Supplementary Material (ESI) for Chemical Communications

Room Temperature Synthesis of Enantioenriched Non-Protected Cyanohydrins Using Vanadium(salalen) Catalyst

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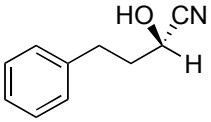
General Information

All reactions were carried out in oven-dried glassware with magnetic stirring. ^{1}H and ^{13}C NMR spectra were measured on a JEOL AL-400 or EX-270 spectrometer. Tetramethylsilane (TMS) served as the internal standard (0 ppm) for ^{1}H NMR and $CDCl_3$ was used as the internal standard (77.0 ppm) for ^{13}C NMR. Optical rotations were measured on a JASCO P-1020 polarimeter. All aldehydes and acetone cyanohydrin were purified by distillation or sublimation before use. The spectroscopic data of all the cyanohydrins were in agreement with those reported in the literature[1-5] and only their optical rotation values are given.

General Procedure for Asymmetric Cyanation of Aliphatic Aldehydes with Acetone Cyanohydrin Using V(salalen) 2

Vanadium(salalen) complex **2** (0.7 mg, 0.2 mol%) was dissolved in CH_2Cl_2 (1.0 mL) under molecular oxygen. Then, aldehyde (0.5 mmol) and acetone cyanohydrin (229 μL, 2.5 mmol) were added and the reaction mixture was stirred at 25 ˚C. After the reaction completion, the mixture was quenched by 1N HCl and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were evaporated in vacuo and the residue was chromatographed on silica gel (*n*-hexane/*i*-Pr_2O = 2:1) to give the cyanohydrin. The enantiomeric excess was determined by GC or HPLC analysis after conversion to the corresponding acetate or benzoate.

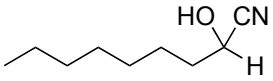
(*S*)-2-hydroxy-4-phenylbutanenitrile[1]



95% yield, 89% *ee*[*]
(SUPELCO BETA-DEX 325, 140°C (1 min) – 2 °C/min – 170 °C)
$[\alpha]_D^{21}$ +6.8 (c=1.83, $CHCl_3$)
[lit.[1] $[\alpha]_D^{27}$ –6.38 (c=1.03, $CHCl_3$), 85% ee, (*R*)-isomer]

[*] Determined after conversion to the corresponding acetate.

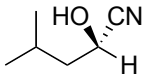
2-hydroxynonanenitrile[1]



92% yield, 91% *ee*[*]
(SUPELCO BETA-DEX 325, 130 °C (30 min) – 45 °C/min – 175 °C)
$[\alpha]_D^{21}$ –3.2 (c=0.80, $CHCl_3$)

[*] Determined after conversion to the corresponding acetate.

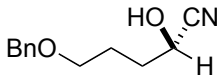
(*S*)-2-hydroxy-4-methylpentanenitrile[2]



87% yield, 89% *ee**
(SUPELCO BETA-DEX 325, 120 °C)
$[\alpha]_D^{20}$ –24.3 (c=0.80, $CHCl_3$)
[lit.[2] $[\alpha]_D^{20}$ –24.9 (c=1.5, $CHCl_3$), 92% ee, (*S*)-isomer]

* Determined after conversion to the corresponding acetate.

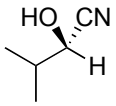
5-(benzyloxy)-2-hydroxypentanenitrile[3]



87% yield,* 89% *ee*
(DAICEL CHIRALPAK AD-H , hexane/*i*PrOH 98:2)

* Isolated by PTLC using CH_2Cl_2 as eluent.

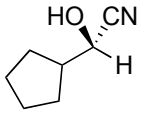
(*S*)-2-hydroxy-3-methylbutanenitrile[5]



85% yield, 94% *ee**
(DAICEL CHIRALCEL OJ-H, hexane/*i*PrOH 98:2)
$[\alpha]_D^{23}$ –15.1 (c=0.93, $CHCl_3$)
[lit.[5] $[\alpha]_D^{19}$ –15.4 (c=2.1, $CHCl_3$), 90% ee, (*S*)-isomer]

* Determined after conversion to the corresponding benzoate.

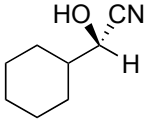
(*S*)- 2-cyclopentyl-2-hydroxyacetonitrile[6]



92% yield, 92% *ee**
(SUPELCO BETA-DEX 325, 130 °C)
$[\alpha]_D^{23}$ –10.4 (c=1.15, $CHCl_3$)
[lit.[6] $[\alpha]_D^{25}$ +11.2 (c=1.0, $CHCl_3$), 94% ee, (*R*)-isomer]

* Determined after conversion to the corresponding acetate.

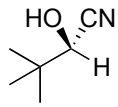
(*S*)- 2-cyclohexyl-2-hydroxyacetonitrile[1]



92% yield, 95% *ee**
(SUPELCO BETA-DEX 325, 130 °C)
$[\alpha]_D^{23}$ –9.5 (c=0.77, $CHCl_3$)
[lit.[1] $[\alpha]_D^{27}$ +8.12 (c=0.77, $CHCl_3$), 79% ee, (*R*)-isomer]

* Determined after conversion to the corresponding acetate.

(*S*)- 3,3-dimethyl-2-hydroxybutanenitrile[1]



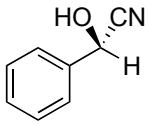
89% yield, 93% *ee**
(DAICEL CHIRALCEL OJ-H, hexane/*i*PrOH 99:1)
$[\alpha]_D^{21}$ –21.6 (c=0.90, $CHCl_3$)
[lit.[1] $[\alpha]_D^{28}$ +16.82 (c=1.17, $CHCl_3$), 72% ee, (*R*)-isomer]

* Determined after conversion to the corresponding benzoate.

General Procedure for Asymmetric Cyanation of Aromatic Aldehydes with Acetone Cyanohydrin Using V(salalen) 2

Vanadium(salalen) complex **2** (3.7 mg, 1 mol%) was dissolved in CH_2Cl_2 (0.5 mL) and acetone cyanohydrin (458 μL, 5.0 mmol) was added under molecular oxygen and the reaction mixture was stirred for 6 h at 25 ˚C. After aging for 6 h, aldehyde (0.5 mmol) in CH_2Cl_2 (0.5 mL) was added and the reaction mixture was stirred at 25 ˚C for 10 min. The mixture was quenched by 1N HCl, and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were evaporated in vacuo and the crude cyanohydrin was treated with Ac_2O (236 μL, 3.0 mmol), pyridine (242 μL, 3.0 mmol) and a catalytic amount of 4-(*N,N*-dimethylamino)pyridine in CH_2Cl_2 (1.0 mL) at 0 ˚C. After 1.5 h, the reaction was quenched by water and the aqueous phase was extracted with CH_2Cl_2.The combined organic phases were evaporated in vacuo and the residue was chromatographed on silica gel (*n*-hexane/AcOEt = 20:1) to give the acetylated cyanohydrin. The enantiomeric excess was determined by GC analysis (SUPELCO BETA-DEX 325) An analytical sample of non-protected cyanohydrins was obtained by thin layer chromatography of the crude product on Silica gel 60 F_{254}-coated glass plates (Merck).

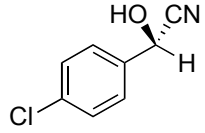
(*S*)-2-hydroxy-2-phenylacetonitrile[1]



74% yield,* 93% *ee**
(SUPELCO BETA-DEX 325, 140 °C (1 min) – 1 °C/min – 160°C)
$[\alpha]_D^{22}$ −41.9 (c=0.50, $CHCl_3$)
[lit.[1] $[\alpha]_D^{27}$ +28.94 (c=1.00, $CHCl_3$), 63% ee, (*R*)-isomer]

* Determined after conversion to the corresponding acetate.

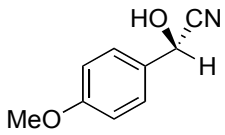
(*S*)-2-hydroxy-2-(*p*-chlorophenyl)acetonitrile[7]



75% yield,* 91% *ee**
(SUPELCO BETA-DEX 325, 140 °C (1 min) – 2 °C/min – 175°C)
$[\alpha]_D^{20}$ −37.6 (c=1.47, $CHCl_3$)
[lit.[7] $[\alpha]_D^{20}$ –28.5 (c=1.10, $CHCl_3$), 70% ee, (*S*)-isomer]

* Determined after conversion to the corresponding acetate.

(*S*)-2-hydroxy-2-(*p*-methoxyphenyl)acetonitrile[1]



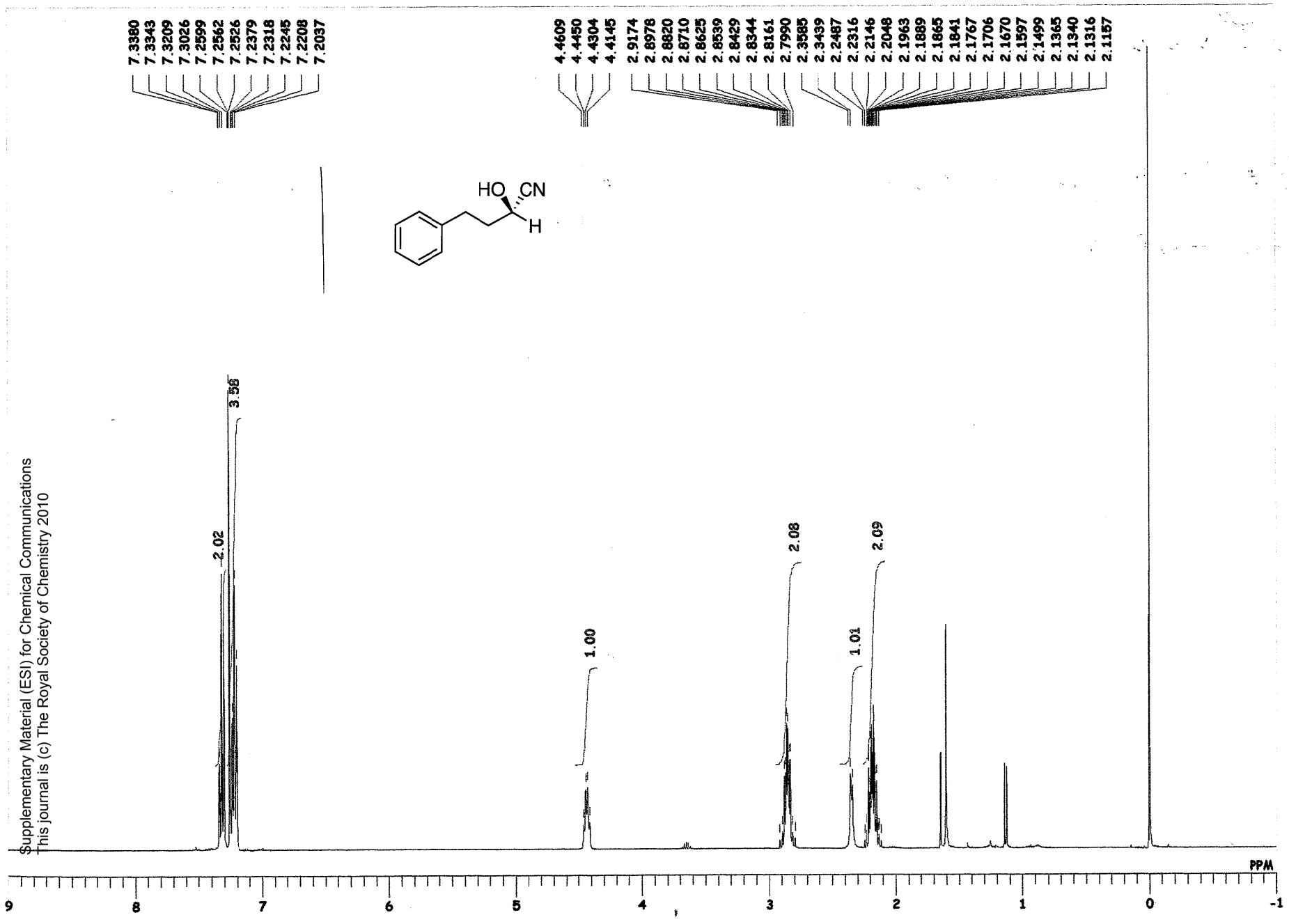
17% yield,* 93% *ee**
(SUPELCO BETA-DEX 325, 175 °C)
$[\alpha]_D^{20}$ −43.6 (c=1.25, $CHCl_3$)
[lit.[2] $[\alpha]_D^{20}$ –38.3 (c=1.04, $CHCl_3$), 81% ee, (*S*)-isomer]

* Determined after conversion to the corresponding acetate.

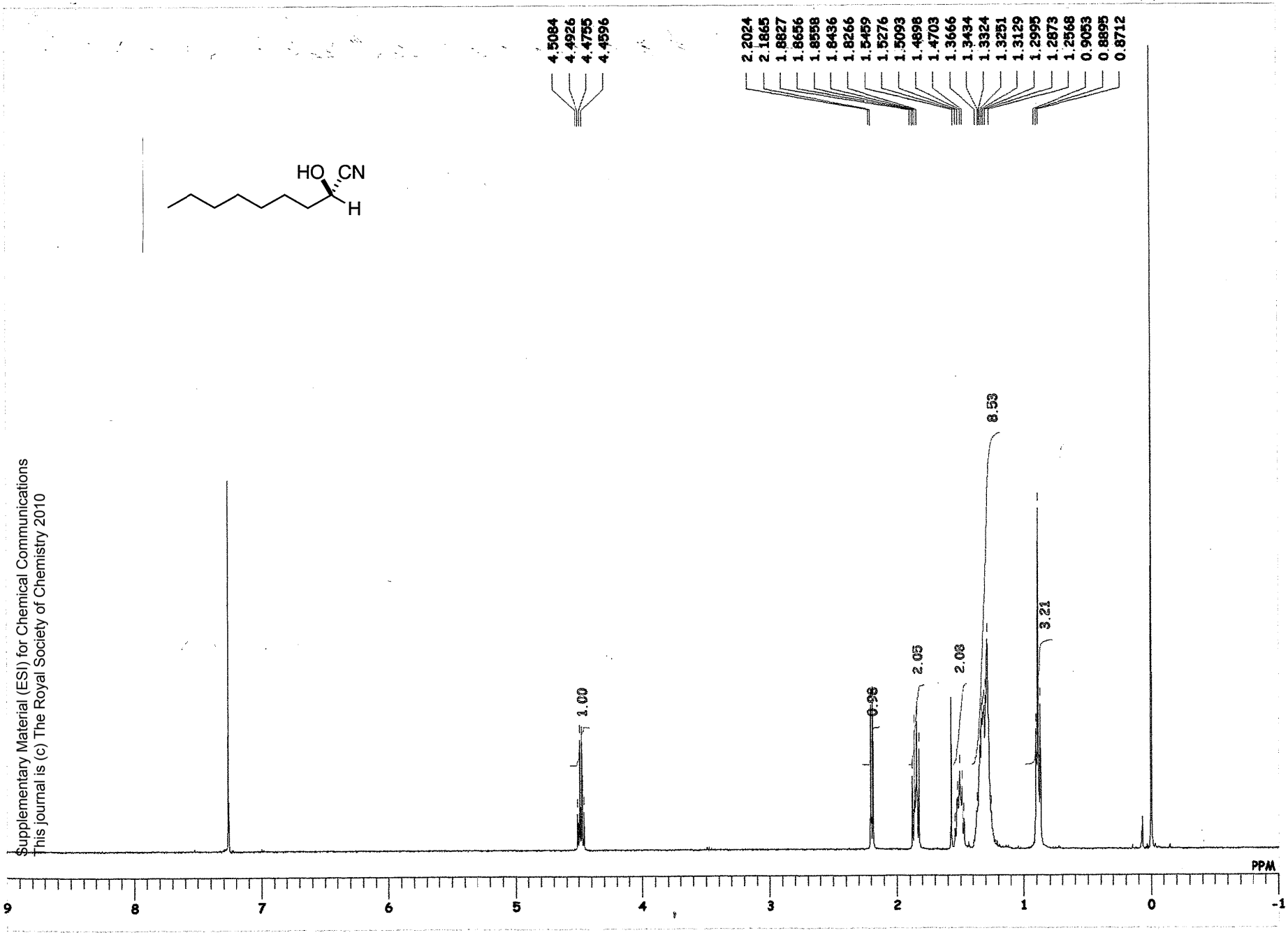
References and Notes

[1] T. Ooi, T. Miura, K. Takaya , H. Ichikawa, K. Maruoka, *Tetrahedron* **2001**, *57*, 867-863.
[2] F. Effenberger, J. Roos, *Tetrahedron: Asymmetry* **2000**, *11,* 1085-1095.
[3] G. Roda, S. Riva, B. Danieli, *Tetrahedron: Asymmetry* **1999**, *10,* 3939-3949.
[4] V. N. Belov, S. M. Korneev, J. Angerer, A. de Meijere, *Eur. J. Org. Chem.* **2008**, 4417-4425.
[5] Y. Hamashima, D. Sawada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **1999**, *121*, 2641-2642.
[6] S. Nanda, Y. Kato, Y. Asano, *Tetrahedron: Asymmetry* **2006**, *17,* 735-741.
[7] Z. Zeng, G. Zhao, Z. Zhou, C. Tang, *Eur. J. Org. Chem*. **2008**, 1615-1618.

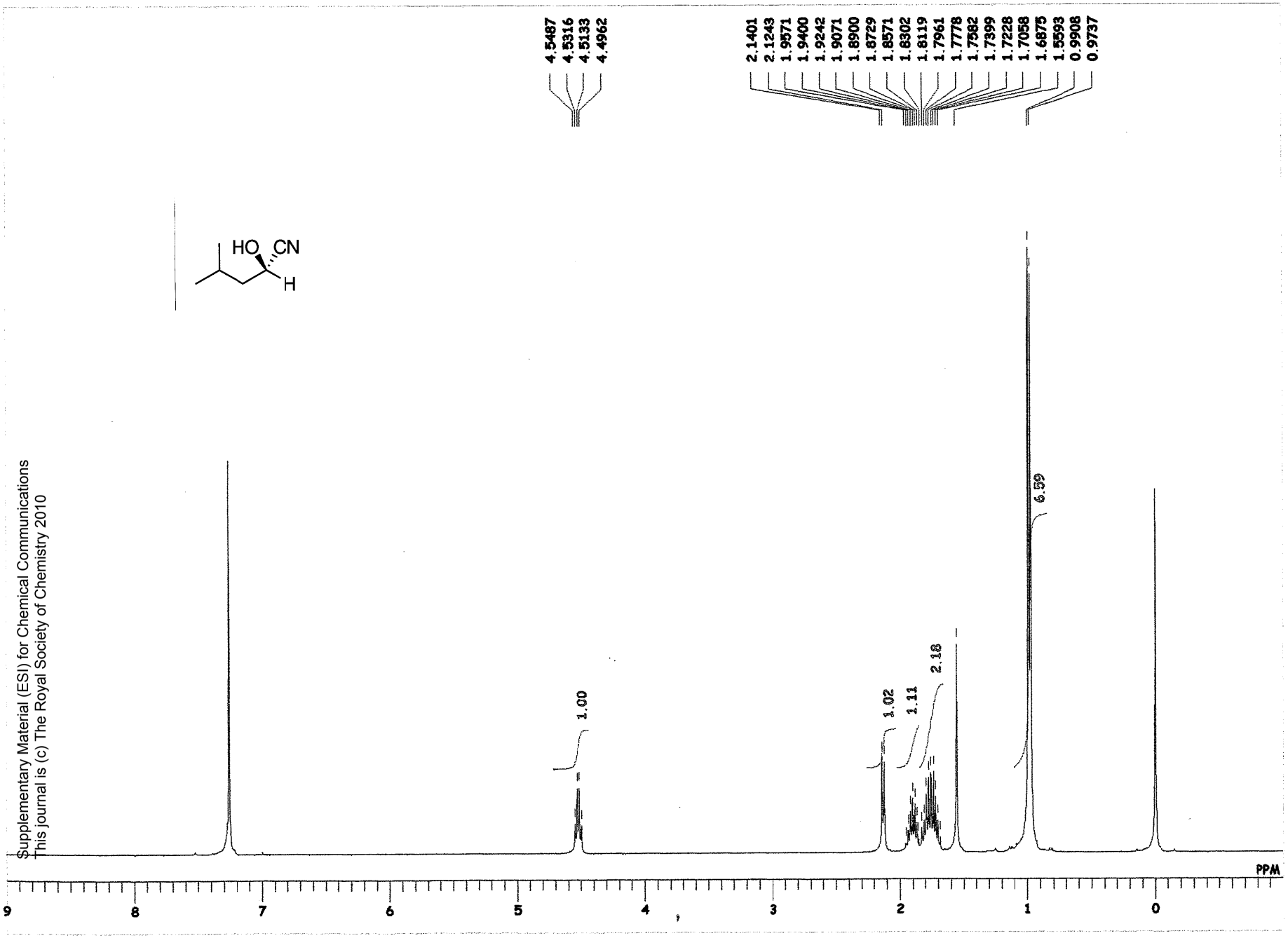
2-hydroxy-4-phenylbutanenitrile



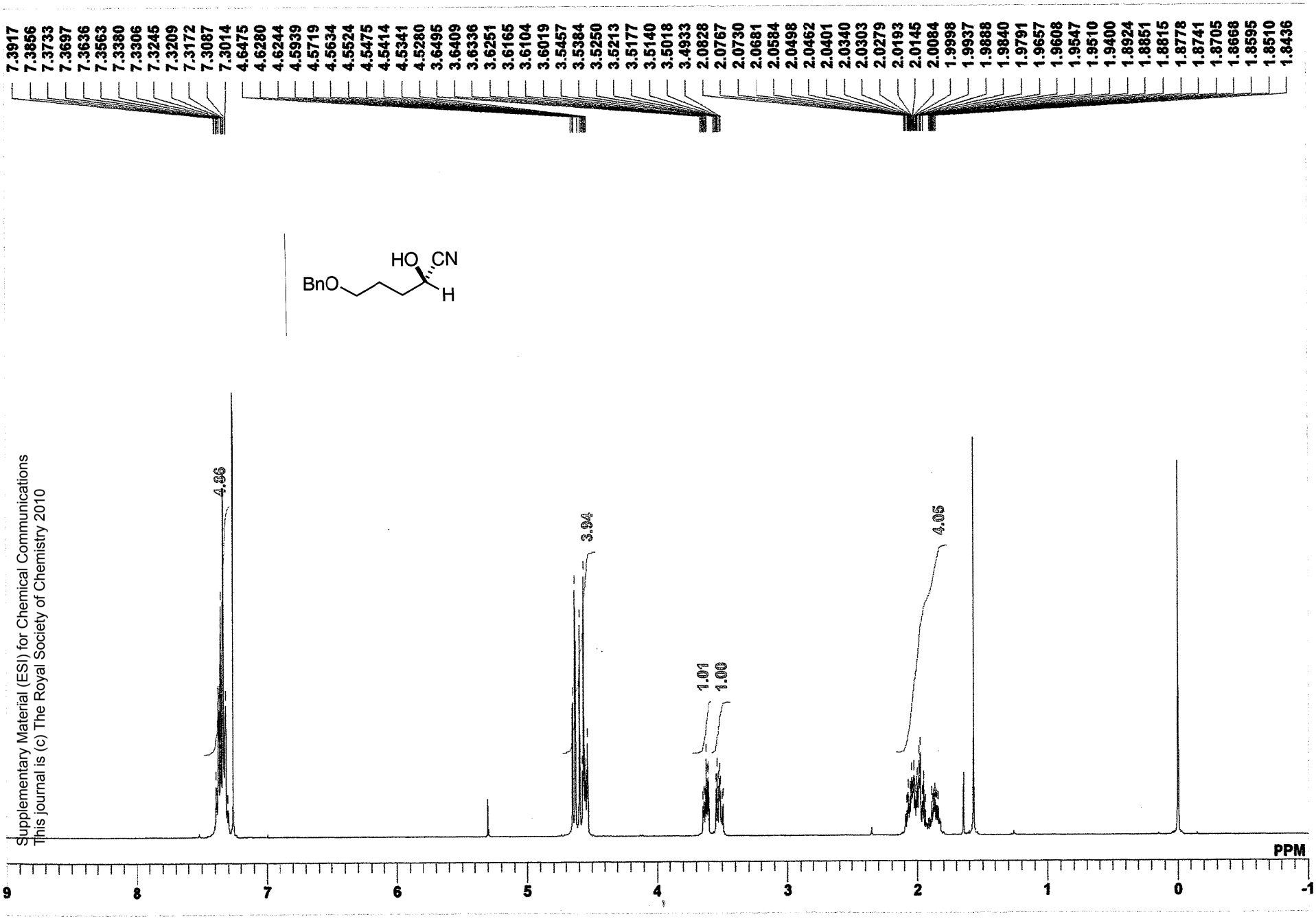
2-hydroxynonanenitrile



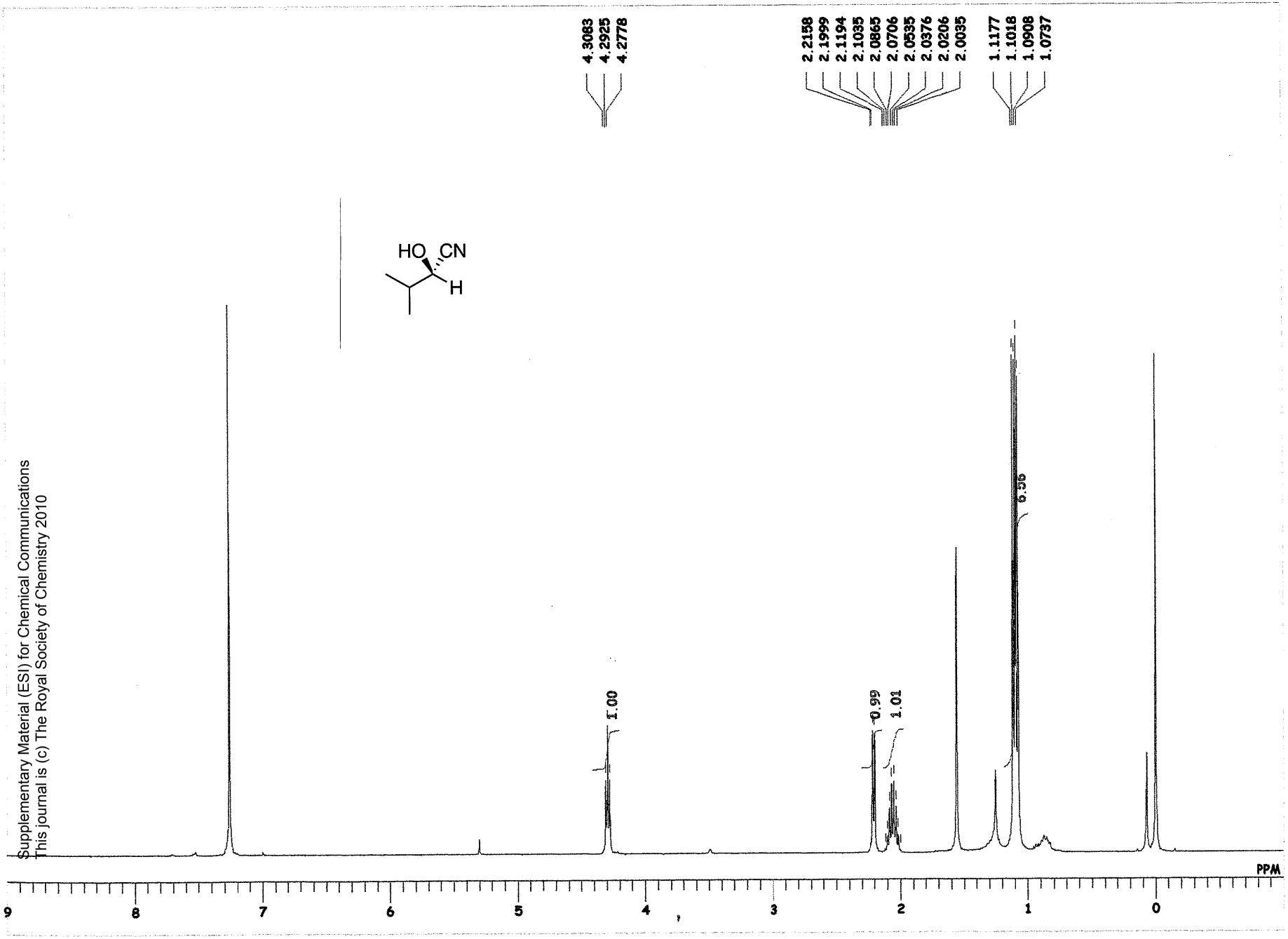
2-hydroxy-4-methylpentanenitrile



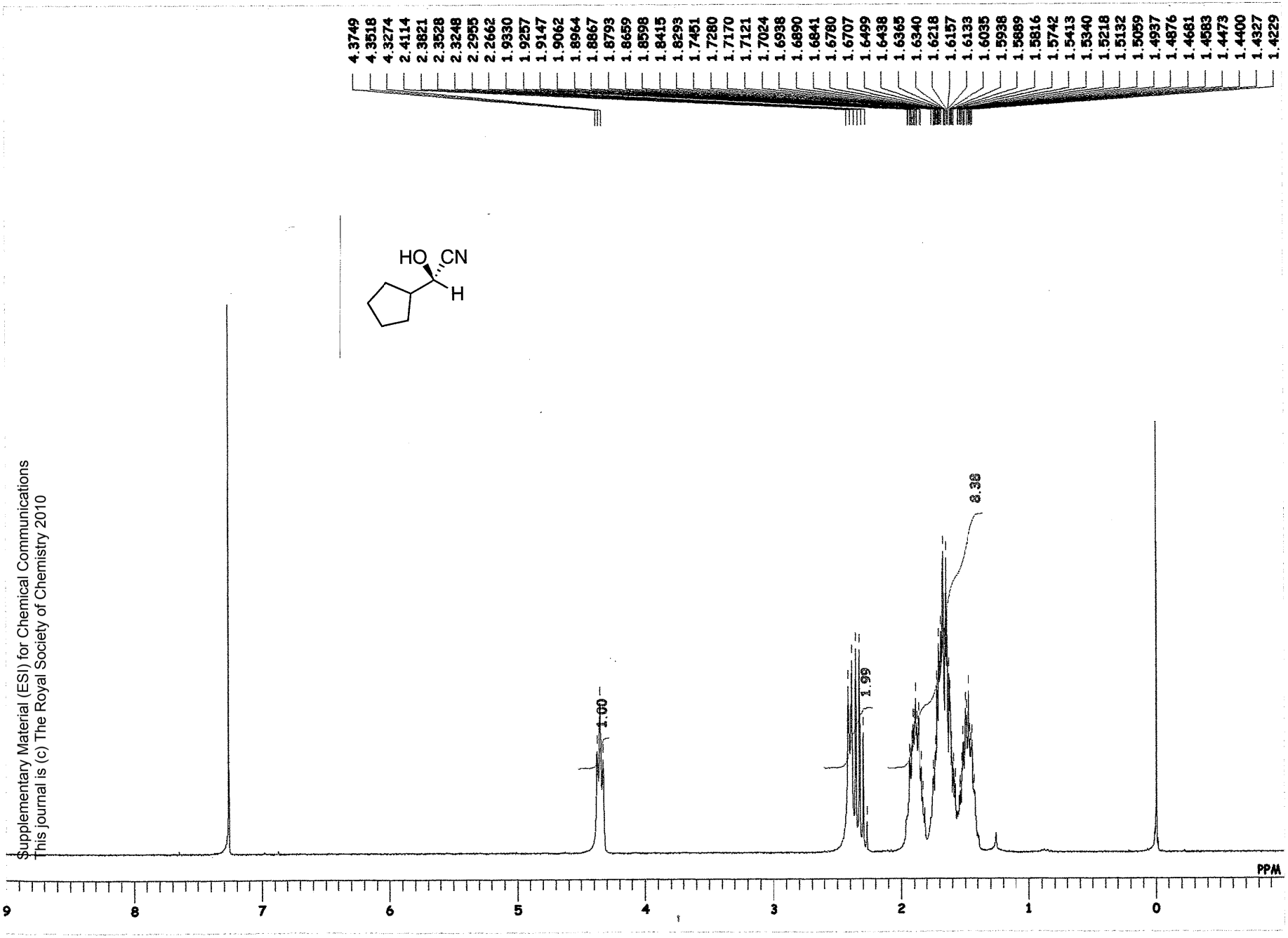
5-(benzyloxy)-2-hydroxypentanenitrile



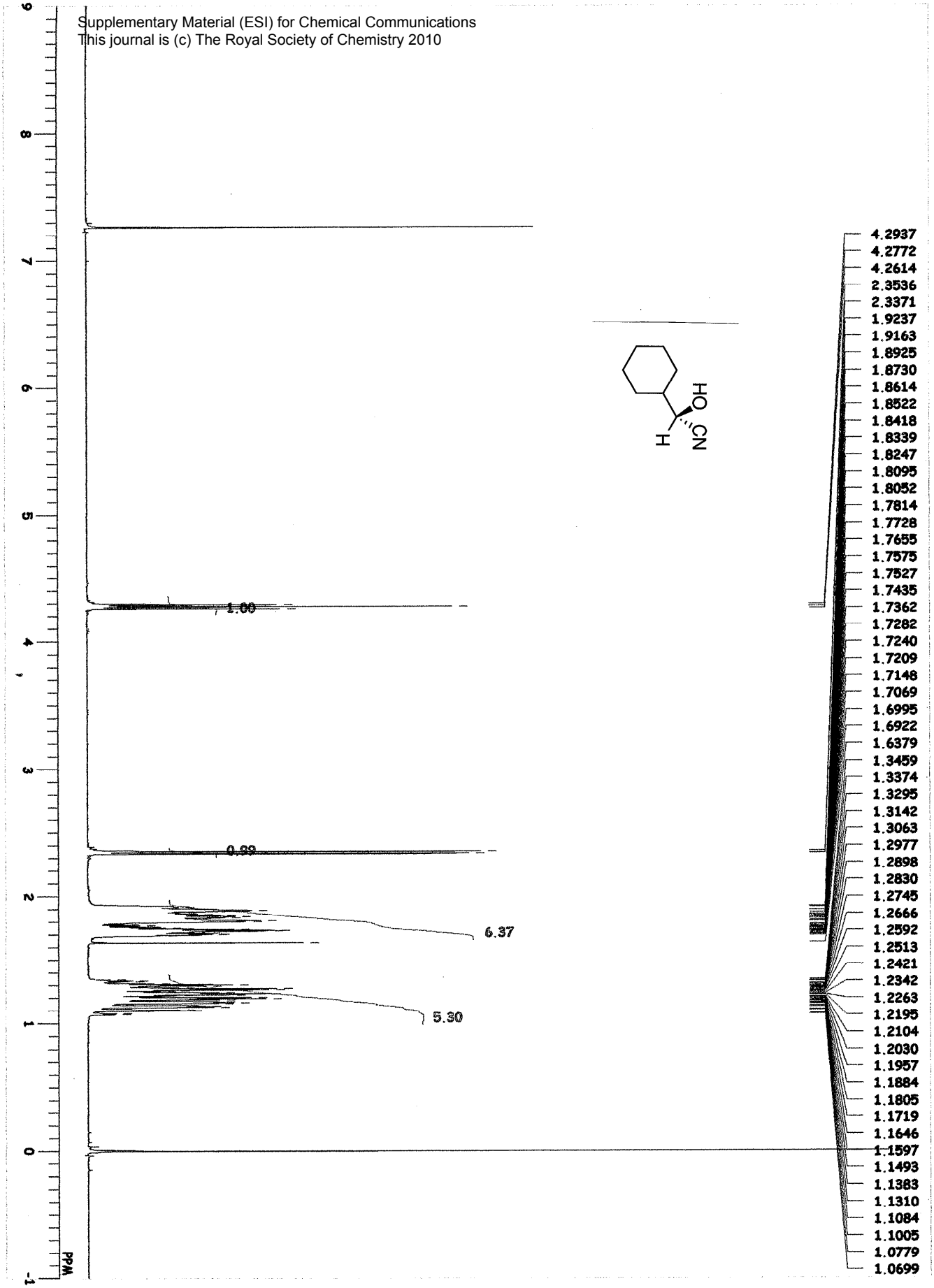
2-hydroxy-3-methylbutanenitrile



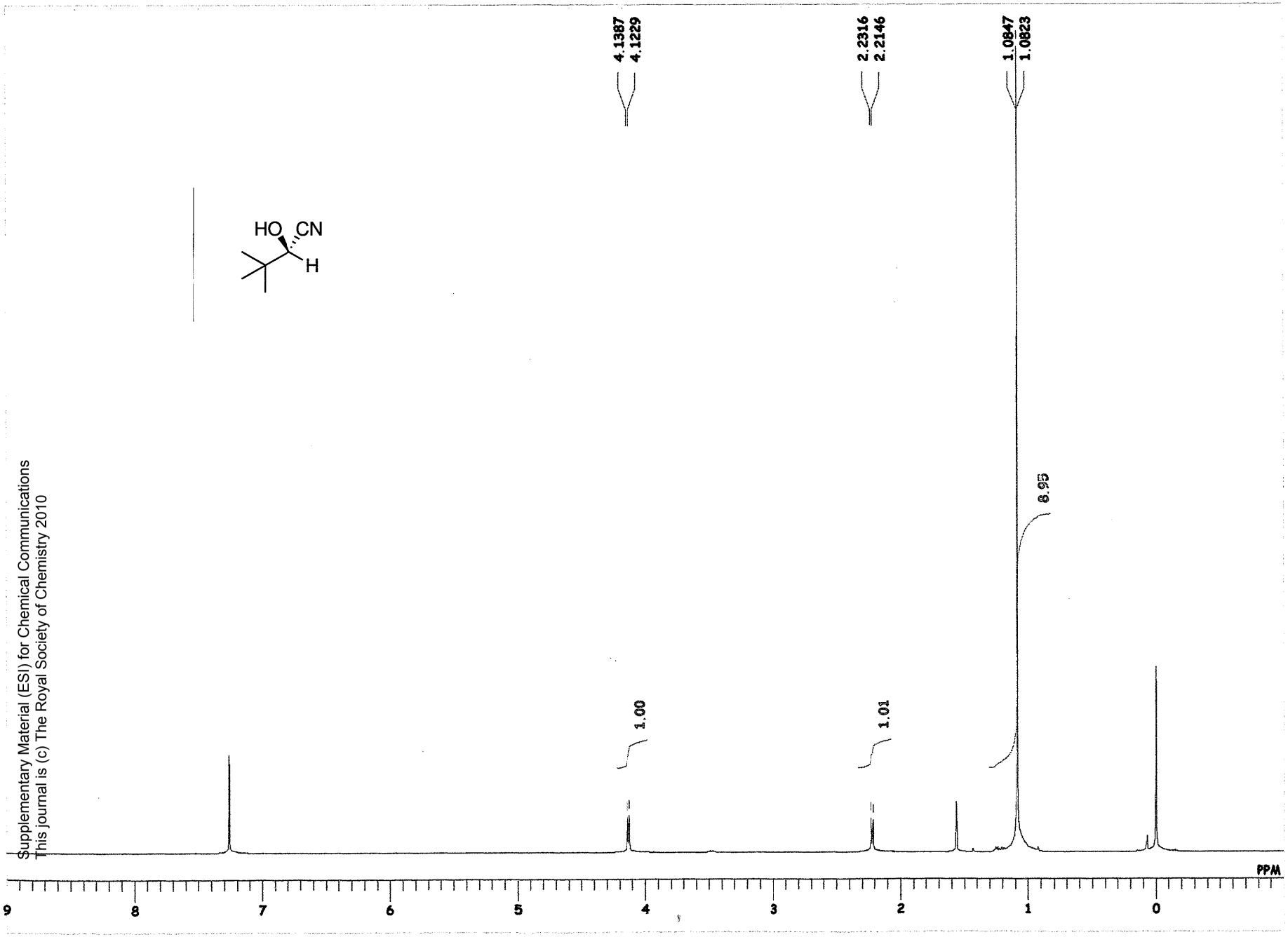
2-cyclopentyl-2-hydroxyacetonitrile



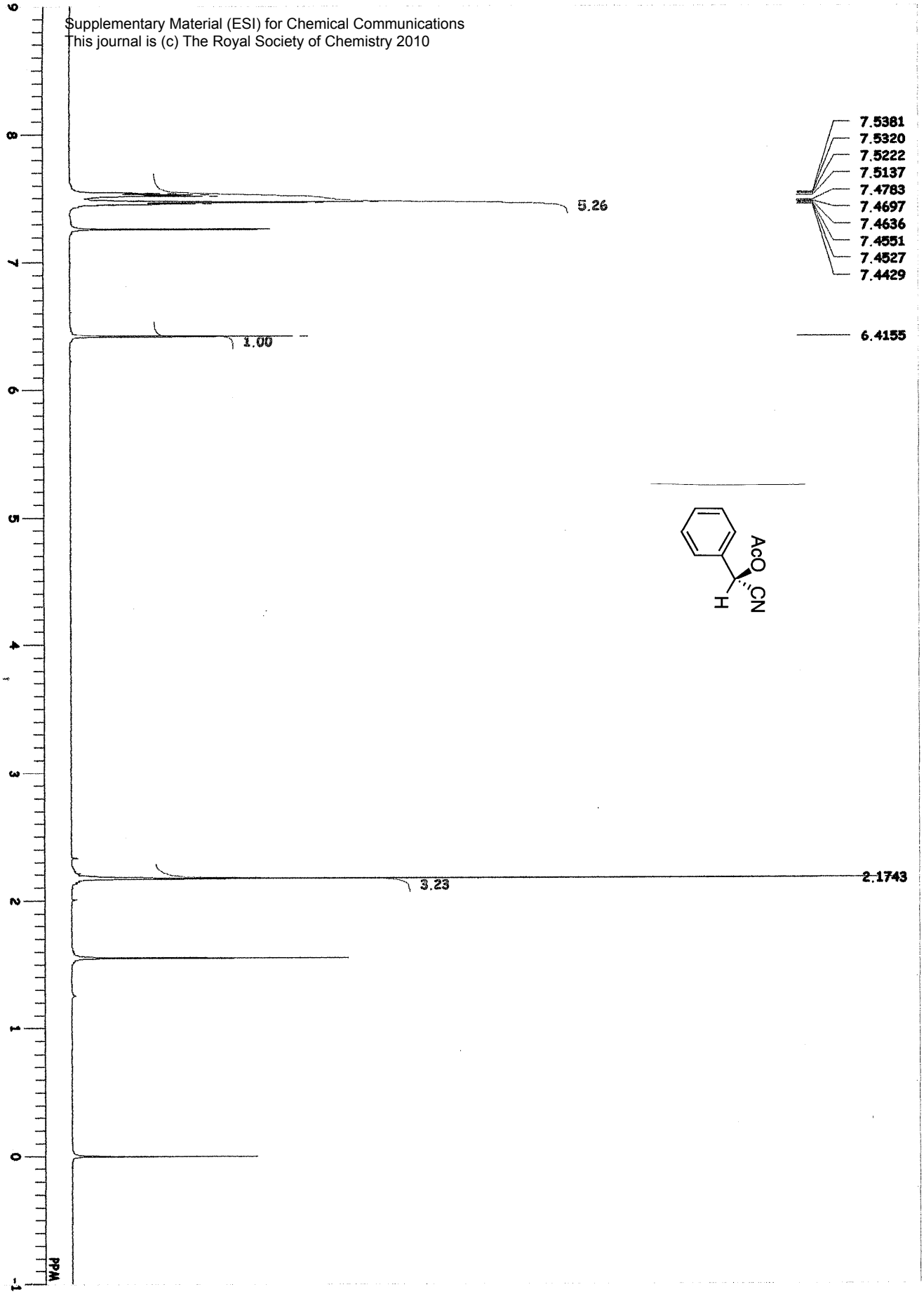
2-cyclohexyl-2-hydroxyacetonitrile



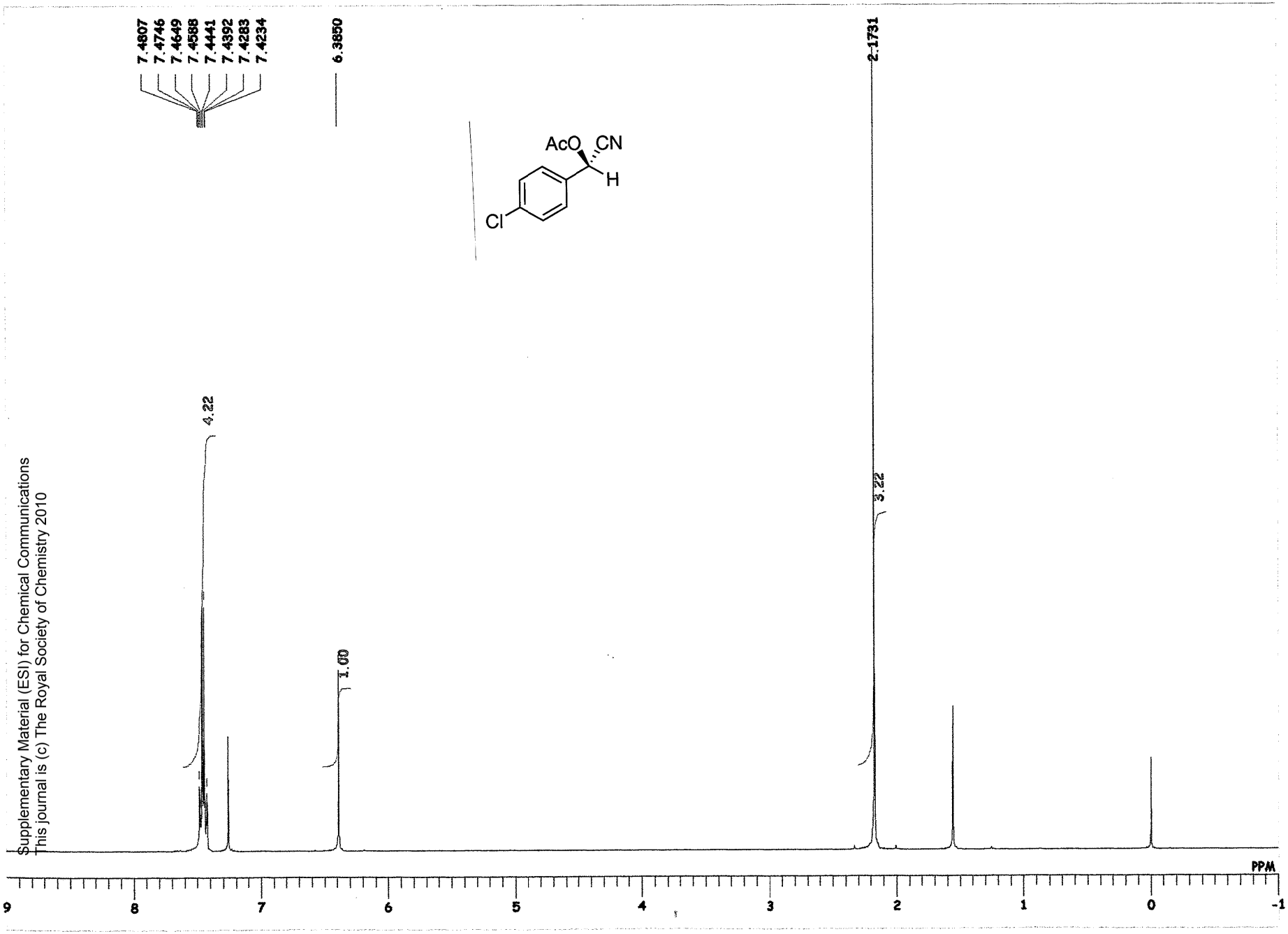
3,3-dimethyl-2-hydroxybutanenitrile



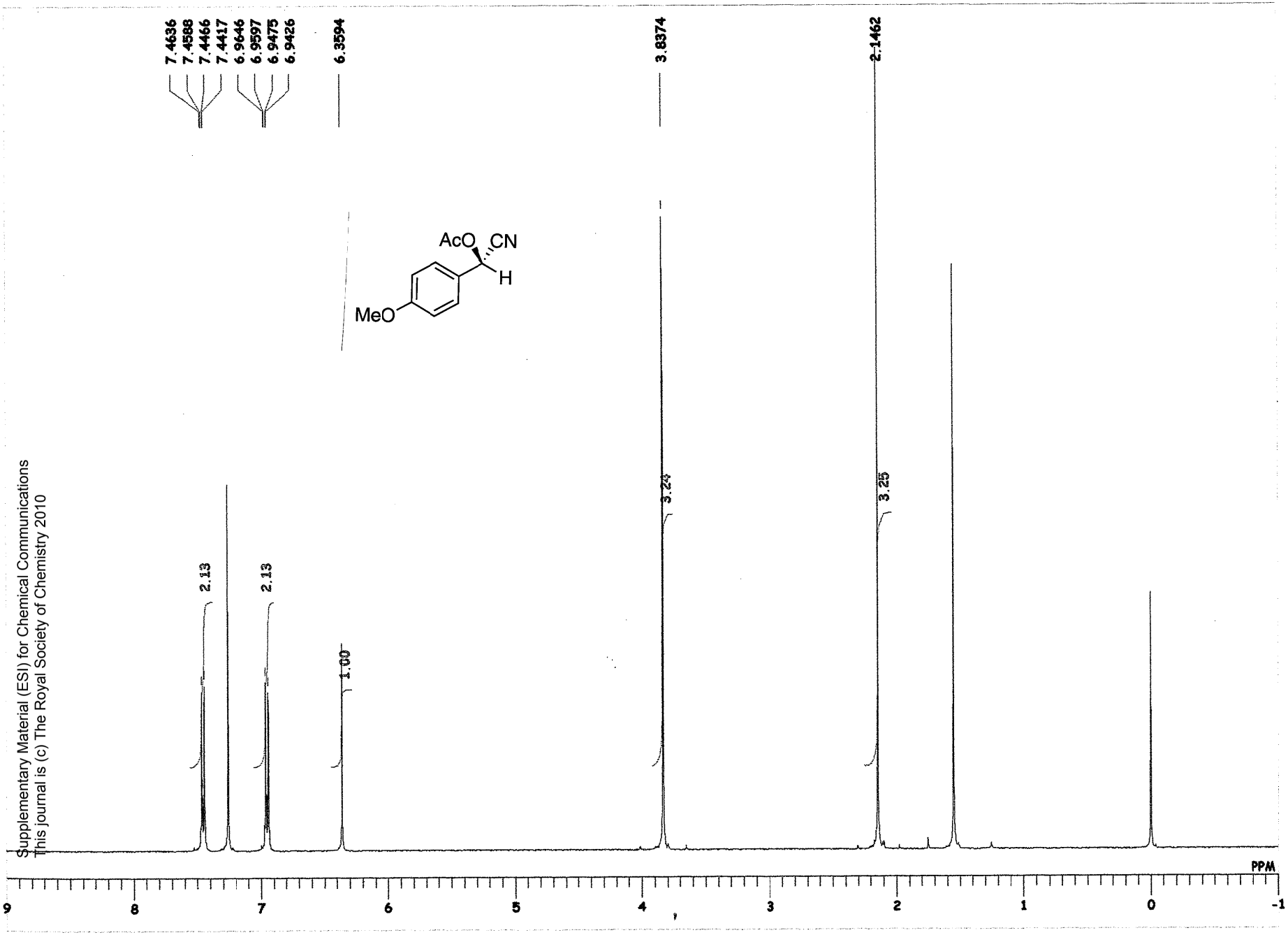
2-acetoxy-2-phenylacetonitrile



2-acetoxy-2-(p-chlorophenyl)acetonitrile



2-acetoxy-2-(p-methoxyphenyl)acetonitrile



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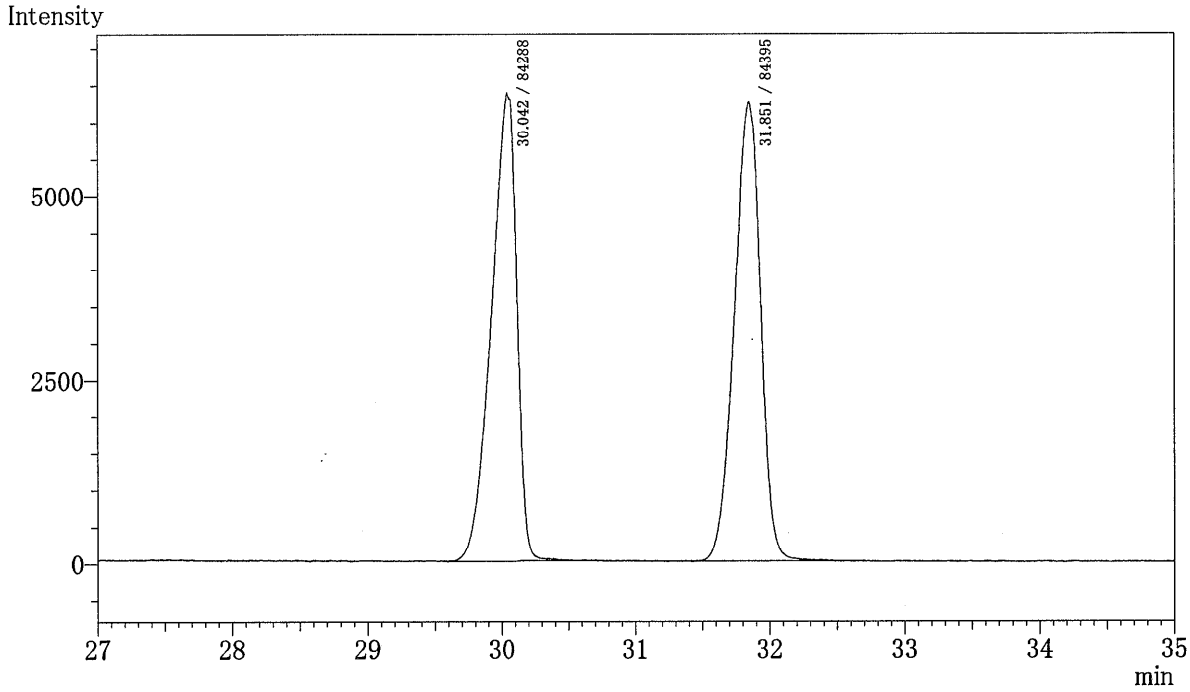

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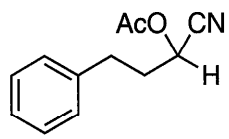

racemic

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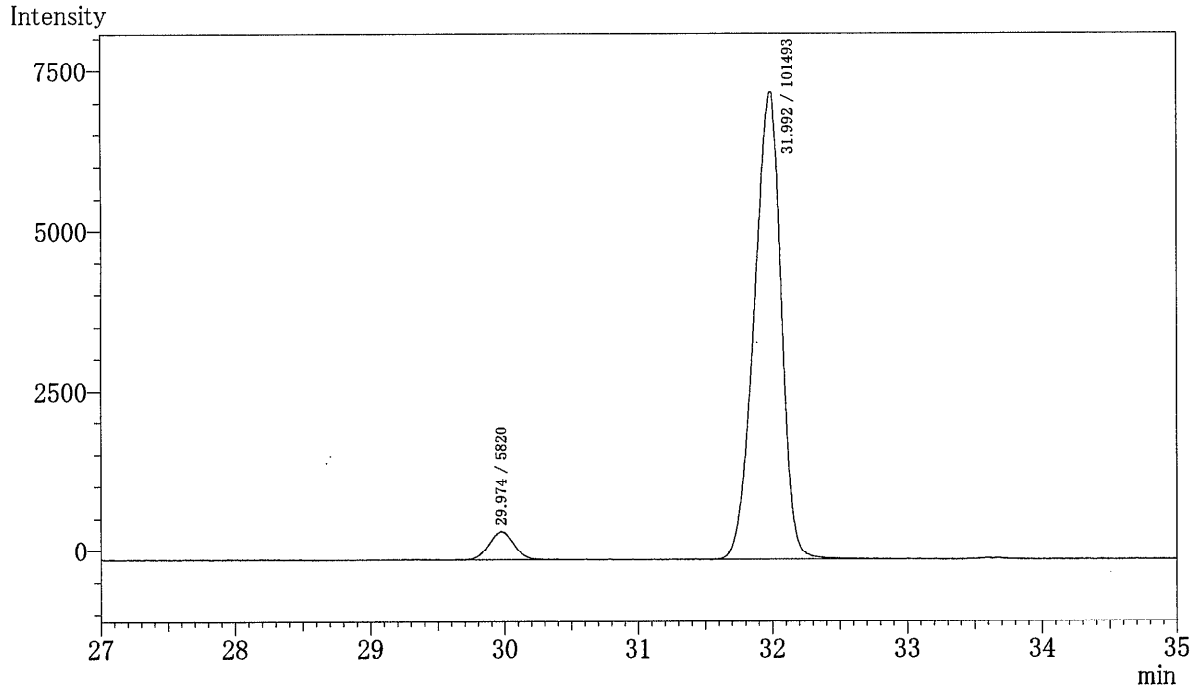

保持時間	面積	面積%
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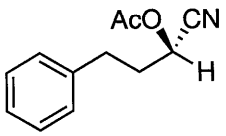

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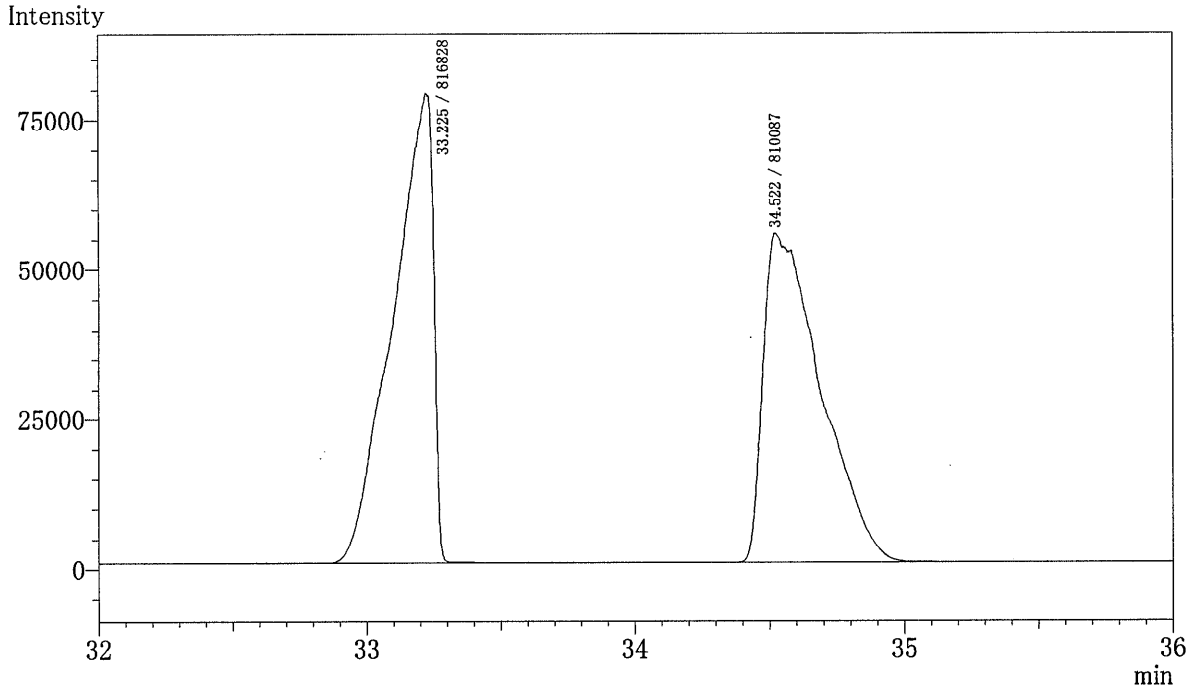

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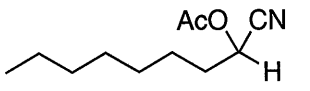

racemic

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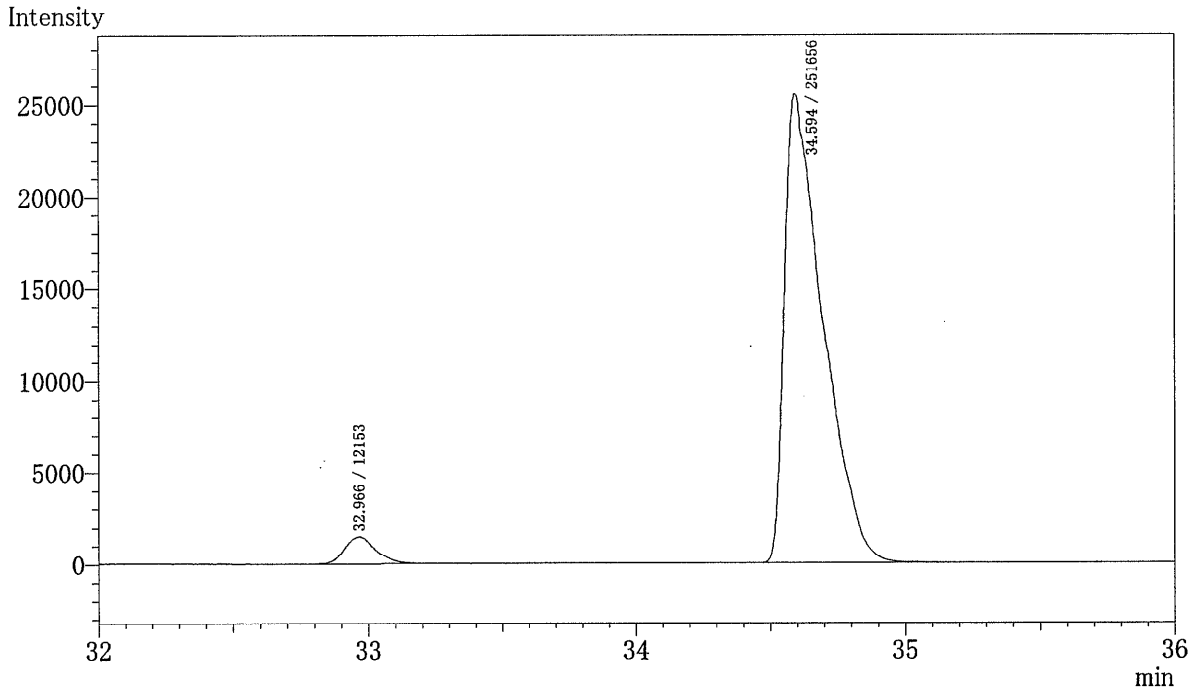

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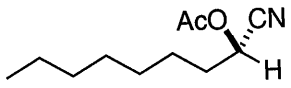

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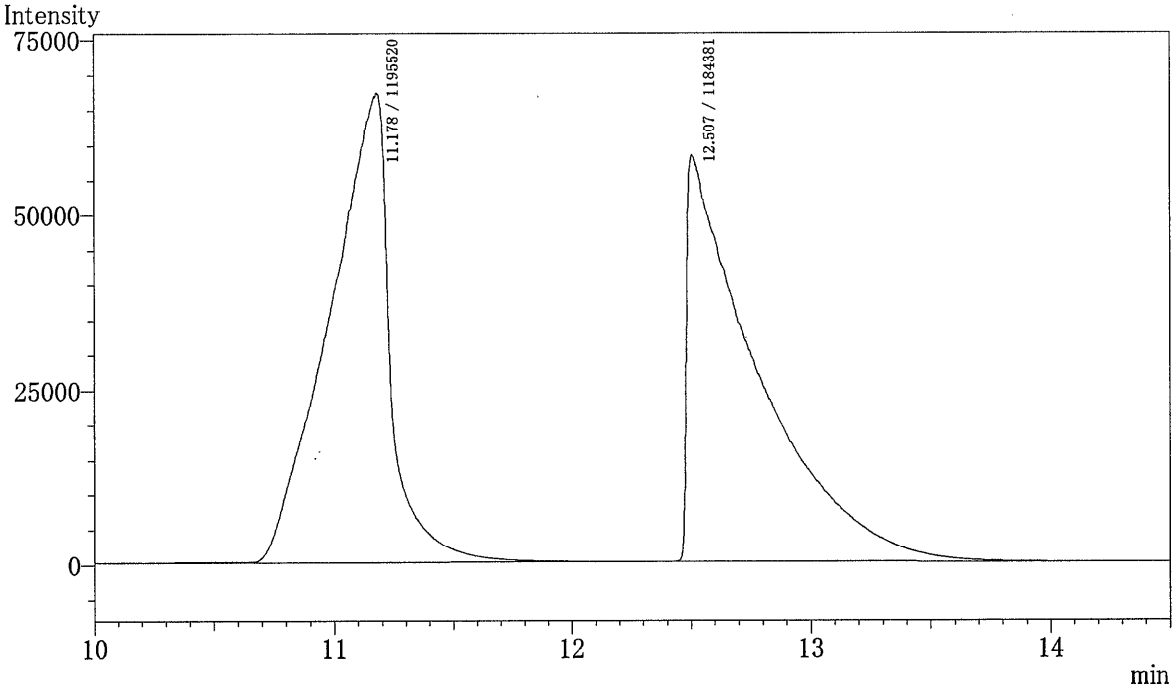

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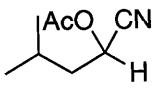

racemic

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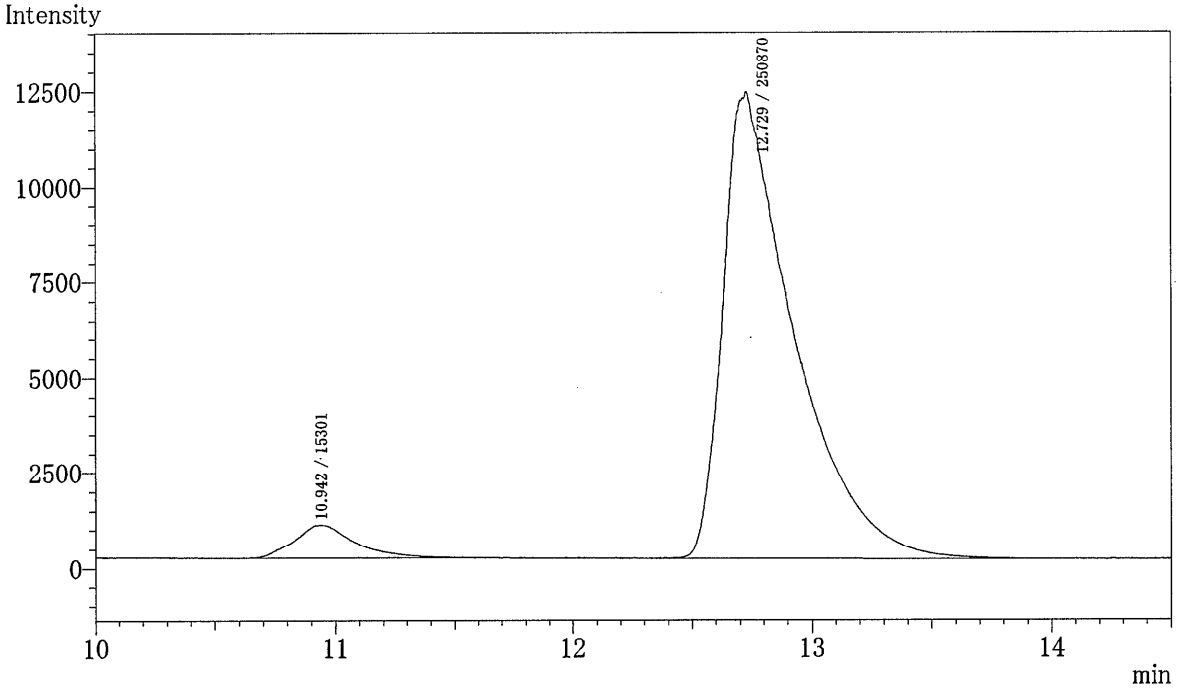

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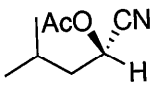
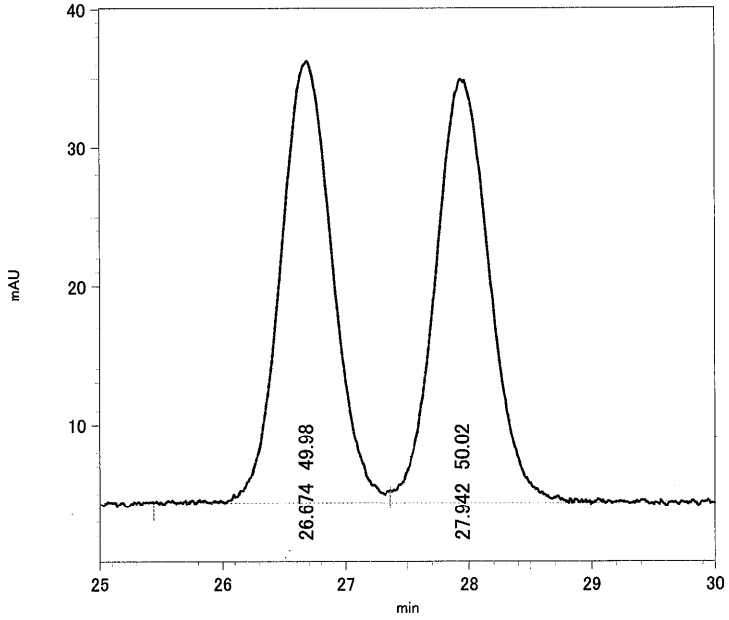


Column: CHIRALPAK AD-H
Eluent: hexane/iPrOH 98/2
Flow Rate: 1.0 mL/min
Press.: 43 kgf
Temp.: 35 degree



検出器 A-210 nm

保持時間	面積	面積%
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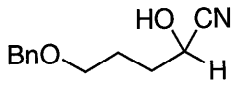
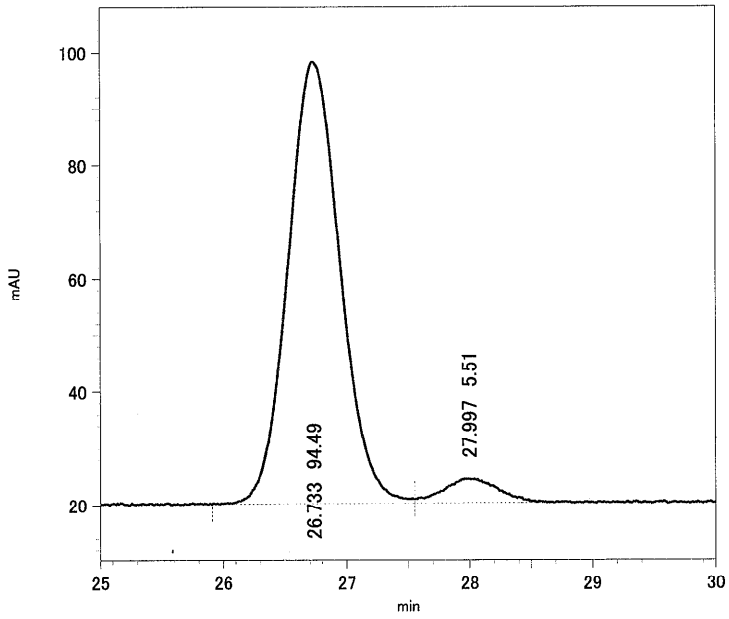
27.942	931833	50.02

Total	1862781	100.00



racemic

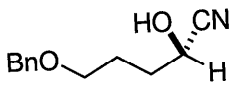
Column: CHIRALPAK AD-H
Eluent: hexane/iPrOH 98/2
Flow Rate: 1.0 mL/min
Press.: 43 kgf
Temp.: 35 degree



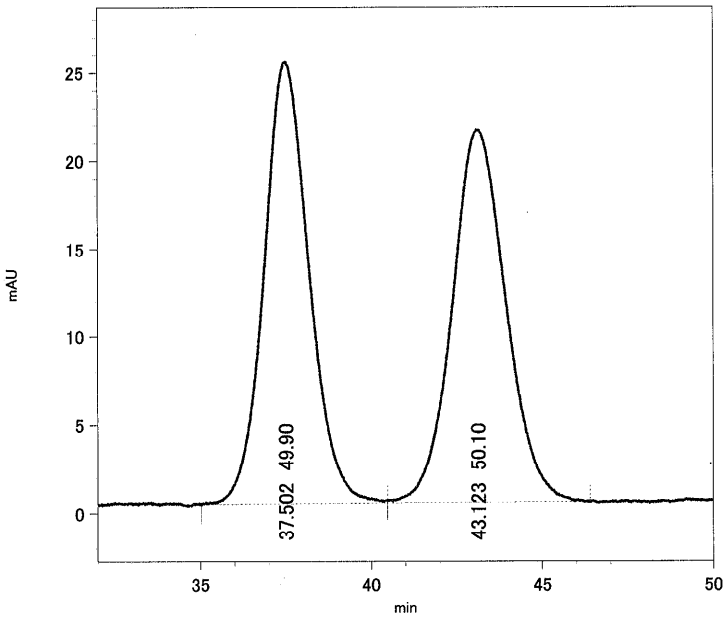
検出器 A-210 nm

保持時間	面積	面積%
26.733	2286173	94.49
27.997	133251	5.51

Total	2419423	100.00



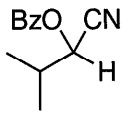
Column: CHIRALCEL OJ-H
Eluent: hexane/iPrOH 98/2
Press.: 14 kgf
Flow Rate: 0.25 mL/min
Temp.: 25 degree



検出器 A-254 nm

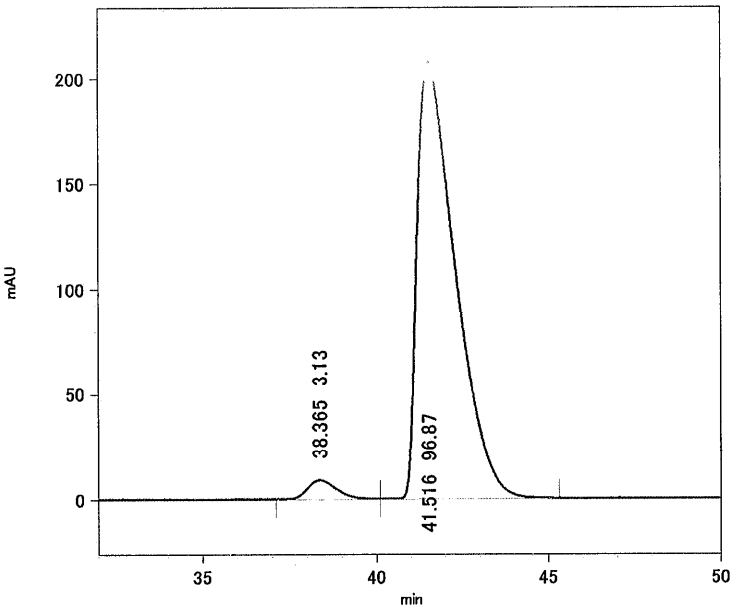
保持時間	面積	面積%
37.502	2287637	49.90
43.123	2296991	50.10

Total	4584628	100.00



racemic

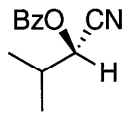
Column: CHIRALCEL OJ-H
Eluent: hexane/iPrOH 98/2
Press.: 11 kgf
Flow Rate: 0.25mL/min
Temp.: RT



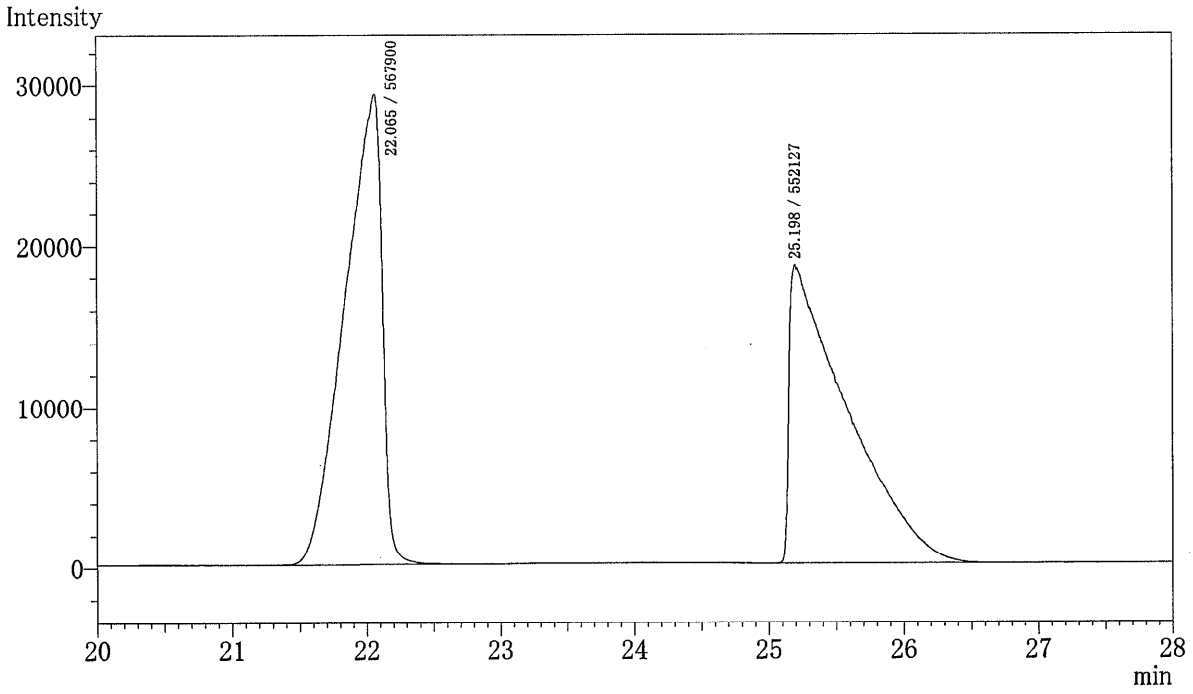
検出器 A-254 nm

保持時間	面積	面積%
38.365	515518	3.13
41.516	15961477	96.87

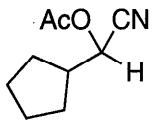
Total	16476994	100.00



データファイル　　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyanation racemi¥c-pentanecarboxyaldehyd
メソッドファイル　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyclopentanecarboxyaldehyde-Ac.gcm

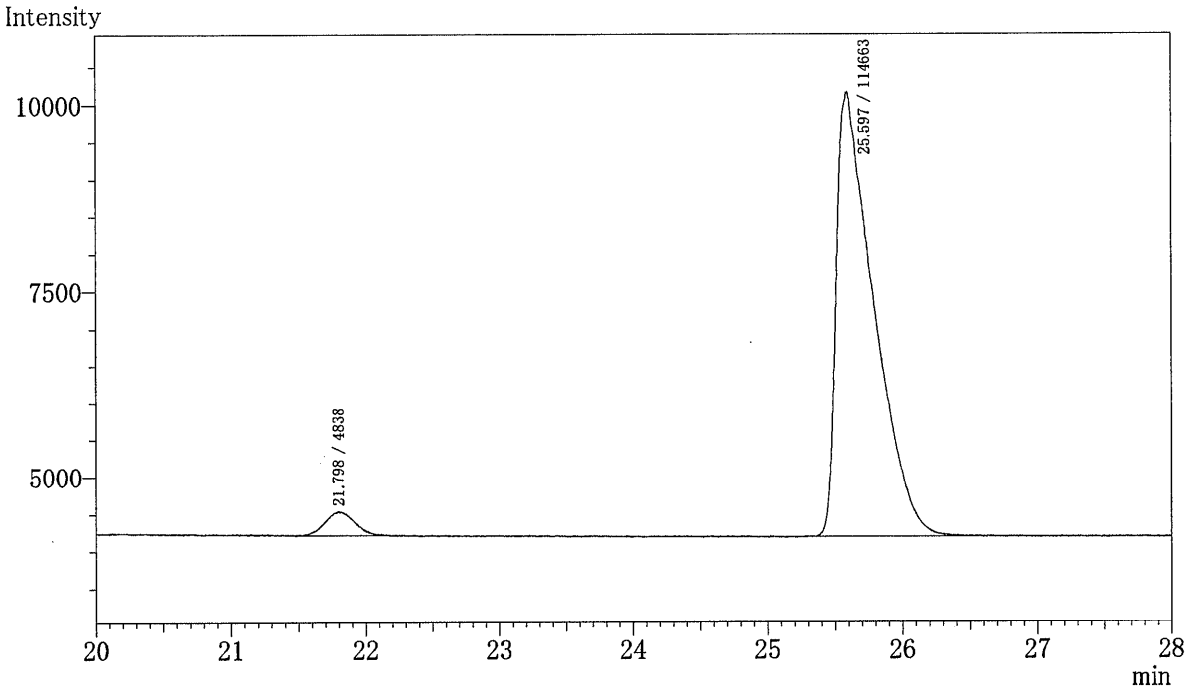


ピーク番号	保持時間	面積	面積%
1	22.065	567900	50.7041
2	25.198	552127	49.2959
合計		1120027	100.0000

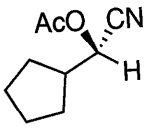


racemic

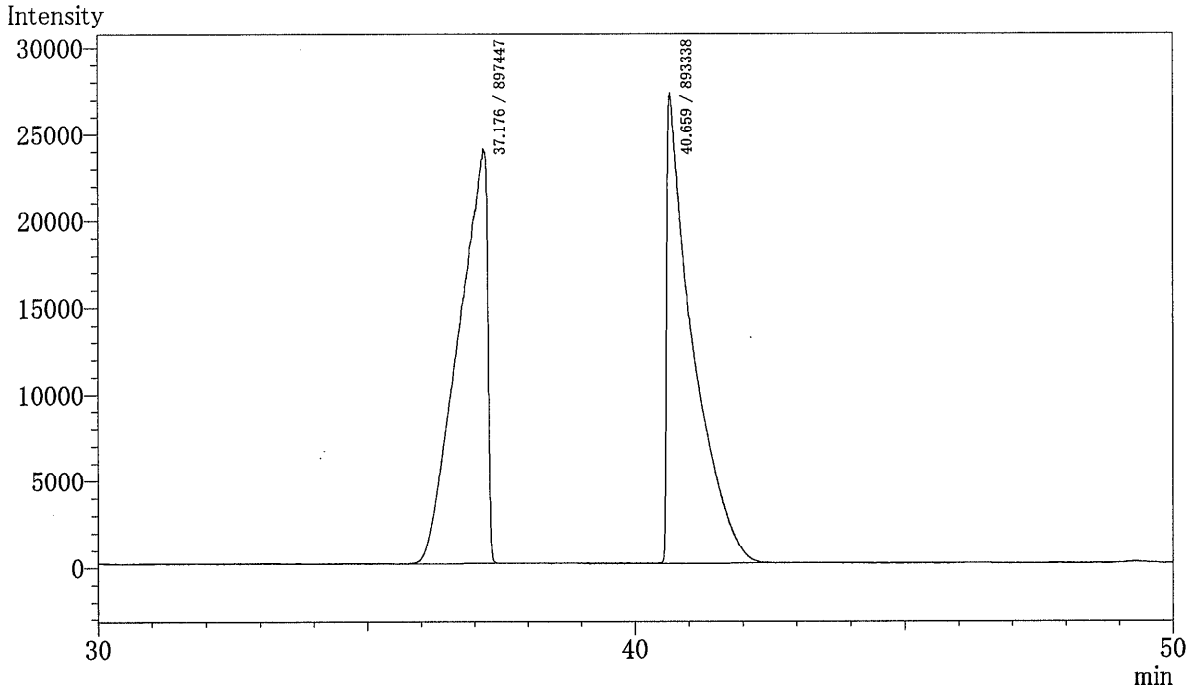
データファイル　　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥S-1167-2.gcd
メソッドファイル　　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyclopentanecarboxyaldehyde-Ac.gcm



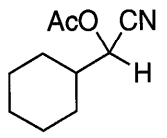
ピーク番号	保持時間	面積	面積%
1	21.798	4838	4.0488
2	25.597	114663	95.9512
合計		119501	100.0000



データファイル　　：C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyanation racemi¥c-hexancarboxyaldehyde-
メソッドファイル　　：C:¥GCsolution¥Data¥sakai¥Cyanation¥GC2-1-cyanocyclohexanol-Ac-new1.gcm

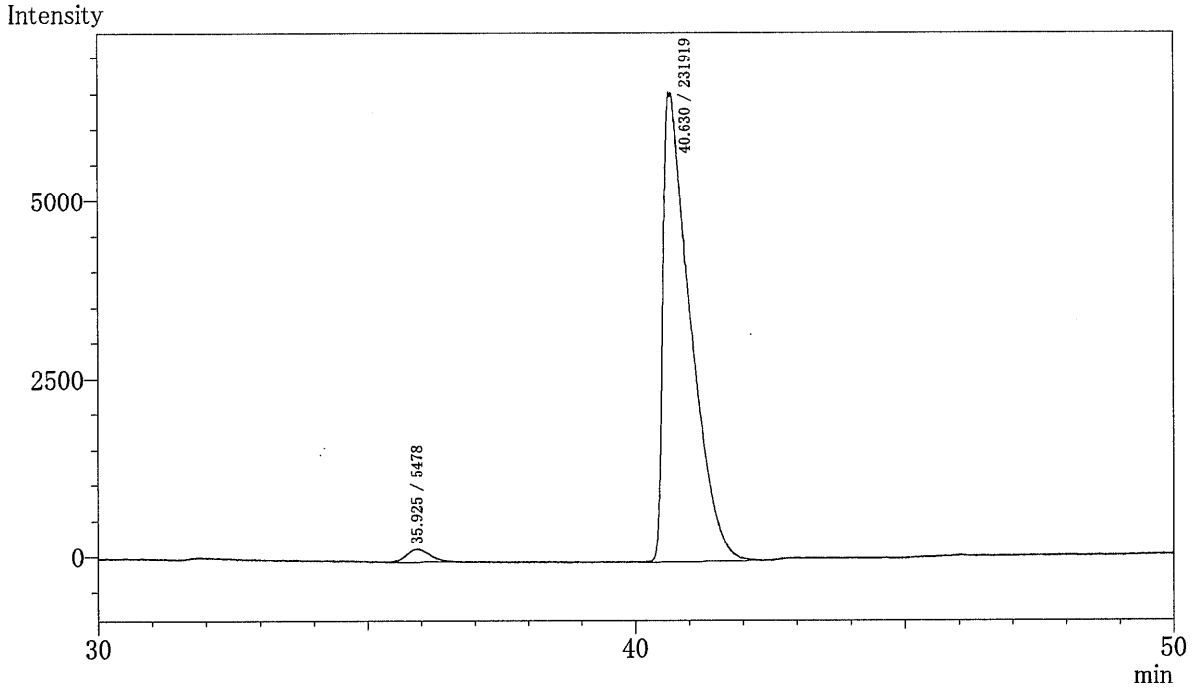


ピーク番号	保持時間	面積	面積%
1	37.176	897447	50.1147
2	40.659	893338	49.8853
合計		1790785	100.0000

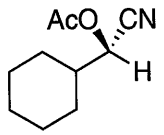


racemic

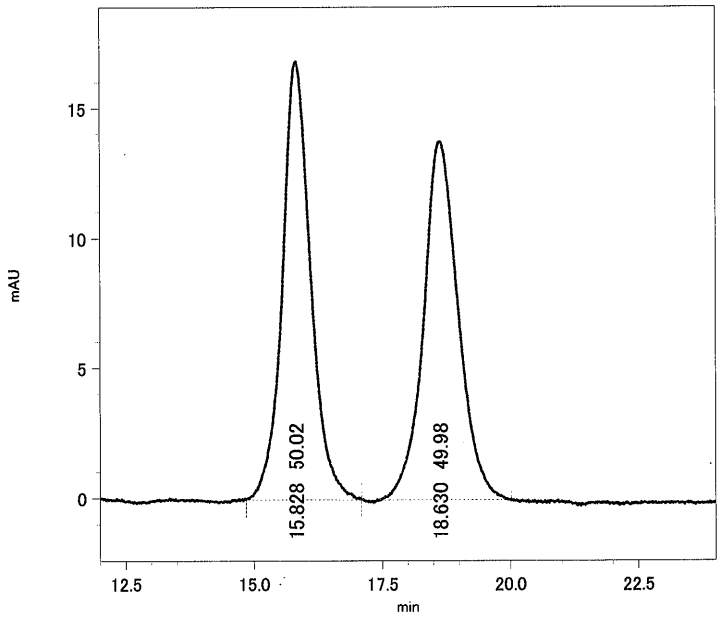
データファイル　　：C:¥GCsolution¥Data¥sakai¥Transcyanation¥S-1152-2.gcd
メソッドファイル　　：C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyclohexanecarboxyaldehyde-Ac.gcm



保持時間	面積	面積%
35.925	5478	2.3076
40.630	231919	97.6924
合計	237397	100.0000



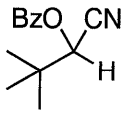
Column: CHIRALCEL OJ-H
Eluent: hexane/iPrOH 99/1
fPress.: 22 kgf
Flow Rate: 0.50 mL/min
Temp.: 25 degree



検出器 A-254 nm

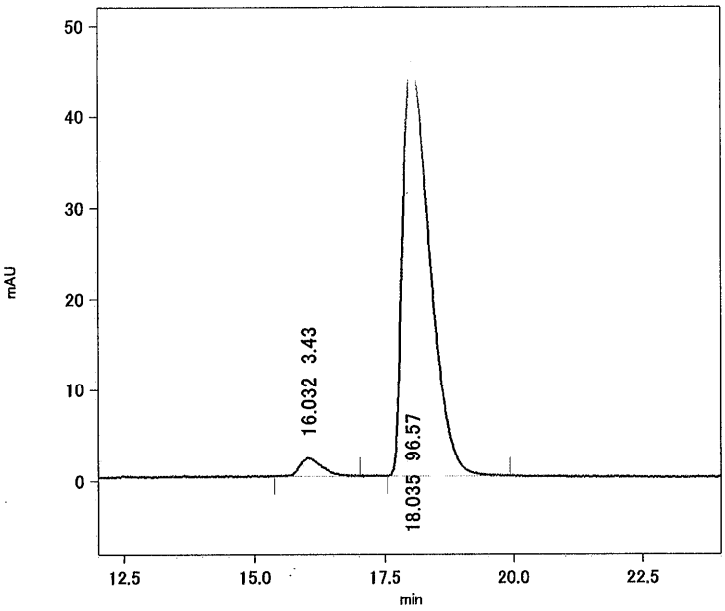
保持時間	面積	面積%
15.828	643180	50.02
18.630	642590	49.98

Total	1285770	100.00



racemic

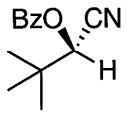
Column: CHIRALCEL OJ-H
Eluent: hexane/iPrOH 99/1
Press.: 22 kgf
Flow Rate: 0.50 mL/min
Temp.: RT



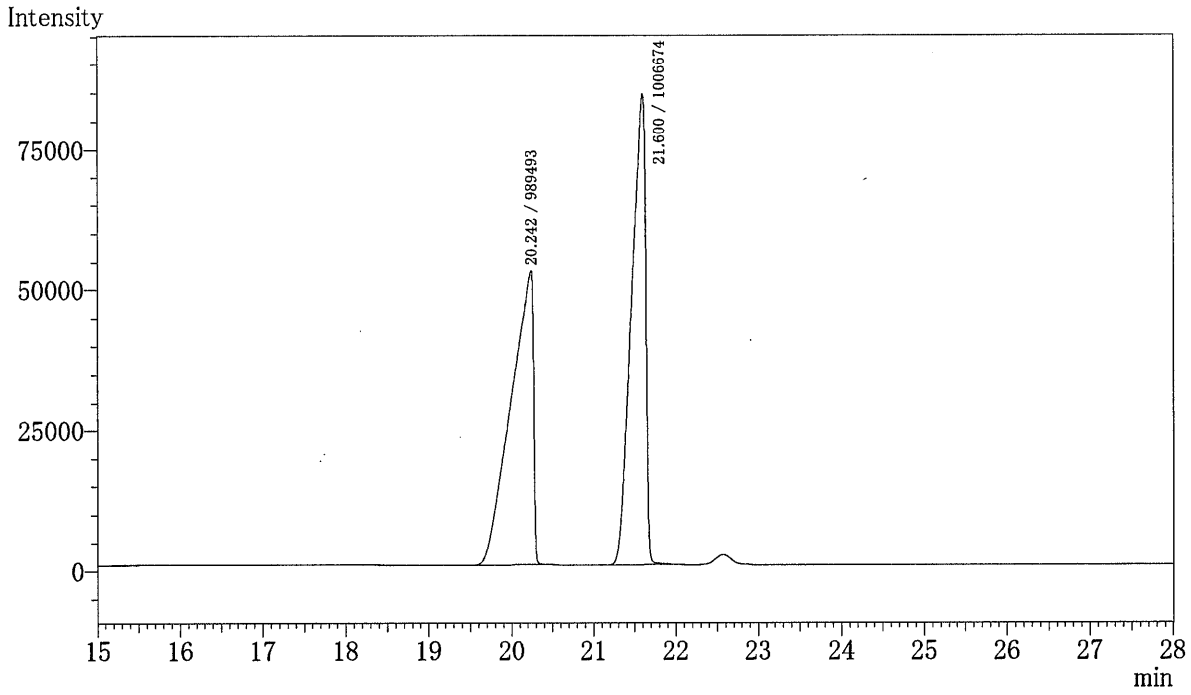
検出器 A-254 nm

保持時間	面積	面積%
16.032	58558	3.43
18.035	1647618	96.57

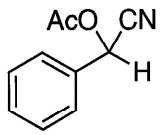
Total	1706176	100.00



データファイル　　: C:¥GCsolution¥Data¥Matsumoto¥Mk-6008-1.gcd
メソッドファイル　　: C:¥GCsolution¥Data¥Matsumoto¥matsumoto.gcm

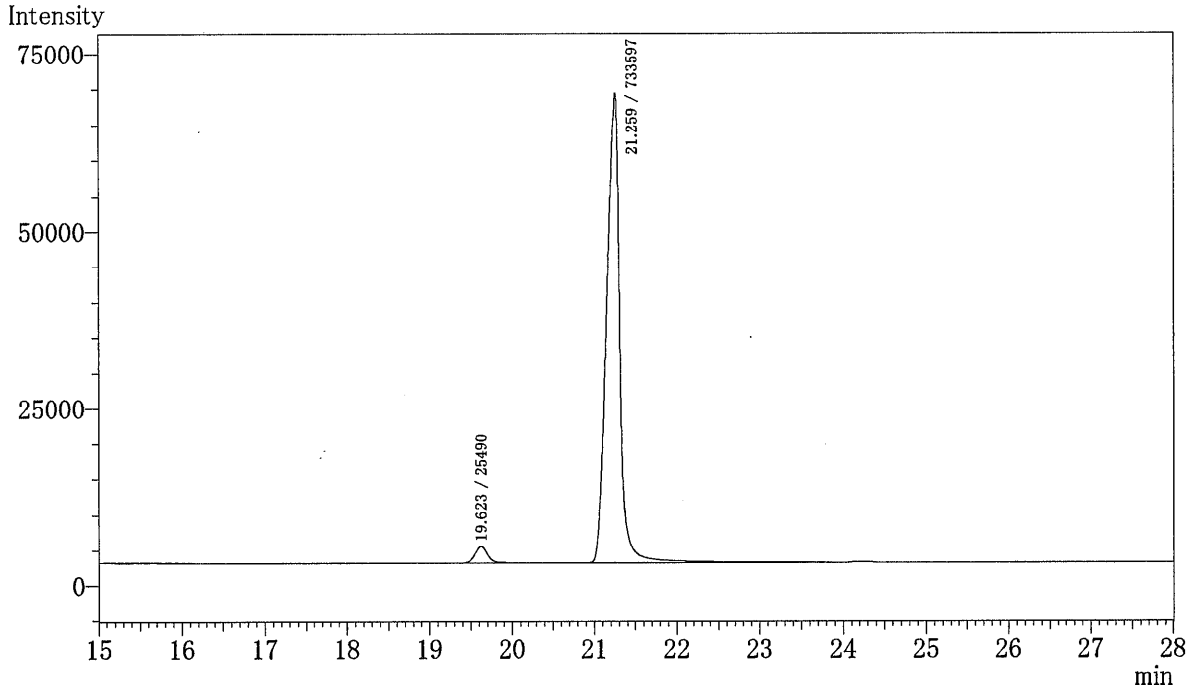


保持時間	面積	面積%
20.242	989493	49.5696
21.600	1006674	50.4304
合計	1996167	100.0000

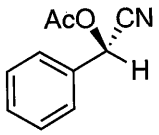


racemic

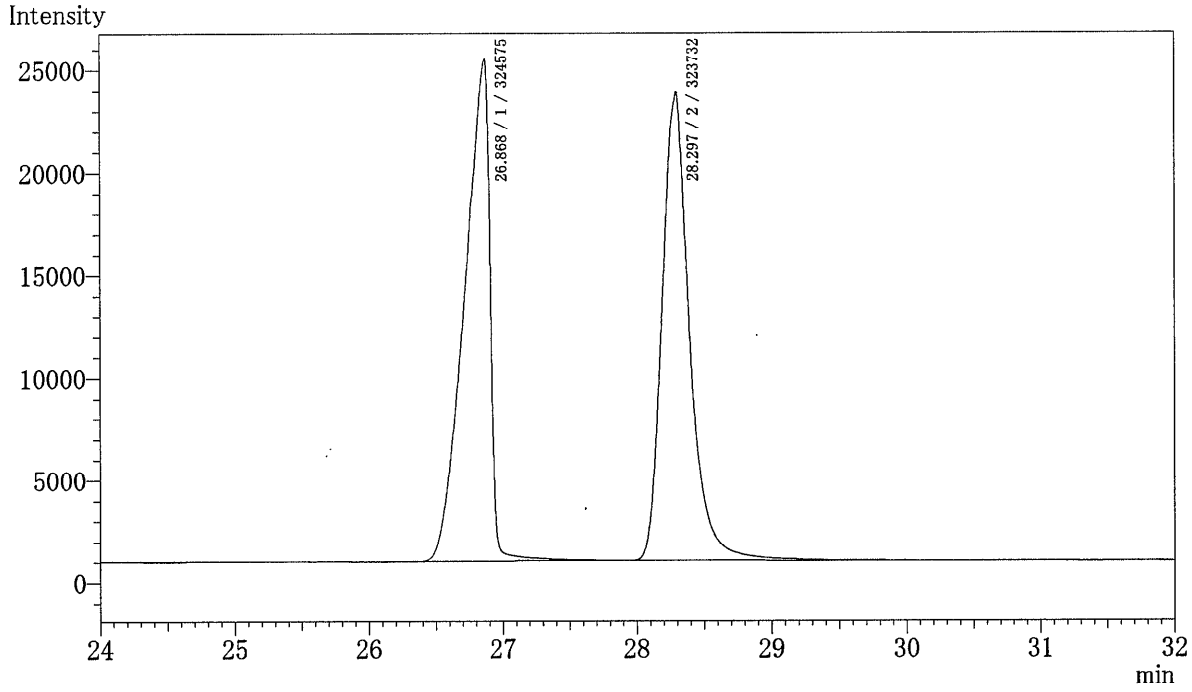
データファイル　　: C:¥GCsolution¥Data¥sakai¥090916-cyanation¥S-1660-1.gcd
メソッドファイル　　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥benzaldehyde-Ac091115.gcm



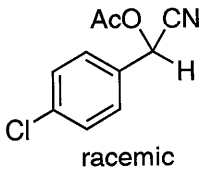
ピーク番号	保持時間	面積	面積%
1	19.623	25490	3.3580
2	21.259	733597	96.6420
合計		759087	100.0000



データファイル　　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyanation racemi¥p-Clbenzaldehyde-cynoh
メソッドファイル　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥test-benzaldehyde-Ac.gcm

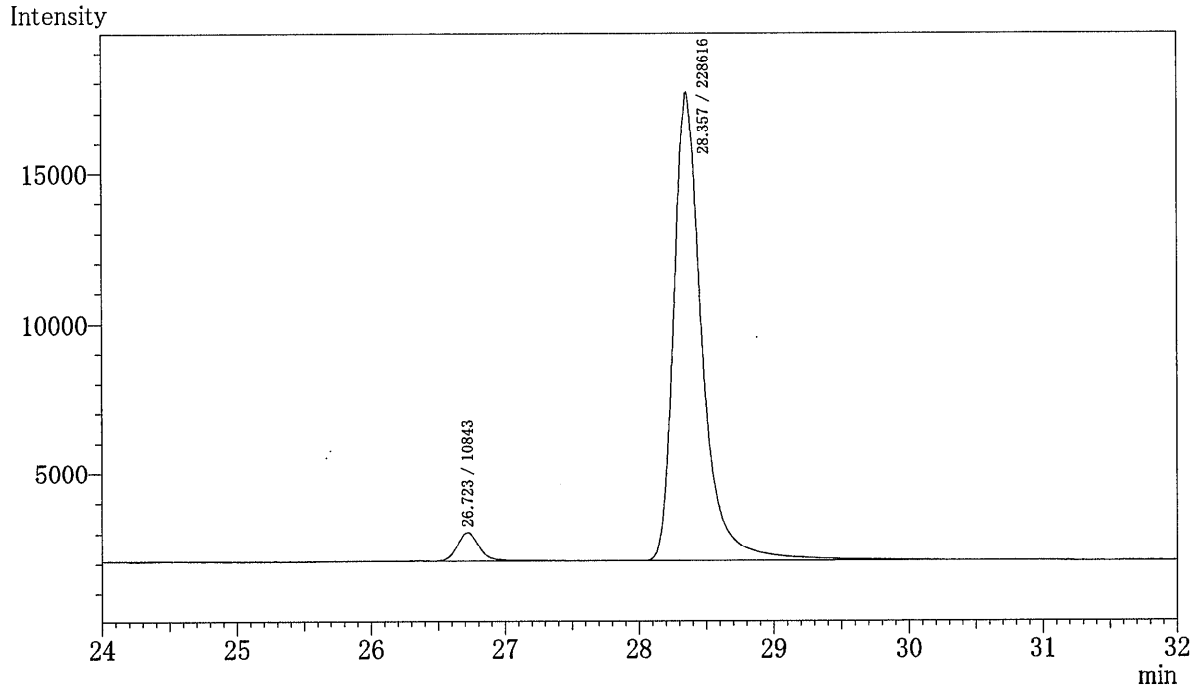


ピーク番号	保持時間	面積	面積%
1	26.868	324575	50.0651
2	28.297	323732	49.9349
合計		648307	100.0000

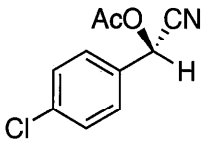


racemic

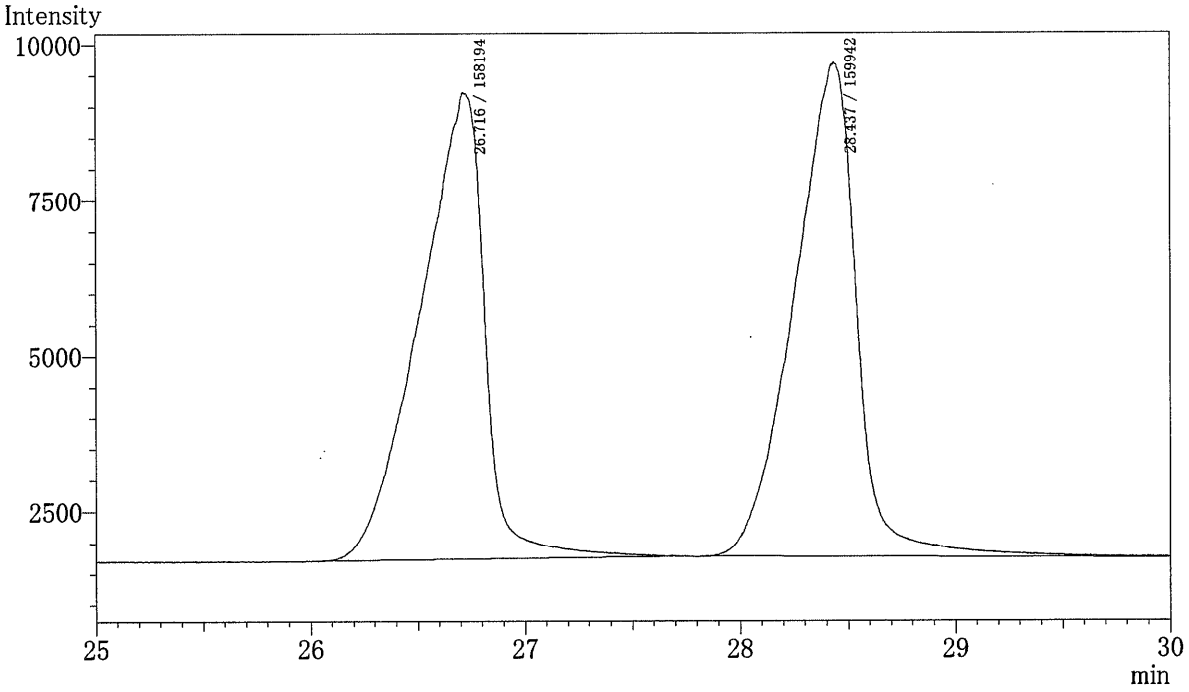
データファイル　　：C:¥GCsolution¥Data¥sakai¥090916-cyanation¥S-1661-2.gcd
メソッドファイル　　：C:¥GCsolution¥Data¥sakai¥Transcyanation¥test-benzaldehyde-Ac.gcm



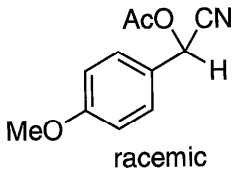
ピーク番号	保持時間	面積	面積%
1	26.723	10843	4.5283
2	28.357	228616	95.4717
合計		239459	100.0000



データファイル　　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥cyanation racemi¥p-MeO-cynohydrin-2.gc
メソッドファイル　: C:¥GCsolution¥Data¥sakai¥Transcyanation¥p-MeObenzaldehyde-Ac.gcm

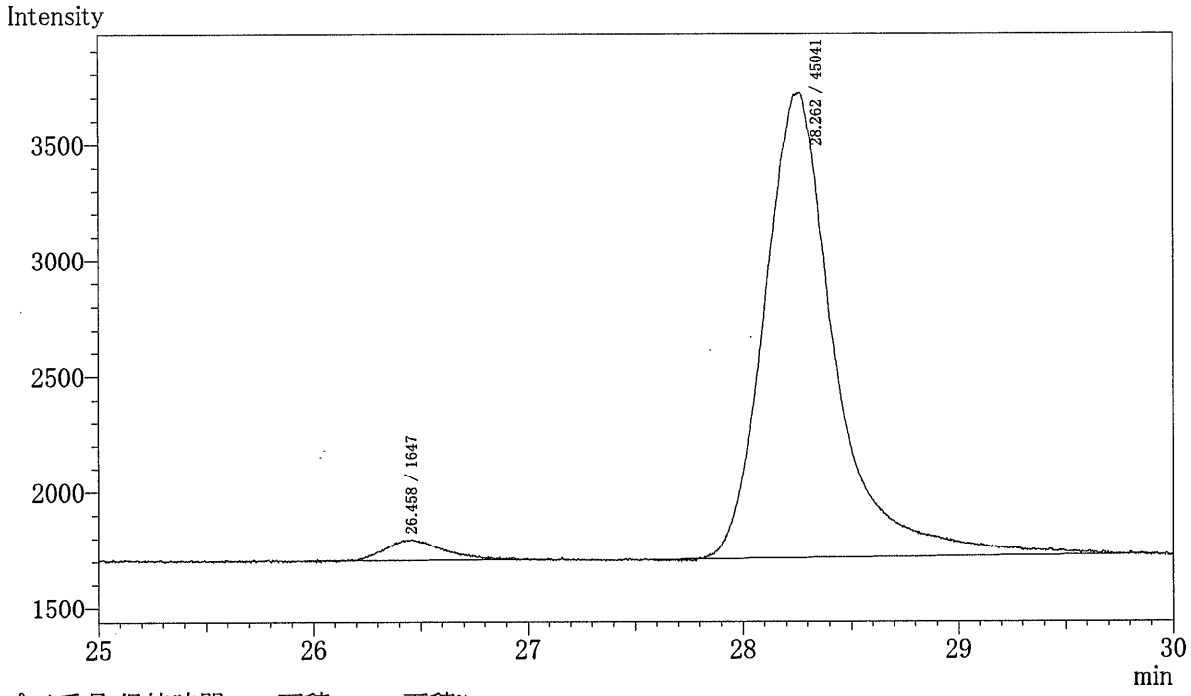


ピーク番号	保持時間	面積	面積%
1	26.716	158194	49.7253
2	28.437	159942	50.2747
合計		318136	100.0000



racemic

データファイル　　：C:¥GCsolution¥Data¥sakai¥090916-cyanation¥S-1659-2.gcd
メソッドファイル　　：C:¥GCsolution¥Data¥sakai¥Transcyanation¥p-MeObenzaldehyde-Ac.gcm



ピーク番号	保持時間	面積	面積%
1	26.458	1647	3.5277
2	28.262	45041	96.4723
合計		46688	100.0000