Supporting Information for *Angew. Chem. Int. Ed.* Z 17713

A Highly Enantioselective and General Conjugate Addition of Thiols to Cyclic Enones with an Organic Catalyst

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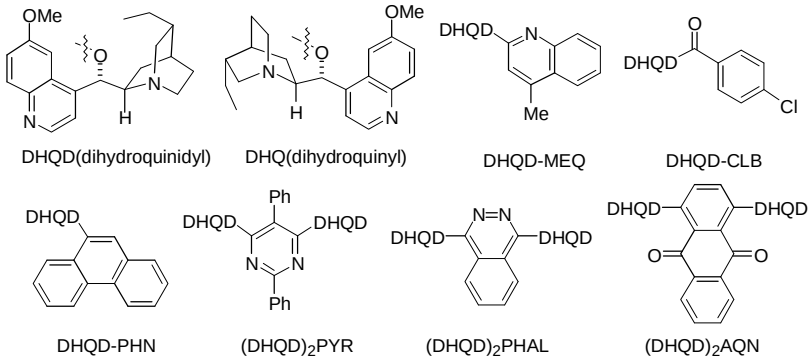
General Information. ^{1}H and ^{13}C NMR were recorded on Varian instruments (400 MHz and 100 MHz, respectively) and internally referenced to a tetramethylsilane signal. Data for ^{1}H NMR are reported as chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported as chemical shift from tetramethylsilane with the solvent as the internal standard. Exact mass spectra for all the new compounds done by 20 eV on a VG 7070 high resolution mass spectrometer. Specific rotations were measured on a Jasco Digital Polarimeter.

Liquid chromatography was performed using forced flow (flash chromatography) on EM Science silica gel 60 (SiO_2, 230-400 mesh). Thin layer chromatography was performed on EM Science 0.25 mm silica gel 60 F_{254} plates. Visualization was achieved with anisaldehyde stain followed by heating. High pressure liquid chromatography (HPLC) analysis was performed on a Hewlett-Packard 1100 Series instrument equipped with an isostatic pump using the chiral columns indicated. UV detection was monitored at 254 nm.

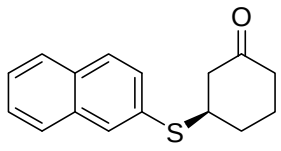
Cycloalkenones listed in entries 1, 2, 3, 5, 6, 7 of table 3 were purchased from Aldrich (Milwaukee) and were distilled before use. Cycloalkenone listed in entry 4 of table 3 was prepared by converting enol silane[1] that was derived from commercially available cyclononanone to the enone, according a literature procedure[2]. 2-Naphthalene-thiol was purchased from Alfa Aesar and used without further purification.

Structure of Modified Cinchona Alkaloids



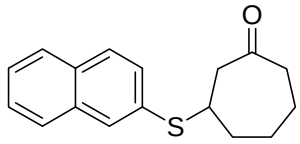
General Procedure for the Catalytic Asymmetric Michael Addition of 2-Naphthalenethiol to Cycloalkenones Catalyzed by $(DHQD)_2PYR$

2-Naphthalenethiol (105.7 mg, 0.66 mmol) is added in one portion to a stirred solution of enone (0.33 mmol) and $(DHQD)_2PYR$ (1 mol %) in Toluene (0.5 mL) at the temperature indicated in Table 3. The reaction mixture is stirred at that temperature until the starting material is consumed as indicated by TLC analysis. The reaction is quenched by partitioning the reaction mixture between Toluene (5 mL) and 1N HCl (0.5 mL). The organic phase is separated, washed with water (1 mL), dried over $MgSO_4$ and concentrated. The resulting oil is purified by column chromatography to provide the desired product.

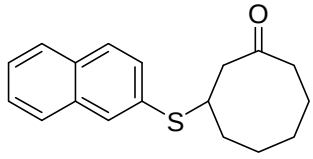


(+)-3-(b-Naphthylthio)cyclohexanone

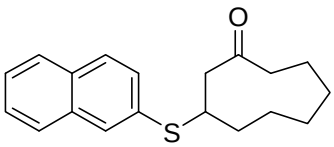
The product was obtained in 77% yield as a white solid and in 94% ee as determined by HPLC analysis (Chiralpak AS, 1:1, Hexanes:IPA, 1.0 mL/min, t(minor) = 6.99 min, t(major) = 11.77 min); mp 71-72 ^oC; $[\alpha]_D^{25}$= +79.6^o (c 3.1, $CHCl_3$); IR (thin film) 3056, 2947, 1711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.69-1.83 (m, 2H), 2.11-2.22 (m, 2H), 2.27-2.46 (m, 3H), 2.71-2.76 (m, 1H), 3.35-3.58 (m, 1H), 7.26-7.51 (m, 3H), 7.78-7.83 (m, 3H), 7.91 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ23.93, 31.20, 40.79, 46.00, 47.67, 126.38, 126.55, 127.40, 127.62, 128.57, 130.14, 130.32, 132.07, 132.47, 133.52, 208.54; HRMS m/z (M^+) Calcd for $C_{16}H_{16}OS$ 256.0922, Found 256.0926. The absolute configuration was established by comparison of the product with an authentic sample prepared by a literature procedure[3].



(+)-3-(b-Naphthylthio)cycloheptanone
The product was obtained in 86% yield as a clear oil and in 97% ee as determined by HPLC analysis (Chiralpak AS, 1:1, Hexanes:IPA, 1.0 mL/min, t(minor) = 7.48 min, t(major) = 9.26 min); $[\alpha]_D^{25}$= +39.3^o (c 3.3, $CHCl_3$); IR (thin film) 3048, 2933, 1698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47-1.58 (m, 1H), 1.62-1.88 (m, 3H), 1.93-2.01 (m, 1H), 2.13-2.21 (m, 1H), 2.46-2.61 (m, 2H), 2.76 (dd, J = 14.6 and 10.2 Hz, 1H), 2.84 (ddd, J = 14.6, 3.2 and 1.2 Hz, 1H), 3.52 (tt, J = 10.2 and 3.2 Hz, 1H), 7.44-7.51 (m, 3H), 7.76-7.81 (m, 3H), 7.88(m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ23.83, 28.06, 36.84, 43.95, 44.09, 49.42, 126.25, 126.54, 127.39, 127.63, 128.62, 129.51, 131.20, 131.38, 132.36, 133.60, 211.32; HRMS m/z (M^+) Calcd for $C_{17}H_{18}OS$ 270.1078, Found 270.1073.

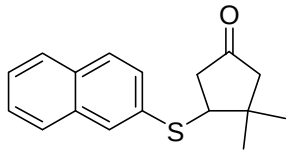


(-)-3-(b-Naphthylthio)cyclooctanone
The product was obtained in 82% yield as a clear oil and in >99% ee as determined by HPLC analysis (Chiralpak AS, 30;1, Hexanes:IPA, 1.0 mL/min, t(major) = 12.01 min, t(minor) = 14.09 min); $[\alpha]_D^{25}$= -41.0^o (c 4.4, $CHCl_3$); IR (thin film) 3054, 2939, 1698, 1422 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31-1.73 (m, 5H), 1.82-1.90 (m, 1H), 1.94-2.11 (m, 2H), 2.33-2.45 (m, 2H), 2.61 (dd, J = 3.8 and 11.8 Hz, 1H), 2.78 (t, J = 11.8 Hz, 1H), 3.69 (tt, J = 3.8 and 11.8 Hz, 1H), 7.47-7.52 (m, 1H), 7.78-7.82 (m, 1H), 7.91 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 23.87, 24.14, 27.60, 33.17, 43.32, 46.62, 126.29, 126.57, 127.44, 127.67, 128.66, 129.70, 131.32, 131.46, 132.41, 133.63, 214.21; HRMS m/z (M^+) Calcd for $C_{18}H_{20}OS$ 284.1235, Found 284.1238.



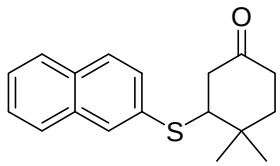
(-)-3-(b-Naphthylthio)cyclononanone
The product was obtained in 91% yield as a clear oil and in 97% ee as determined by HPLC analysis. [Chiralpak AD, Hexane:IPA, 100:1, 1.0 mL/min, t(minor) = 18.90 min, t(major) = 23.94 min.]; $[\alpha]_D^{25}$= -68.3^o (c 2.5, $CHCl_3$); IR (thin film) 3053, 2932, 1670, 1468, 1443 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33-1.98 (m, 10H), 2.35-2.41 (m, 1H), 2.45-2.52 (m, 1H), 2.62 (dd, J = 3 and 13.6 Hz, 1H), 2.86 (dd, J = 11.6 and 13.6 Hz, 1H), 3.87-3.94 (m,1H), 7.44-7.51 (m, 3H), 7.78-7.52 (m, 3H), 7.92(m, 1H); ^{13}C NMR (100MHz, $CDCl_3$)

δ 23.03, 24.10, 25.76, 25.96, 32.66, 44.31, 44.36, 48.24, 126.09, 126.56, 127.38, 127.67, 128.60, 128.95, 130.02, 132.16, 132.21, 133.70, 214.64; HRMS m/z (M^+) Calcd for $C_{19}H_{22}OS$ 298.1391, Found 298.1379.



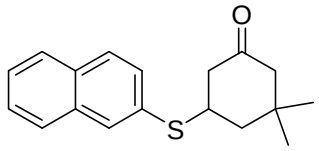
(-)-3-(b-Naphthylthio)-4,4-Dimethylcyclopentanone

The product was obtained in 71% yield as a clear oil and in 92% ee as determined by HPLC analysis (Chiralpak AS, 1:1, Hexanes:IPA, 0.5 mL/min, t(major) = 18.03 min, t(minor) = 21.26min); $[\alpha]_D^{25}$= +198.0^o (c 1.9, $CHCl_3$); IR(thin film) 3054, 2961, 1745, 1402 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.28 (s, 3H), 2.17 (d, J = 18 Hz, 1H), 2.35 (d, J = 18 Hz, 1H), 2.47 (ddd, J = 1.4, 9.2 and 19.4 Hz, 1H), 2.79 (dd, J = 8 and 19.4 Hz, 1H), 3.68 (dd, J = 8 and 9.2 Hz, 1H), 7.43-7.50 (m, 3H), 7.74-7.80 (m, 3H), 7.86 (m,1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 23.14, 27.69, 40.55, 45.34, 53.81, 54.55, 126.13, 126.63, 127.18, 127.65, 128.62, 128.93, 129.89, 132.12, 132.70, 133.63, 215.10; HRMS m/z (M^+) Calcd for $C_{17}H_{18}OS$ 270.1078, Found 270.1077.



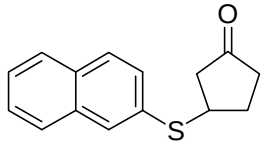
(+)-3-(b-Naphthylthio)-4,4-Dimethylcyclohexanone

The reaction is quenched by adding diluted reaction mixture (1.5 mL) dropwise to well stirred 1 N HCl (25 mL). The product was obtained in 88% yield as a white solid and in 95% ee as determined by HPLC analysis (Chiralpak AS, 50:1, Hexanes:IPA, 1.0 mL/min, t(major) = 23.01min, t(minor) = 27.86min); mp 116-117 ^{o}C; $[\alpha]_D^{25}$= +80.0^o (c 3.9, $CHCl_3$); IR (thin film) 3054, 2967, 1711, 1425 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.31 (s, 3H), 1.64-1.72 (m, 1H), 1.90-1.96 (m, 1H), 2.29-2.35 (m, 1H), 2.44-2.52 (m, 1H), 2.57-2.70 (m, 2H), 3.31 (dd, J = 4.8, 1H), 7.45-7.51 (m, 3H), 7.75-7.81 (m, 3H), 7.88 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.06, 29.06, 34.73, 37.86, 38.61, 45.40, 57.43, 126.26, 126.58, 127.35, 127.65, 128.72, 129.78, 131.37, 131.93, 132.37, 133.66, 208.88; HRMS m/z (M^+) Calcd for $C_{18}H_{20}OS$ 284.1235, Found 284.1238.



(+)-3-(b-Naphthylthio)-5,5-Dimethylcyclohexanone

The product was obtained in 88% yield as a white solid and in 93% ee as determined by HPLC analysis (Chiralpak AS, 1:1, Hexanes:IPA, 1.0 mL/min, t(min) = 6.30 min, t(major) = 10.39 min); mp 57-58 ^{o}C; $[\alpha]_D^{25}$= +45.5^{o} (c 3.6, $CHCl_3$); IR (thin film) 3054, 2961, 1712, 1421 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (s, 3H), 1.06 (s, 3H),1.66-1.72 (m, 1H), 1.95-2.00 (m, 1H), 2.10 (dt, J = 2 and 13.4 Hz, 1H), 2.18 (d, J = 13.4Hz, 1H), 2.30(t, J = 12.8 Hz, 1H), 2.68 (ddt, J = 12.8, 4.4 and 2.0 Hz, 1H), 3.54 (tt, J = 4.4 and 12.8 Hz, 1H), 7.46-7.52 (m, 3H), 7.77-7.82 (m, 3H), 7.90 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ25.53, 31.67, 35.14, 42.28, 45.01, 47.53, 53.97, 126.39, 126.57, 127.42, 127.63, 128.59, 130.08, 130.19, 131.96, 132.48, 133.52, 208.67; HRMS m/z (M^+) Calcd for $C_{18}H_{20}OS$ 284.1235, Found 284.1242.



(-)-3-(b-Naphthylthio)cyclopentanone

The product was obtained in 55% yield as a white solid and in 41% ee as determined by HPLC analysis. (Chiralpak OD, Hexane:IPA, 4:1, 0.5 mL/min, t(major) = 15.76 min, t(minor)= 18.16 min.); mp 61-62 ^{o}C; $[\alpha]_D^{25}$= -3.1^{o} (c 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04-2.12 (m, 1H), 2.21-2.56 (m, 3H), 2.48-2.56 (m, 1H), 2.65 (dd, J = 7.6 and 18.4 Hz, 1H), 3.99-4.05 (m, 1H), 7.46-7.51 (m, 3H), 7.77-7.83 (m, 3H), 7.87 (m, 1H); IR (thin film) 3054, 2987, 1743, 1421 cm^{-1}; ^{13}C NMR (100MHz, $CDCl_3$) δ 29.30, 36.71, 43.30, 45.17, 126.29, 126.67, 127.31, 127.69, 128.66, 129.13, 130.54, 131.60, 132.30, 133.60, 216.65; HRMS m/z (M^+) Calcd for $C_{15}H_{14}OS$ 242.0765, Found 242.0762.

Referneces

[1] Ishino, Y.; Kita, Y.; Maekawa, H.; Ohno, T.; Yamasaki, Y.; Miyata, T.; Nishiguchi, I. *Tetrahedron Lett.* **1999**, 40, 1349.

[2] Larock, R. C.; Hightower, T. R.; Kraus, G. A.; Hahn, P.; Zheng, D. *Tetrahedron Lett.* **1995**, 36, 2423.

[3] Hiemstra, H.; Wynberg, H. *J. Am. Chem. Soc.* **1981**, 103, 417.

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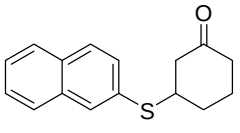

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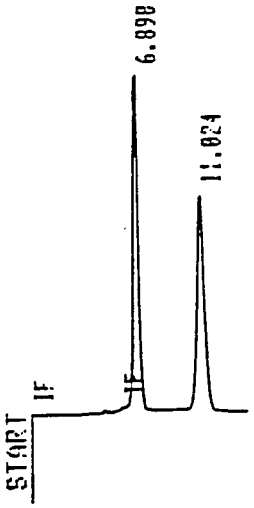

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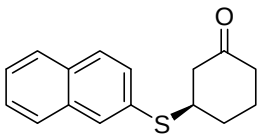

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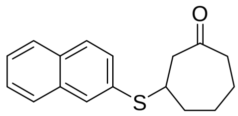

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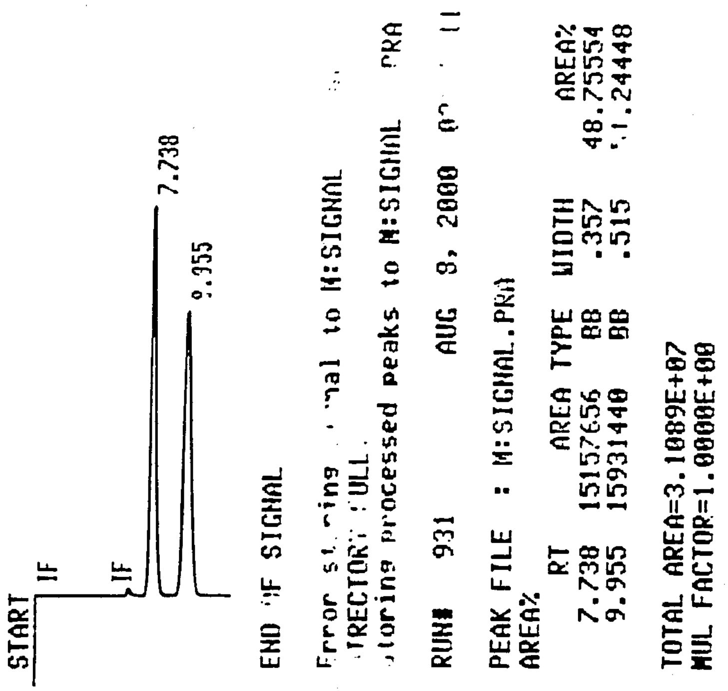

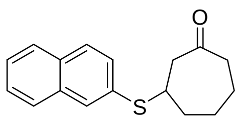

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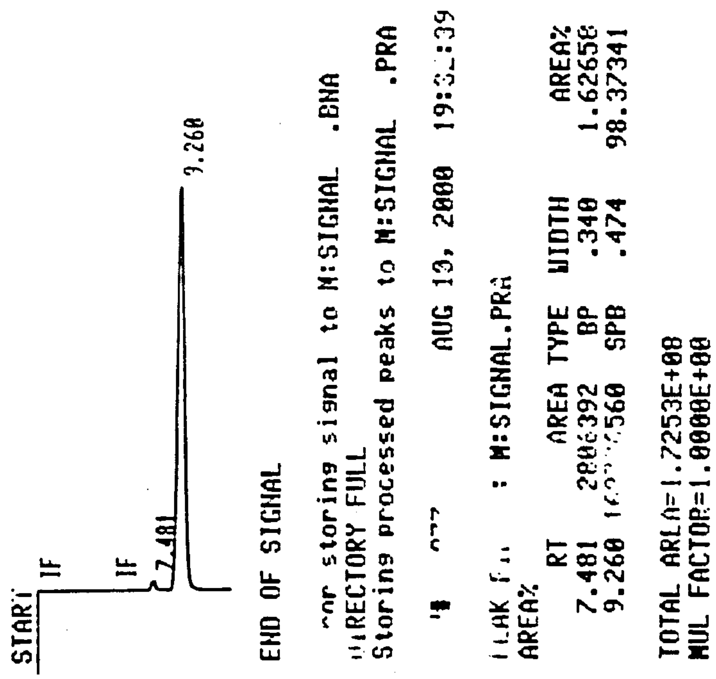

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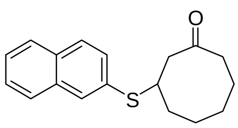

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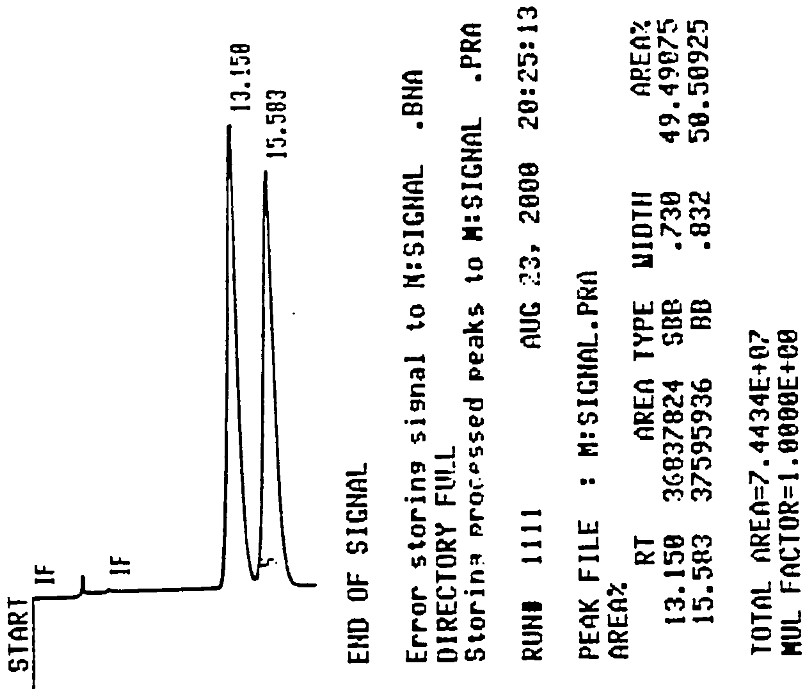

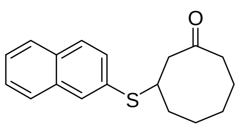

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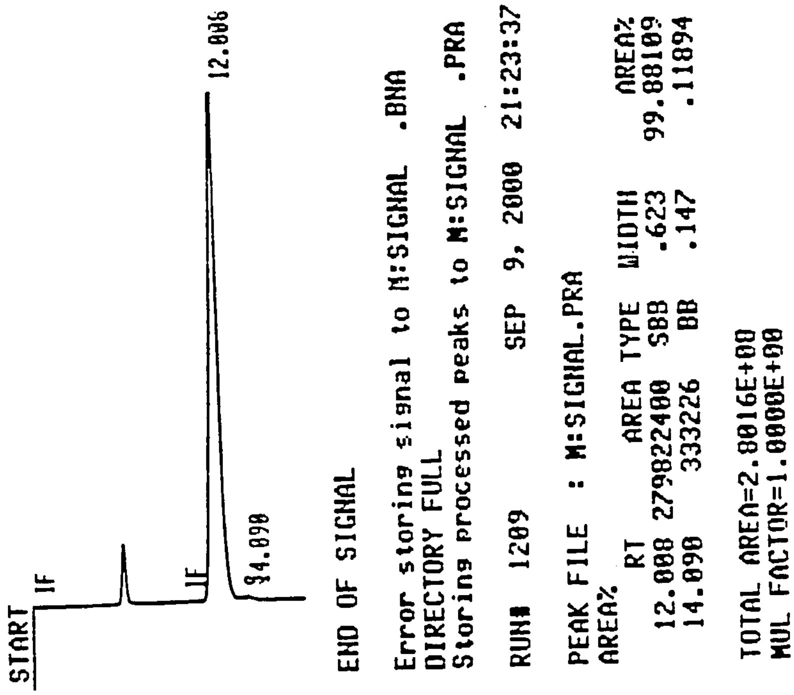

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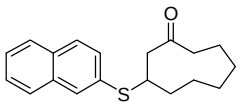
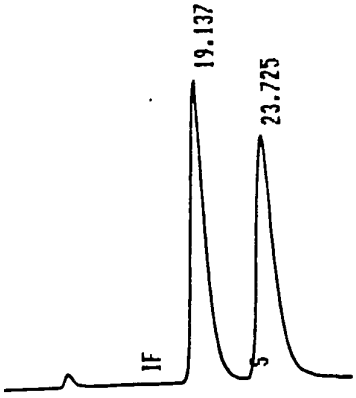


Racemic Product



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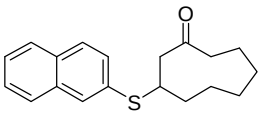

Re
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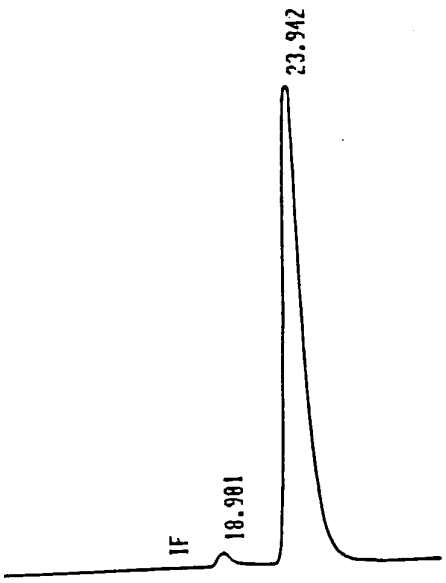

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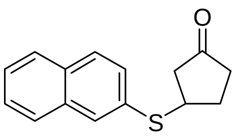

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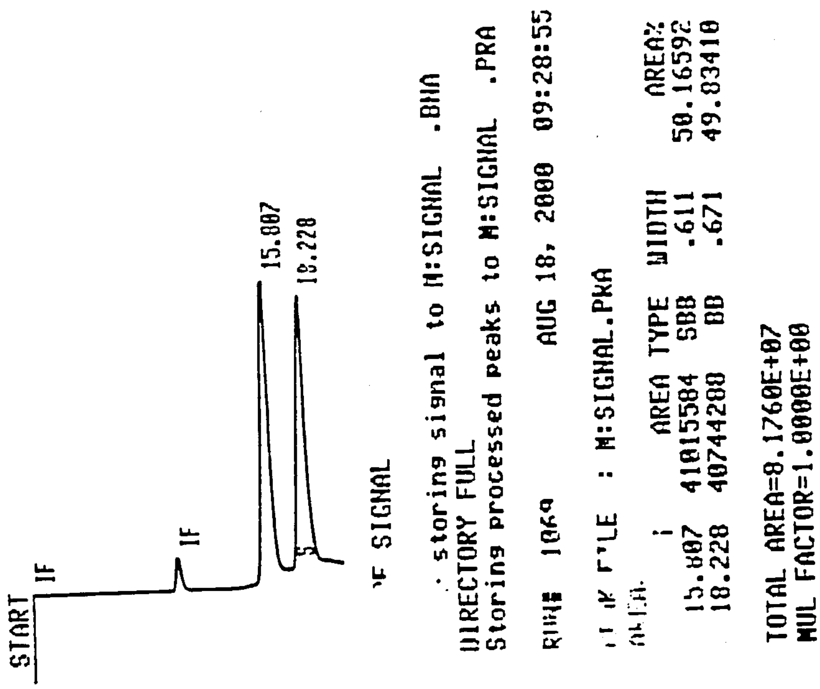
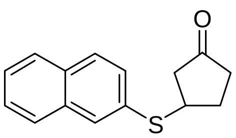
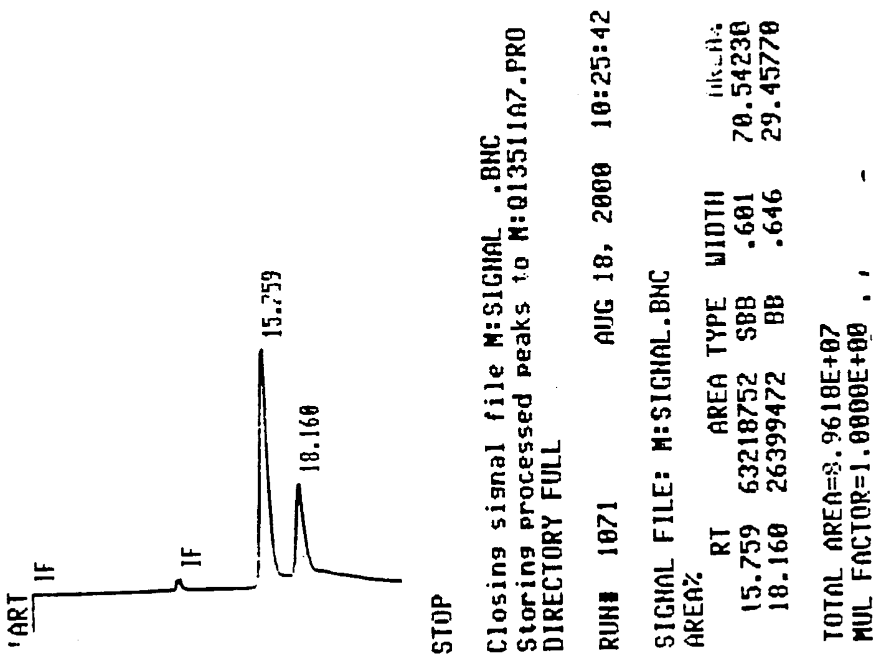
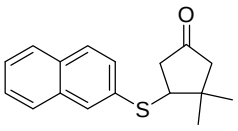




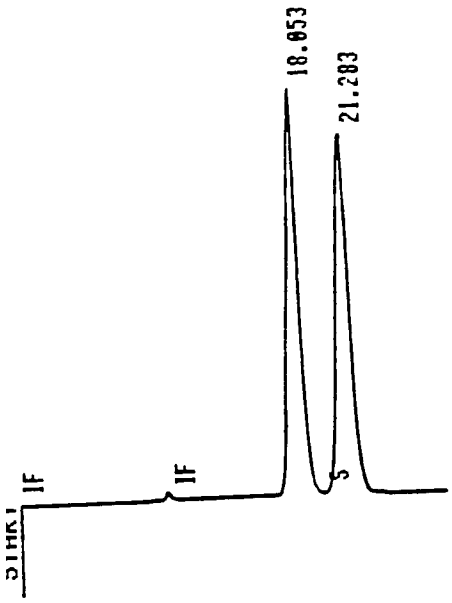
Reaction Product



HPLC Conditions : Chiralpak AS, 1:1, Hexanes:IPA, 0.5ml/min.



Racemic Product



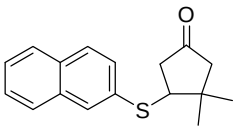
Error storing signal to M:SIGNAL .CHA
TORY FULL
ng processed peaks to M:SIGNAL .PRA

RUN# 995 AUG 12, 2000 06:56:27

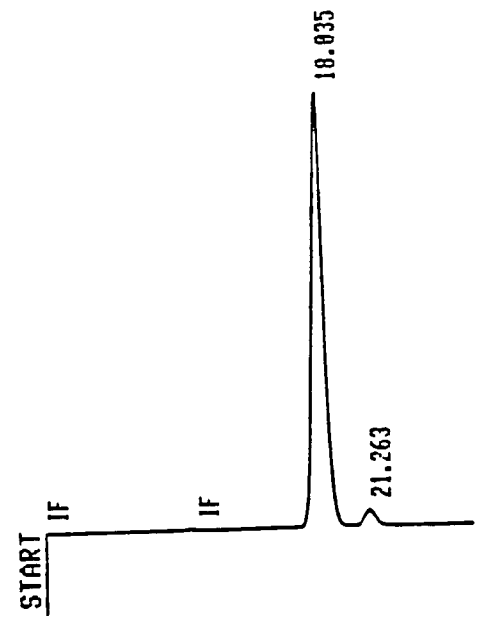
PEAK FILE : M:SIGNAL.PRA
AREA%

	RT	AREA TYPE	WIDTH	AREA%
	18.053	305105440 SPB	.859	50.09637
	21.283	303931600 SPB	.969	49.90365

TOTAL AREA=6.0904E+08
MUL FACTOR=1.0000E+00



Reaction Product



Error storing signal to M:SIGNAL .BHA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA

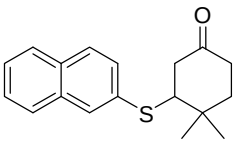
RUN# 997 AUG 12, 2000 08:[illegible]:03

PEAK FILE : M:SIGNAL.PRA
AREA%

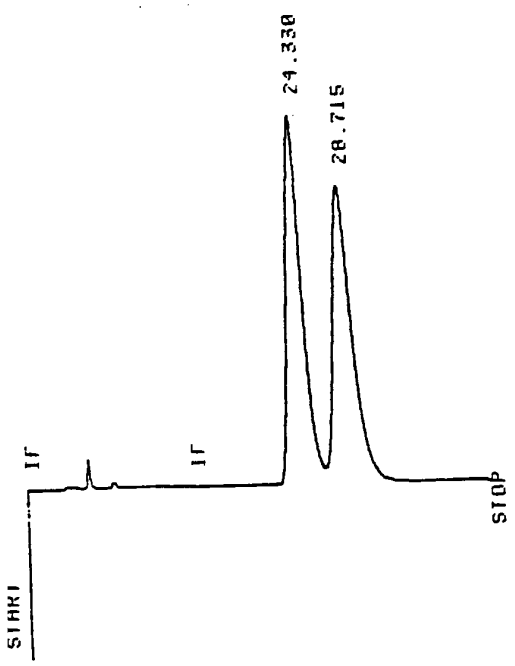
	RT	AREA TYPE	WIDTH	AREA%
	18.035	20030464 BB	.842	96.17517
	21.263	796603 BB	.889	3.82485

TOTAL AREA=2.0827E+07
MUL FACTOR=1.0000E+00

HPLC Conditions : Chiralpak AS, 50:1, Hexanes:IPA, 1ml/min.



Racemic Product



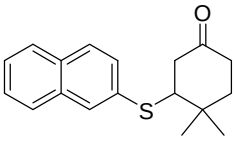
Closing signal file H:SIGNAL .BHC
Storing processed peaks to H:Q1090A77.PRO
DIRECTORY FULL

RUN# 264 DEC 19, 2000 10:14:14

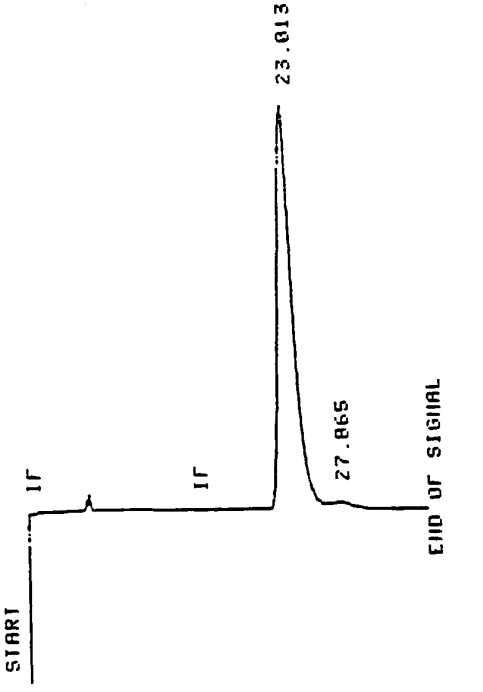
SIGNAL FILE: H:SIGNAL.BHC
PEAK FILE : H:Q1090A77.PRO
AREA%

RT	AREA TYPE	WIDTH	AREA%
24.330	21414912 BV	1.608	49.37005
28.715	21954384 VB	2.043	50.62195

TOTAL AREA=4.3369E+07
MUL FACTOR=1.0000E+00



Reaction Product



Error storing signal to H:SIGNAL .BIA
DIRECTORY FULL
Storing processed peaks to H:SIGNAL .PRA

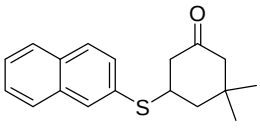
RUN# 266 DEC 19, 2000 23:47:22

PEAK FILE : H:SIGNAL.PRA
AREA%

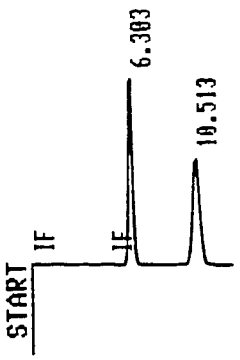
RT	AREA TYPE	WIDTH	AREA%
23.013	45161400 BV	1.562	97.56653
27.865	1126400 VB	2.023	2.43347

TOTAL AREA=4.6288E+07
MUL FACTOR=1.0000E+00

HPLC Conditions : Chiralpak AS, 1:1, Hexanes:IPA, 1ml/min.



Racemic Product



END OF SIGNAL

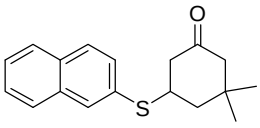
Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA

RUN# 1065 AUG 17, 2000 19:09:49

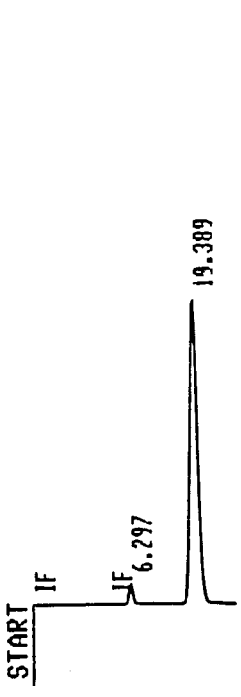
PEAK FILE : M:SIGNAL.PRA
AREA%

RT	AREA	TYPE	WIDTH	AREA%
6.303	12419496	BB	.304	49.86515
10.513	12486664	BB	.538	50.13486

TOTAL AREA=2.4906E+07
MUL FACTOR=1.0000E+00



Reaction Product



END OF SIGNAL

Error storing signal to M:SIGNAL .BNA
DIRECTORY FULL
Storing processed peaks to M:SIGNAL .PRA

RUN# 1064 AUG 17, 2000 18:53:17

PEAK FILE : M:SIGNAL.PRA
AREA%

RT	AREA	TYPE	WIDTH	AREA%
6.297	5507075	BB	.294	3.51446
10.389	151190480	SBB	.563	96.48554

TOTAL AREA=1.5670E+08
MUL FACTOR=1.0000E+00