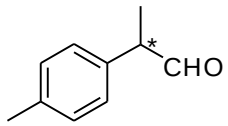
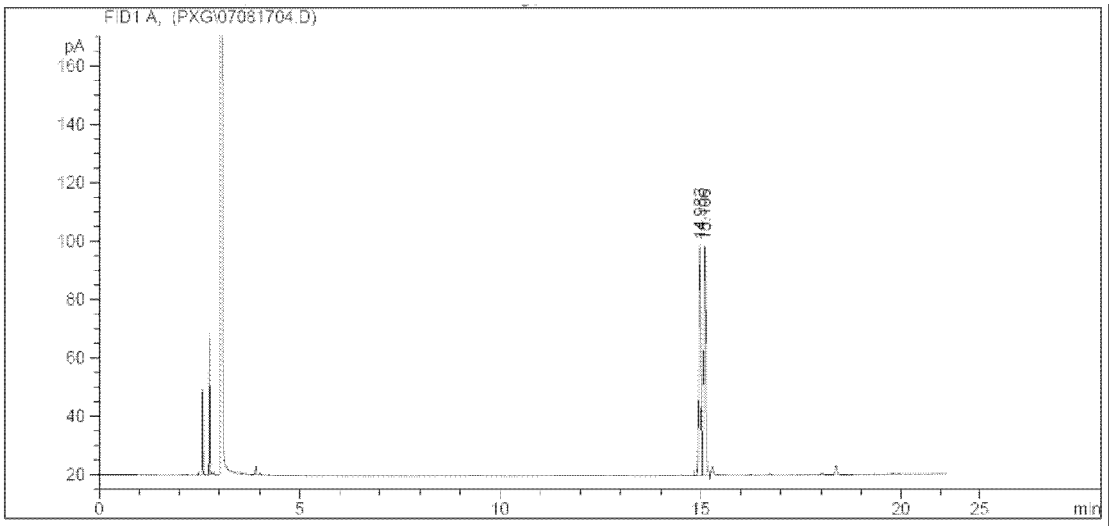


Supelco's Beta Dex 225 column, Temperature program: 100 ^{o}C for 5 min, then 4 ^{o}C/min to160 ^{o}C; Flow rate: 1.0 mL/min



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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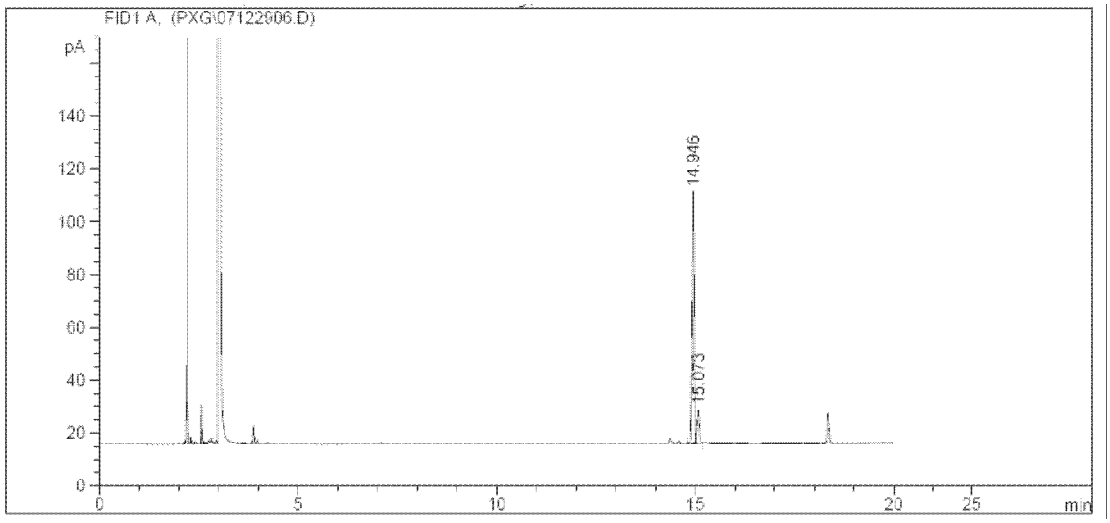
2	15.106	VV	0.0562	287.90646	78.64988	51.43200



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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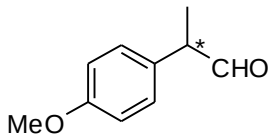
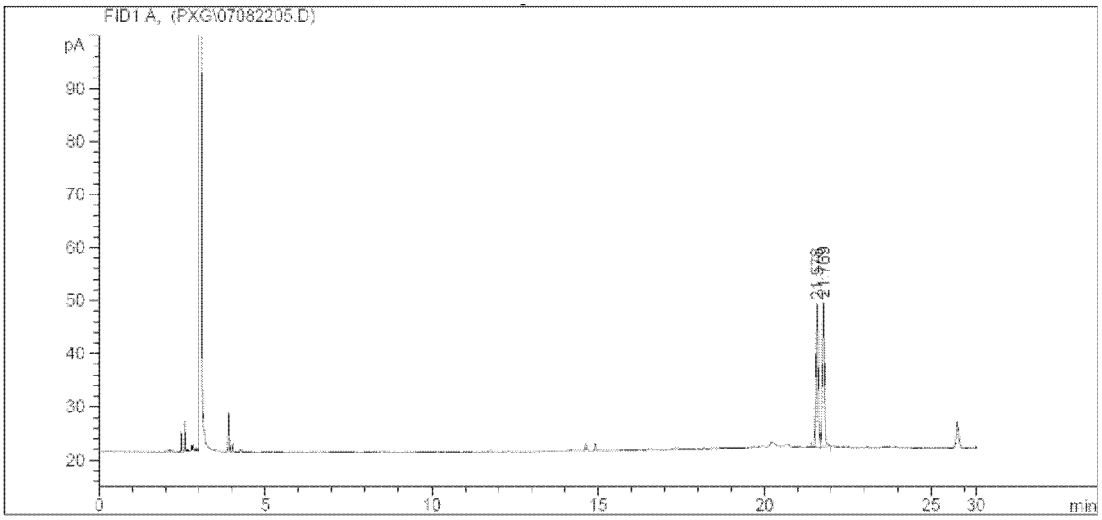


Supelco's Beta Dex 225 column, Temperature program: 100 ^{o}C for 5 min, then 4 ^{o}C/min to160 ^{o}C; Flow rate: 1.0 mL/min



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1	21.579	BV	0.0641	110.11284	26.68889	48.95564
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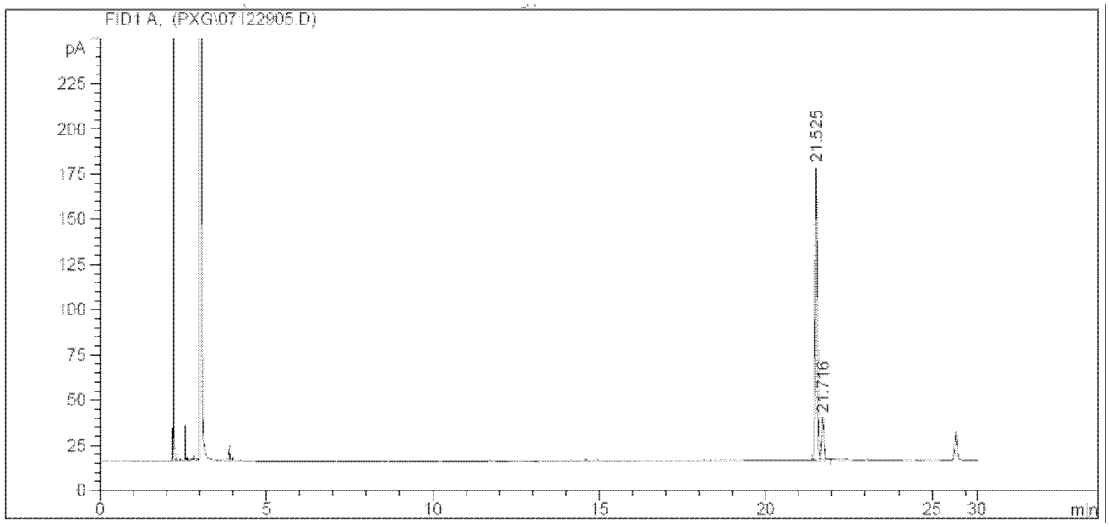

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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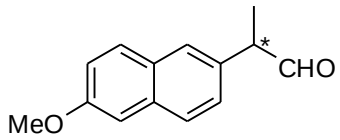
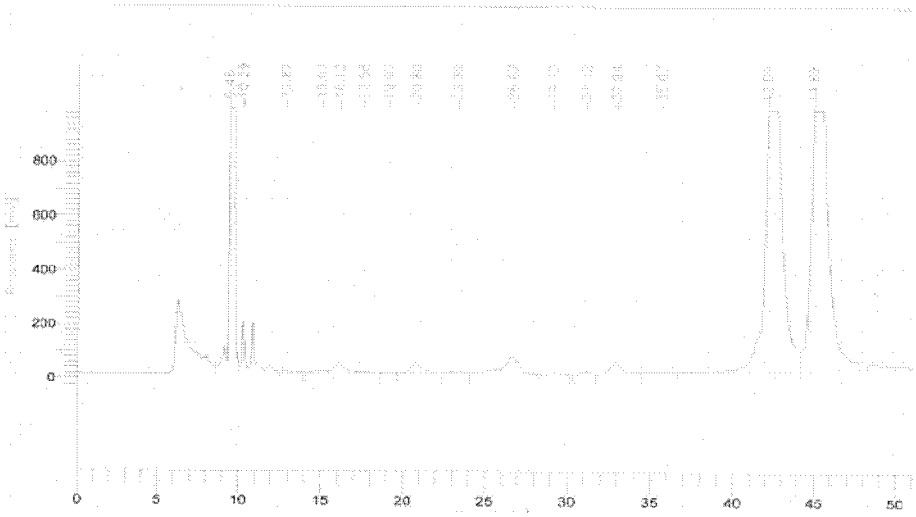
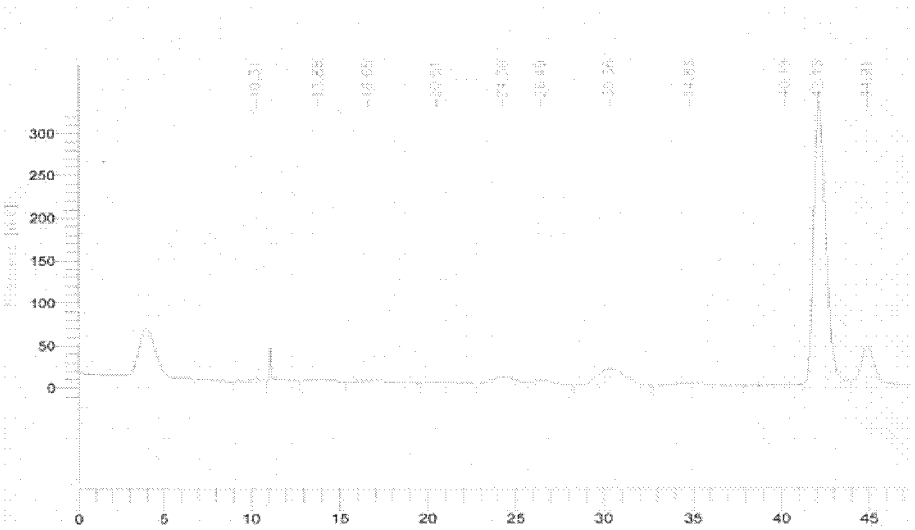
2	21.716	VB	0.0676	107.89881	23.26287	13.63249



HPLC (column, chiraipak IC; eluent, hexane/2-propanol = 99/1; room temperature; flow rate, 0.5mL/min, detection, 214nm UV)



Peak #	Time [min]	Area [uv*sec]	Height [uv]	Area [%]	BL
15	42.092	74971544.21	970113.19	39.62	VV
16	44.892	76754382.92	964064.97	40.57	VB



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10	42.127	16347426.10	328076.60	68.37	VV
11	44.906	2955451.30	48180.47	12.36	VB

References

[1] a) M. T. Reetz, D. Moulin, A. Gosberg, *Org. Lett*. **2001**, *3*, 4083-4085; b) M. T. Reetz, A. Gosberg, *Tetrehedron: Asymmetry* **1999**, *10*, 2129-2137.

[2] a) G. Consiglio, P. Pino, L. I. Flowers, Jr, C. U. Pittman, *J. Chem. Soc. Chem. Commun*. **1983**, 612-613; b) S. G. Cohen, J. Crossley, E. Khedouri, R. Zand, L. H. Klee, *J. Am. Chem. Soc.* **1963**, *85*, 1685-1691.

[3] Z.-F. Xie, H. Suemune, K. Sakai, *Tetrehedron: Asymmetry* **1993**, *4*, 973-980.