

Highly enantioselective direct vinylogous Michael addition of  
 $\gamma$ -substituted deconjugated butenolides to maleimides catalyzed by chiral  
squaramides

Yun-Long Guo,<sup>a,b</sup> Li-Na Jia,<sup>a,b</sup> Lin Peng,<sup>a</sup> Liang-Wen Qi,<sup>a,b</sup> Jing Zhou,<sup>a,b</sup> Fang Tian,<sup>a</sup>  
Xiao-Ying Xu,<sup>\*a</sup> Li-Xin Wang,<sup>\*a</sup>

<sup>a</sup> Key Laboratory of Asymmetric Synthesis & Chirotechnology of Sichuan Province,  
Chengdu

Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, PR  
China;

<sup>b</sup> University of Chinese Academy of Sciences, Beijing 100039, PR China  
wlxioc@cioc.ac.cn, xuxy@cioc.ac.cn

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## General Methods

Commercial grade solvent was dried and purified by standard procedures as specified in Purification of Laboratory Chemicals, 4th Ed (Armarego, W. L. F.; Perrin, D. D. Butterworth Heinemann: 1997). NMR spectras were recorded with tetramethylsilane as the internal standard.  $^1\text{H}$  NMR spectras were recorded at 300 MHz, and  $^{13}\text{C}$  NMR spectras were recorded at 75 MHz (Bruker Avance). Chemical shifts ( $\delta$ ) are reported in ppm downfield from  $\text{CDCl}_3$  ( $\delta = 7.26$  ppm) for  $^1\text{H}$  NMR and relative to the central  $\text{CDCl}_3$  resonance ( $\delta = 77.0$  ppm) for  $^{13}\text{C}$  NMR spectroscopy. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. High-resolution mass spectra were obtained with the microTOF-Q mass spectrometer. Reactions were monitored by TLC and visualized with ultraviolet light. Enantiomeric excess was determined by HPLC analysis on chiralpak AD-H and IC-H columns.

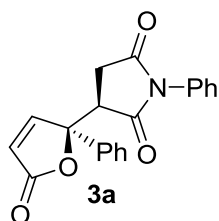
The catalysts **4a-f**<sup>1</sup> and  $\gamma$ -substituted deconjugated butenolides<sup>2</sup> were synthesized according to the literature.

## General procedure for the direct vinylogous Michael addition

Catalyst **4b** (1 mol %), maleimides **1** (0.22 mmol) and  $\gamma$ -substituted deconjugated butenolides **2** (0.2 mmol) were dissolved in 0.3 mL DCM at 30 °C and stirred for 5-96 h. The reaction was monitored by TLC analysis. The reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate) to furnish the corresponding products **3**.

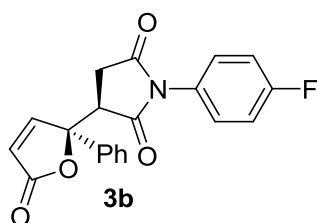
## Characterization of products

3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione (**3a**)



White solid,  $[\alpha]_D^{20} = +249.0$  (c 0.3,  $\text{CH}_2\text{Cl}_2$ ), yield 96 %; 82:18 dr, Enantiomeric excess: 97 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 15.4 min,  $t_R$  (minor) = 18.7 min.  **$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.42 (d,  $J = 5.7$  Hz, 1H), 7.46-7.36 (m, 8H), 7.02-6.98 (m, 2H), 6.21 (d,  $J = 5.6$  Hz, 1H), 3.42 (dd,  $J = 4.7, 8.7$  Hz, 1H), 3.09-2.89 (m, 2H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  174.0, 173.8, 170.4, 158.1, 133.7, 131.1, 129.5, 129.2, 129.2, 129.0, 126.2, 125.8, 120.2, 89.1, 50.5, 30.9; **HRMS** (ESI) calcd. for  $\text{C}_{20}\text{H}_{15}\text{NNaO}_4$   $[\text{M}+\text{Na}]^+$ : 356.0893; found: 356.0892

1-(4-fluorophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione  
(**3b**)

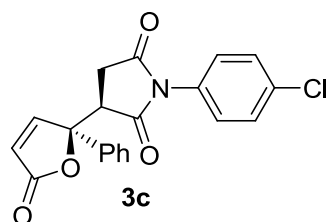


White solid,  $[\alpha]_D^{20} = +220.7$  (c 0.3,  $\text{CH}_2\text{Cl}_2$ ), yield 95 %; 74:26 dr, Enantiomeric excess: 96 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (minor) = 14.7 min,  $t_R$  (major) = 17.6 min.  **$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.40 (d,  $J = 5.7$  Hz, 1H), 7.44-7.39 (m, 5H), 7.14-7.08 (m, 2H), 7.01-6.95 (m, 2H), 6.22 (d,  $J = 5.7$  Hz, 1H), 3.43 (dd,  $J = 4.7, 8.7$  Hz, 1H), 3.09-2.89 (m, 2H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.9, 173.7, 170.4, 163.9 ( $J = 247.8$  Hz), 157.9, 133.7, 129.5, 129.2, 128.1 ( $J = 8.7$

Hz), 126.9, 125.7, 120.3, 116.4 ( $J = 22.8$  Hz), 89.0, 50.3, 30.8; **HRMS** (EI) calcd. for  $C_{20}H_{14}NO_4F$   $[M]^+$ : 351.0907; found: 351.0913

1-(4-chlorophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

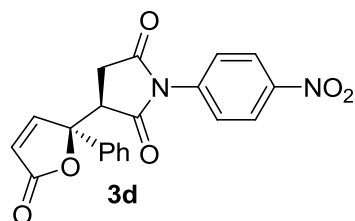
**(3c)**



White solid,  $[\alpha]_D^{20} = +228.0$  (c 0.3,  $CH_2Cl_2$ ), yield 96 %; 78:22 dr, Enantiomeric excess: 96 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (minor) = 16.9 min,  $t_R$  (major) = 21.0 min.  **$^1H$  NMR** (300 MHz,  $CDCl_3$ )  $\delta$  8.39 (d,  $J = 5.7$  Hz, 1H), 7.44-7.38 (m, 7H), 6.97 (d,  $J = 8.6$  Hz, 2H), 6.22 (d,  $J = 5.7$  Hz, 1H), 3.43 (dd,  $J = 4.7, 8.7$  Hz, 1H), 3.09-2.89 (m, 2H);  **$^{13}C$  NMR** (75 MHz,  $CDCl_3$ )  $\delta$  173.7, 173.4, 170.3, 157.9, 134.8, 133.6, 129.5, 129.4, 129.2, 127.4, 125.7, 124.4, 120.3, 88.9, 50.4, 30.8; **HRMS** (EI) calcd. for  $C_{20}H_{14}NO_4Cl$   $[M]^+$ : 367.0611; found: 367.0616

1-(4-nitrophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

**(3d)**

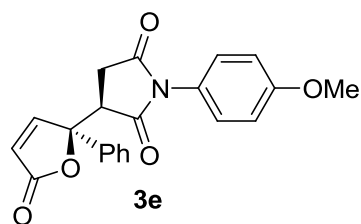


Light yellow solid,  $[\alpha]_D^{20} = +164.2$  (c 0.24,  $CH_2Cl_2$ ), yield 94 %; 81:19 dr, Enantiomeric excess: 95 %, determined by HPLC (Chiralcel AD-H column,

hexane/*i*-propanol= 70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (minor) = 24.6 min,  $t_R$  (major) = 33.9 min.  **$^1H$  NMR** (300 MHz,  $CDCl_3$ )  $\delta$  8.37 (d,  $J$  = 5.7 Hz, 1H), 8.29 (d,  $J$  = 8.0 Hz, 2H), 7.41 (m, 5H), 7.29 (d,  $J$  = 8.9 Hz, 2H), 6.25 (d,  $J$  = 5.6 Hz, 1H), 3.50 (dd,  $J$  = 4.6, 8.8 Hz, 1H), 3.15-2.94 (m, 2H);  **$^{13}C$  NMR** (75 MHz,  $CDCl_3$ )  $\delta$  173.2, 172.8, 170.2, 157.6, 147.1, 136.5, 133.6, 129.6, 129.3, 126.8, 125.6, 124.0, 120.6, 88.8, 50.3, 30.9; **HRMS** (EI) calcd. for  $C_{20}H_{14}N_2O_6$   $[M]^+$ : 378.0852; found: 378.0848

1-(4-methoxyphenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

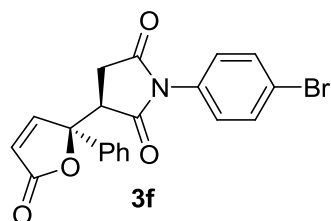
(**3e**)



White solid,  $[\alpha]_D^{20}$  = +211.3 (c 0.3,  $CH_2Cl_2$ ), yield 96 %; 77:23 dr, Enantiomeric excess: 96 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol= 70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (minor) = 19.3 min,  $t_R$  (major) = 20.2 min.  **$^1H$  NMR** (300 MHz,  $CDCl_3$ )  $\delta$  8.42 (d,  $J$  = 5.6 Hz, 1H), 7.42-7.39 (m, 5H), 6.95-6.88 (m, 4H), 6.21 (d,  $J$  = 5.6 Hz, 1H), 3.80 (s, 3H), 3.40 (dd,  $J$  = 4.7, 8.7 Hz, 1H), 3.06-2.87 (m, 2H);  **$^{13}C$  NMR** (75 MHz,  $CDCl_3$ )  $\delta$  174.3, 174.1, 170.4, 159.7, 158.1, 133.7, 129.4, 129.2, 127.4, 125.7, 123.6, 120.1, 114.5, 89.1, 55.4, 50.4, 30.8; **HRMS** (EI) calcd. for  $C_{21}H_{17}NO_5$   $[M]^+$ : 363.1107; found: 363.1115

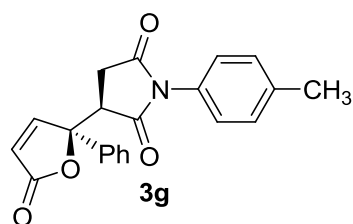
1-(4-bromoxyphenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

(**3f**)



White solid,  $[\alpha]_D^{20} = +214.1$  (c 0.34,  $\text{CH}_2\text{Cl}_2$ ), yield 93 %; 77:23 dr, Enantiomeric excess: 96 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 18.1 min,  $t_R$  (minor) = 20.9 min.  **$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.39 (d,  $J = 5.6$  Hz, 1H), 7.56 (d,  $J = 8.4$  Hz, 2H), 7.41 (s, 5H), 6.91 (d,  $J = 8.5$  Hz, 2H), 6.22 (d,  $J = 5.5$  Hz, 1H), 3.43 (dd,  $J = 4.7, 8.7$  Hz, 1H), 3.08-2.89 (m, 2H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.7, 173.4, 170.4, 157.9, 133.7, 132.4, 130.0, 129.5, 129.2, 127.7, 125.7, 122.9, 120.3, 89.0, 50.4, 30.8; **HRMS** (EI) calcd. for  $\text{C}_{20}\text{H}_{14}\text{NO}_4\text{Br}$   $[\text{M}]^+$ : 411.0106; found: 411.0106

3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)-1-*p*-tolylpyrrolidine-2,5-dione (**3g**)

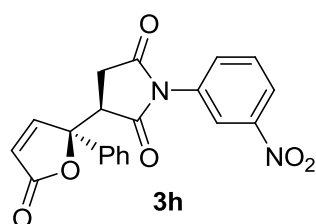


White solid,  $[\alpha]_D^{20} = +214.1$  (c 0.34,  $\text{CH}_2\text{Cl}_2$ ), yield 95 %; 81:19 dr, Enantiomeric excess: 97 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 15.1 min,  $t_R$  (minor) = 17.5 min.  **$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.43 (d,  $J = 5.6$  Hz, 1H), 7.45-7.39 (m, 5H), 7.24 (d,  $J = 8.1$  Hz, 2H), 6.88-6.21 (d,  $J = 5.6$  Hz, 1H), 3.41 (dd,  $J = 4.7, 8.6$  Hz, 1H), 3.08-2.88 (m, 2H), 2.36 (s, 3H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$

174.2, 173.9, 170.5, 158.2, 139.1, 133.7, 129.8, 129.5, 129.2, 128.4, 126.0, 125.8,  
120.2, 89.1, 50.5, 30.8, 21.1; **HRMS** (EI) calcd. for  $C_{21}H_{17}NO_4$   $[M]^+$ : 347.1158;  
found: 347.1158

1-(3-nitrophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

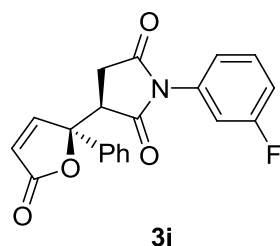
**(3h)**



Light yellow solid, yield 93 %; 82:18 dr, Enantiomeric excess: 92 %, determined by  
HPLC (Chiralcel IC-H column, hexane/*i*-propanol=50/50, flow rate 0.7 mL/min, 35  
°C, UV detection at 220 nm),  $t_R$  (minor) = 32.3 min,  $t_R$  (minor) = 36.4 min.  **$^1H$  NMR**  
(300 MHz,  $CDCl_3$ )  $\delta$  8.38 (d,  $J$  = 5.6 Hz, 1H), 8.24 (d,  $J$  = 7.8 Hz, 1H), 7.93 (s, 1H),  
7.64-7.58 (m, 1H), 7.48-7.39 (m, 6H), 6.24 (d,  $J$  = 5.7 Hz, 1H), 3.51 (dd,  $J$  = 4.6, 8.9  
Hz, 1H), 3.14-3.00 (m, 2H);  **$^{13}C$  NMR** (75 MHz,  $CDCl_3$ )  $\delta$  173.4, 173.0, 170.3, 158.5,  
148.3, 132.2, 130.0, 129.7, 129.1, 125.7, 124.4, 123., 121.6, 120.6, 119.1, 88.8, 50.3,  
30.9; **HRMS** (EI) calcd. for  $C_{20}H_{14}N_2O_6$   $[M]^+$ : 378.0852; found: 378.0856

1-(3-fluorophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

**(3i)**

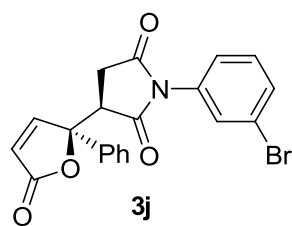


White solid,  $[\alpha]_D^{20}$  = +228.4 (c 0.33,  $CH_2Cl_2$ ), yield 95 %; 81:19 dr, Enantiomeric

excess: 96 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol=70/30, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 14.8 min,  $t_R$  (minor) = 23.4 min.  **$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.40 (d,  $J = 5.7$  Hz, 1H), 7.42-7.36 (m, 6H), 7.10-7.09 (m, 1H), 6.84-6.74 (m, 2H), 6.22 (d,  $J = 5.7$  Hz, 1H), 3.43 (dd,  $J = 4.7, 8.7$  Hz, 1H), 3.09-2.90 (m, 2H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.6, 173.5, 170.3, 164.1 ( $J = 246.6$ ), 157.9, 133.6, 132.3 ( $J = 9.9$  Hz), 130.4 ( $J = 8.7$  Hz), 129.6, 129.2, 125.7, 121.9 ( $J = 3.3$  Hz), 120.3, 116.2 ( $J = 20.8$  Hz), 114.0 ( $J = 24.1$  Hz), 88.9, 50.4, 30.8; **HRMS** (EI) calcd. for  $\text{C}_{20}\text{H}_{14}\text{NO}_4\text{F}$   $[\text{M}]^+$ : 351.0907; found: 351.0900

1-(3-bromophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

(3j)

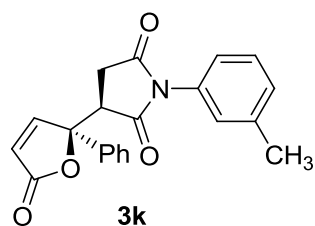


White solid,  $[\alpha]_D^{20} = +189.1$  (c 0.33,  $\text{CH}_2\text{Cl}_2$ ), yield 91 %; 78:22 dr, Enantiomeric excess: 94 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=50/50, flow rate 0.6 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 13.3 min,  $t_R$  (minor) = 20.4 min.  **$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.39 (d,  $J = 5.3$  Hz, 1H), 7.50 (d,  $J = 7.9$  Hz, 1H), 7.42 (m, 5H), 7.32-7.27 (m, 1H), 7.16 (s, 1H), 6.97 (d,  $J = 7.9$  Hz, 1H), 6.22 (d,  $J = 5.3$  Hz, 1H), 3.43 (dd,  $J = 4.7, 8.6$  Hz, 1H), 3.09-2.90 (m, 2H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.6, 173.3, 170.3, 157.9, 133.6, 132.2, 132.0, 130.3, 129.6, 129.3, 129.2, 125.7, 124.9, 122.4, 120.3, 88.9, 50.4, 30.8; **HRMS** (EI) calcd.



for  $C_{20}H_{14}NO_4Br$   $[M]^+$ : 411.0106; found: 411.0126

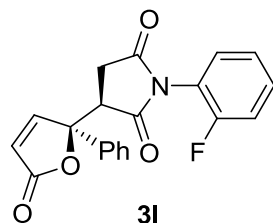
3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)-1-*m*-tolylpyrrolidine-2,5-dione (**3k**)



White solid,  $[\alpha]_D^{20} = +220.3$  (c 0.3,  $CH_2Cl_2$ ), yield 93 %; 80:20 dr, Enantiomeric excess: 97 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 22.9 min,  $t_R$  (minor) = 37.4 min.  **$^1H$  NMR** (300 MHz,  $CDCl_3$ )  $\delta$  8.42 (d,  $J = 5.3$  Hz, 1H), 7.42 (s, 5H), 7.34-7.29 (m, 1H), 7.21-7.19 (m, 1H), 6.79 (s, 2H), 6.21 (dd,  $J = 4.3, 7.6$  Hz, 1H), 3.08-2.88 (m, 2H), 2.35 (s, 3H);  **$^{13}C$  NMR** (75 MHz,  $CDCl_3$ )  $\delta$  174.1, 173.9, 170.5, 158.1, 139.3, 133.7, 130.9, 129.8, 128.4, 129.2, 129.0, 126.8, 125.8, 123.3, 120.1, 8.1, 50.4, 30.8, 21.1; **HRMS** (EI) calcd. for  $C_{21}H_{17}NO_4$   $[M]^+$ : 347.1158; found: 347.1162

1-(2-fluorophenyl)-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione

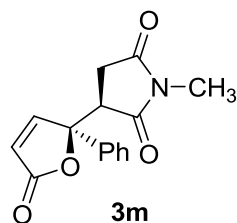
(**3l**)



White solid,  $[\alpha]_D^{20} = +173.0$  (c 0.3,  $CH_2Cl_2$ ), yield 88 %; 79:21 dr, Enantiomeric excess: 95 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 22.1 min,

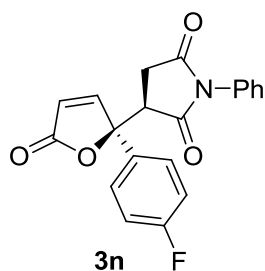
$t_R$  (minor) = 36.5 min.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.41 (s, 1H), 7.44-7.41 (m, 6H), 7.22-7.16 (m, 3H), 6.21 (d,  $J = 5.3$  Hz, 1H), 3.46 (s, 1H), 3.15-2.91 (m, 2H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.2, 173.0, 170.4, 158.8 ( $J = 251.7$  Hz), 158.3, 157.9, 133.7, 131.3 ( $J = 7.8$  Hz), 129.5, 128.7, 125.7, 124.6 ( $J = 3.7$  Hz), 120.3 ( $J = 13.6$  Hz), 119.0 ( $J = 13.2$  Hz), 116.8 ( $J = 19.2$  Hz), 89.0, 50.8 ( $J = 24.5$  Hz), 31.0; **HRMS** (EI) calcd. for  $\text{C}_{20}\text{H}_{14}\text{NO}_4\text{F}$   $[\text{M}]^+$ : 351.0907; found: 351.0927

1-methyl-3-(5-oxo-2-phenyl-2,5-dihydrofuran-2-yl)pyrrolidine-2,5-dione (**3m**)



White solid,  $[\alpha]_D^{20} = +233.8$  (c 0.2,  $\text{CH}_2\text{Cl}_2$ ), yield 82 %; 44:56 dr, Enantiomeric excess: 95 %, determined by HPLC (Chiralcel AD-H column, hexane/*i*-propanol=70/30, flow rate 0.8 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 9.4 min,  $t_R$  (minor) = 10.1 min.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.39 (d,  $J = 5.6$  Hz, 1H), 7.35 (s, 5H), 6.19 (d,  $J = 5.6$  Hz, 1H), 3.27 (dd,  $J = 4.5, 8.7$  Hz, 1H), 2.91 (dd,  $J = 8.9, 18.6$  Hz, 1H), 2.85 (s, 3H), 2.75 (dd,  $J = 4.6, 18.6$  Hz, 1H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  175.0, 174.8, 170.5, 158.2, 133.8, 129.3, 129.1, 125.5, 120.1, 89.1, 50.4, 30.6, 24.9; **HRMS** (EI) calcd. for  $\text{C}_{15}\text{H}_{13}\text{NO}_4$   $[\text{M}]^+$ : 271.0845; found: 271.0847

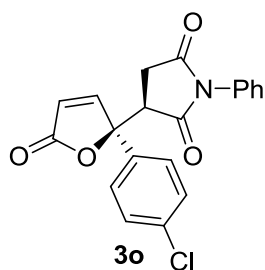
3-(2-(4-fluorophenyl)-5-oxo-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione (**3n**)



White solid, yield 80 %; 75:25 dr, Enantiomeric excess: 95 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 18.8 min,  $t_R$  (minor) = 34.7 min.  **$^1\text{H NMR}$**  (300 MHz, d-DMSO)  $\delta$  8.46 (d,  $J$  = 5.5 Hz, 1H), 7.70-7.40 (m, 5H), 7.32-7.27 (m, 2H), 7.12 (d,  $J$  = 7.3 Hz, 2H), 6.48 (d,  $J$  = 5.5 Hz, 1H), 3.94 (d,  $J$  = 5.0 Hz, 1H), 3.01-2.87 (m, 1H), 2.61-2.55 (m, 1H);  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  174.2, 173.8, 170.8, 163.7 ( $J$  = 244.1 Hz), 157.6, 132.6, 131.9 ( $J$  = 3.0 Hz), 129.0, 128.5, 128.2 ( $J$  = 8.5 Hz), 126.8, 121.3, 115.8 ( $J$  = 21.5 Hz), 89.2, 47.5, 30.8; **HRMS** (EI) calcd. for  $\text{C}_{20}\text{H}_{14}\text{NO}_4\text{F}$   $[\text{M}]^+$ : 351.0907; found: 351.0911

3-(2-(4-chlorophenyl)-5-oxo-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione

**(3o)**

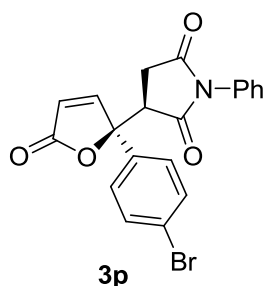


White solid, yield 86 %; 77:23 dr, Enantiomeric excess: 94 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 20.3 min,  $t_R$  (minor) = 39.4 min.  **$^1\text{H NMR}$**  (300 MHz, d-DMSO)  $\delta$  8.35 (d,  $J$  = 5.4 Hz, 1H), 7.56-7.44 (m, 7H), 7.17-7.11 (m, 2H),

6.33 (d,  $J = 5.4$  Hz, 1H), 3.88 (dd,  $J = 3.6, 8.7$  Hz, 1H), 3.05-2.96 (m, 1H), 2.54 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.6, 173.3, 170.1, 157.3, 134.3, 133.8, 131.4, 128.8, 128.6, 128.1, 127.1, 126.3, 120.5, 88.6, 47.7, 30.4; **HRMS** (EI) calcd. for  $\text{C}_{20}\text{H}_{14}\text{NO}_4\text{Cl}$   $[\text{M}]^+$ : 367.0611; found: 367.0633

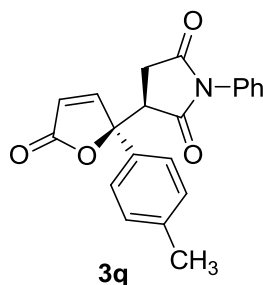
3-(2-(4-bromophenyl)-5-oxo-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione

(**3p**)



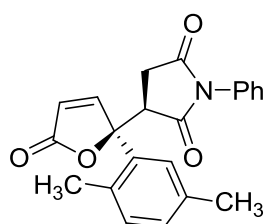
White solid, yield 83 %; 78:22 dr, Enantiomeric excess: 95 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_{\text{R}}$  (major) = 22.0 min,  $t_{\text{R}}$  (minor) = 43.3 min.  $^1\text{H}$  NMR (300 MHz,  $d\text{-DMSO}$ )  $\delta$  8.41 (d,  $J = 5.3$  Hz, 1H), 7.67 (d,  $J = 8.0$  Hz, 2H), 7.50-7.40 (m, 5H), 7.14 (d,  $J = 7.2$  Hz, 2H), 6.49 (d,  $J = 5.5$  Hz, 1H), 3.98 (dd,  $J = 3.8, 9.0$  Hz, 1H), 3.02-2.88 (m, 1H), 2.58-2.54 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  174.2, 173.7, 170.9, 157.6, 135.8, 131.7, 129.0, 128.5, 128.0, 127.4, 126.8, 122.1, 121.3, 89.2, 47.1, 30.8; **HRMS** (EI) calcd. for  $\text{C}_{20}\text{H}_{14}\text{NO}_4\text{Br}$   $[\text{M}]^+$ : 411.0106; found: 411.0110

3-(5-oxo-2-*p*-tolyl-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione (**3q**)



White solid, yield 87 %; 79:21 dr, Enantiomeric excess: 97 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 24.3 min,  $t_R$  (minor) = 46.3 min.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.41 (d,  $J$  = 5.7 Hz, 1H), 7.48-7.39 (m, 3H), 7.34-7.31 (m, 2H), 7.22-7.04 (m, 2H), 7.03 (d,  $J$  = 6.7 Hz, 2H), 6.19 (d,  $J$  = 5.7 Hz, 1H), 3.40 (dd,  $J$  = 4.9, 8.6 Hz, 1H), 3.09-2.90 (m, 2H), 2.35 (s, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  174.1, 173.9, 170.6, 158.3, 139.6, 131.2, 130.7, 129.9, 129.2, 129.0, 126.2, 125.6, 120.0, 89.2, 50.5, 30.9, 21.0; **HRMS** (ESI) calcd. for  $\text{C}_{21}\text{H}_{17}\text{NNa}_4$  [ $\text{M}+\text{Na}$ ]: 370.1050; found: 370.1036

3-(2-(2,5-dimethylphenyl)-5-oxo-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione (**3r**)



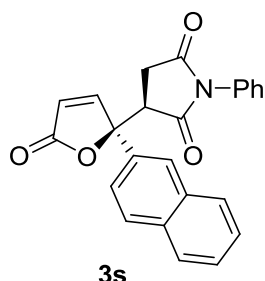
**3r**

White solid, yield 96 %; 77:23 dr, Enantiomeric excess: 97 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 21.0 min,  $t_R$  (minor) = 28.2 min.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (d,  $J$  = 5.7 Hz, 1H), 7.47-7.36 (m, 3H), 7.14-7.06 (m, 5H), 6.28 (d,  $J$  = 5.6 Hz, 1H), 3.63 (dd,  $J$  = 4.5, 9.0 Hz, 1H), 3.05 (dd,  $J$  = 9.2, 18.6 Hz, 1H), 2.79 (dd,  $J$  = 4.5, 18.6 Hz, 1H), 2.56 (s, 3H); 2.27 (s, 3H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.7, 173.6, 170.5, 157.1, 136.0, 133.8, 132.4, 131.3, 12.9, 129.1, 128.9, 127.4, 127.0, 126.3, 121.3, 91.2, 4.2, 31.1, 22.3, 20.9; **HRMS** (EI) calcd. for  $\text{C}_{22}\text{H}_{19}\text{NNaO}_4$

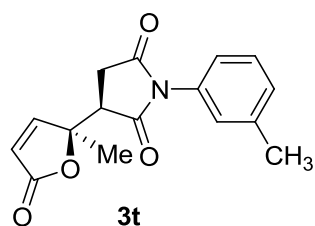
[M+Na]: 384.1206; found: 384.1195

3-(2-(naphthalene-2-yl)-5-oxo-2,5-dihydrofuran-2-yl)-1-phenylpyrrolidine-2,5-dione

(3s)



White solid, yield 95 %; 78:22 dr, Enantiomeric excess: 97 %, determined by HPLC (Chiralcel IC-H column, hexane/*i*-propanol= 50/50, flow rate 0.7 mL/min, 35 °C, UV detection at 220 nm),  $t_R$  (major) = 25.4 min,  $t_R$  (minor) = 46.4 min.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.54 (d,  $J$  = 5.7 Hz, 1H), 7.97-7.84 (m, 4H), 7.57-7.54 (m, 6H), 6.98-6.95 (m, 2H), 6.25 (d,  $J$  = 5.7 Hz, 1H), 3.51 (dd,  $J$  = 5.0, 8.4 Hz, 1H), 3.13-2.90 (m, 2H);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  174.2, 173.6, 170.5, 158.2, 133.2, 133.0, 131.1, 129.7, 129.2, 129.2, 128.9, 128.3, 127.6, 127.3, 127.2, 126.9, 125.6, 122.4, 120.2, 89.4, 50.6, 31.0; **HRMS** (ESI) calcd. for  $\text{C}_{24}\text{H}_{17}\text{NNaO}_4$  [M+Na] 406.1050; found: 406.1049



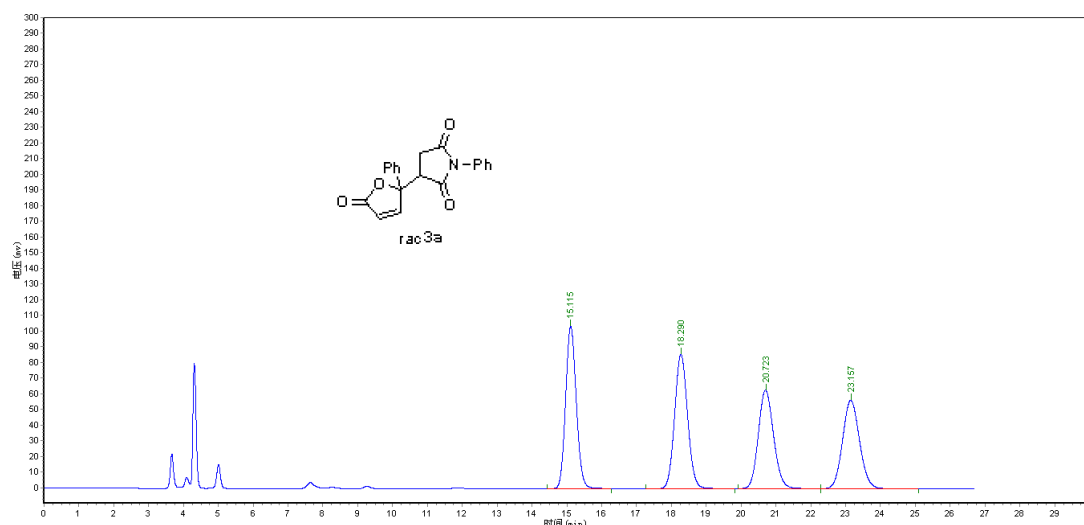
Colorless oil, yield 92 %; 68:32 dr, Enantiomeric excess: 83 %, determined by HPLC (Chiralcel IC-H column, hexane/ethanol= 90/10, flow rate 1.5 mL/min, 35 °C, UV detection at 210 nm),  $t_R$  (major) = 33.2 min,  $t_R$  (minor) = 47.9 min.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85-7.83 (m, 1H), 7.40-7.31 (m, 1H), 7.24-7.19 (m, 1H), 7.05-6.97

(m, 2H), 6.17-6.12 (m, 1H), 3.19 (dd,  $J = 4.8, 9.1$  Hz, 1H), 3.04 (dd,  $J = 9.1, 18.8$  Hz, 1H), 2.88 (dd,  $J = 4.7, 18.4$  Hz, 1H), 2.39 (s, 3H), 1.58 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  174.1, 173.6, 171.0, 159.4, 139.3, 131.1, 129.8, 129.0, 126.9, 123.4, 120.9, 86.8, 46.9, 30.9, 21.2, 19.2; **HRMS** (ESI) calcd. for  $\text{C}_{16}\text{H}_{15}\text{NNaO}_4$  [M+Na] 308.0893; found: 308.0902

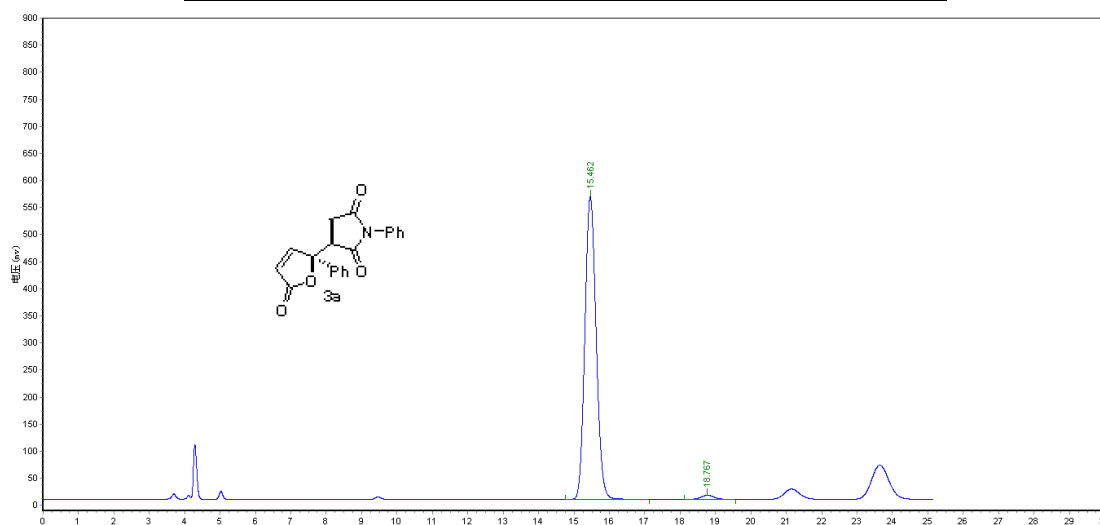
1 W. Yang and D.-M. Du, *Org. Lett.*, 2010, **12**, 5450.

2 A. Tsolomitis and C. Sandris, *J. Heterocyclic. Chem.*, 1983, **20**, 1545.

Copies of HPLC spectra

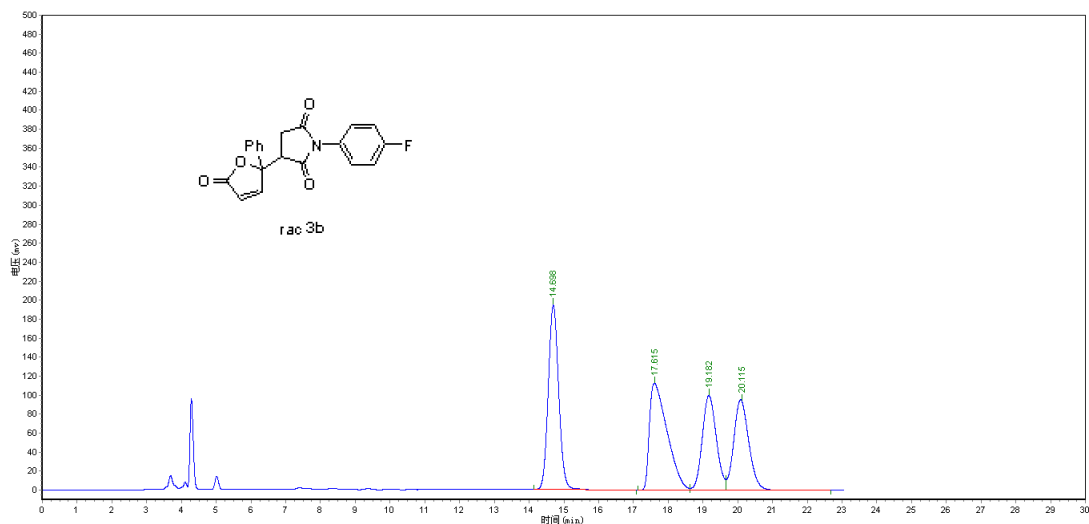


Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	15.115	103582.391	2200679.000	26.7076
2	18.290	85715.898	2215552.000	26.8881
3	20.723	62848.605	1913800.750	23.2260
4	23.157	56362.906	1909866.375	23.1783

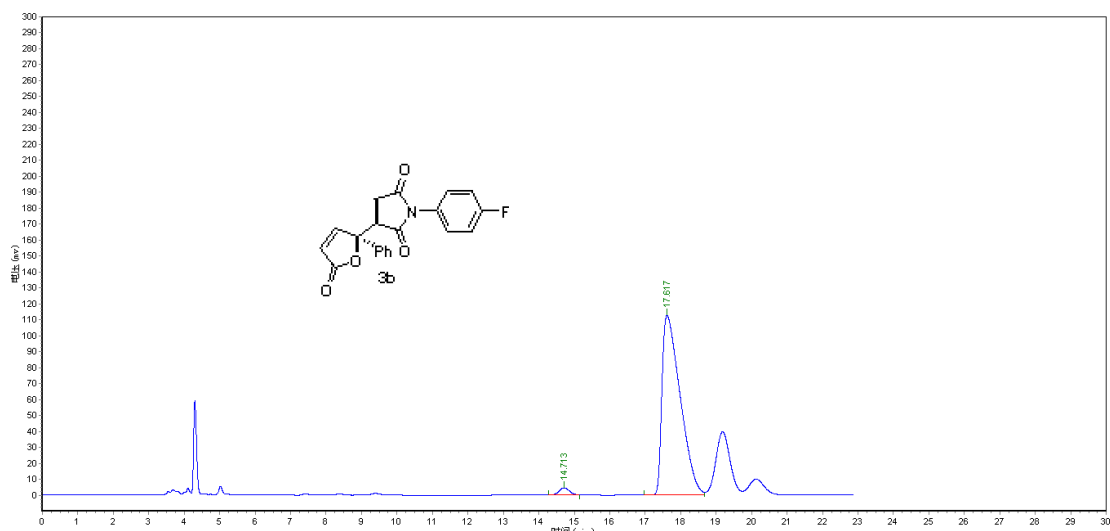


Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	15.462	558764.438	12329913.000	98.4644
2	18.767	7435.787	192290.047	1.5356

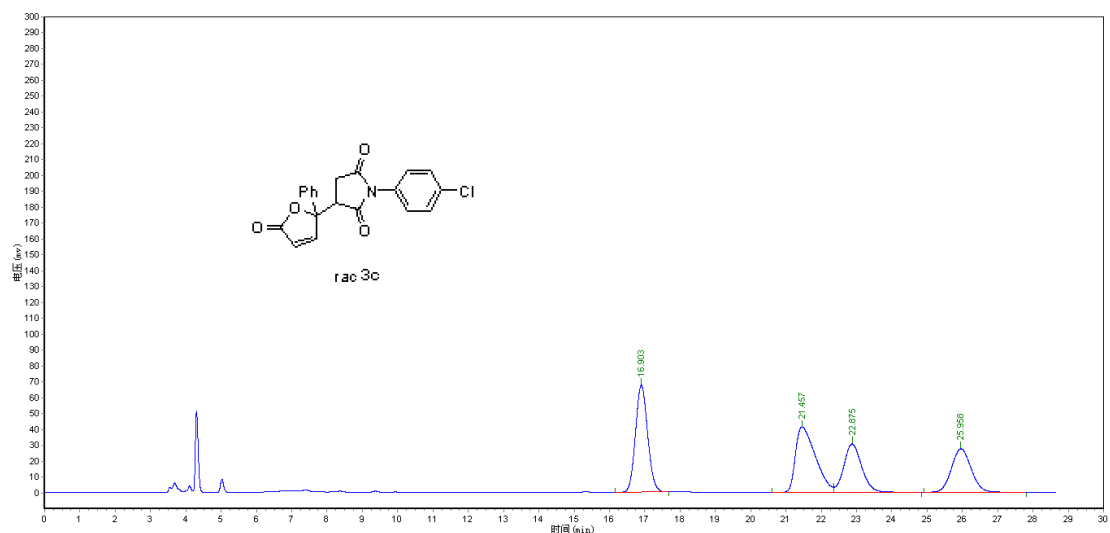




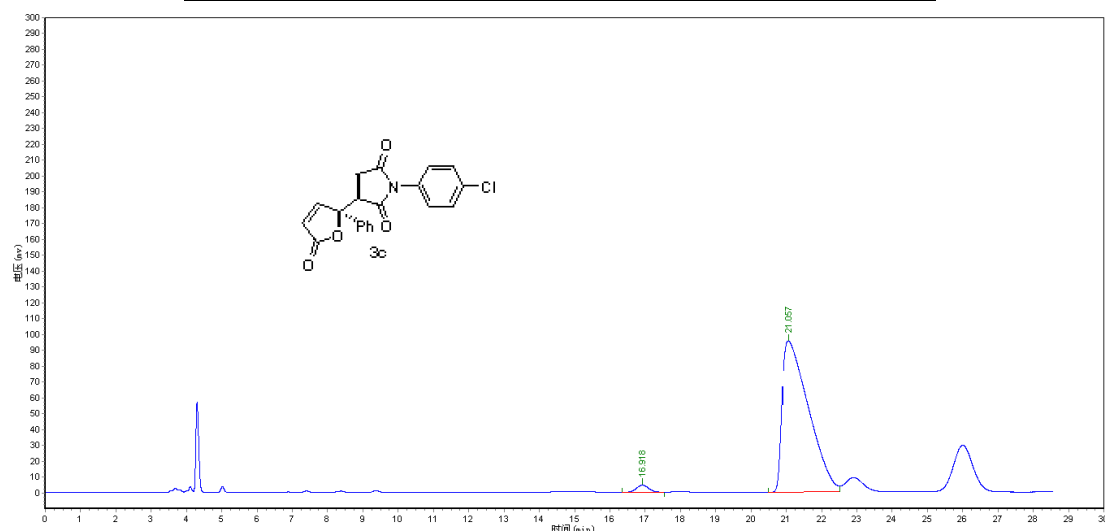
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	14.698	193956.219	4026605.750	29.3664
2	17.615	112718.273	3992043.000	29.1143
3	19.182	99828.594	2815600.750	20.5344
4	20.115	95126.703	2877378.000	20.9849



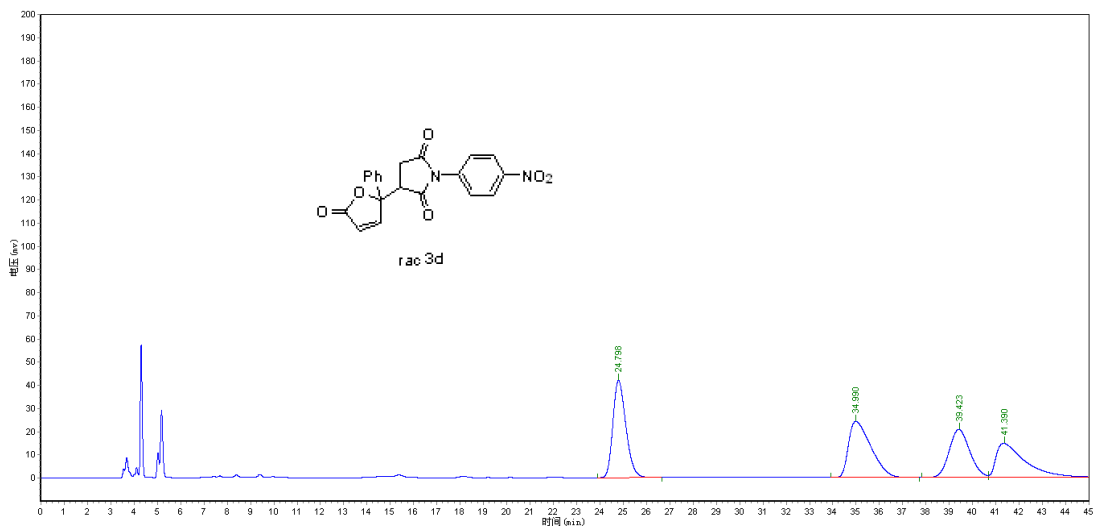
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	14.713	4534.848	92223.875	2.2442
2	17.617	112749.070	4017175.750	97.7558



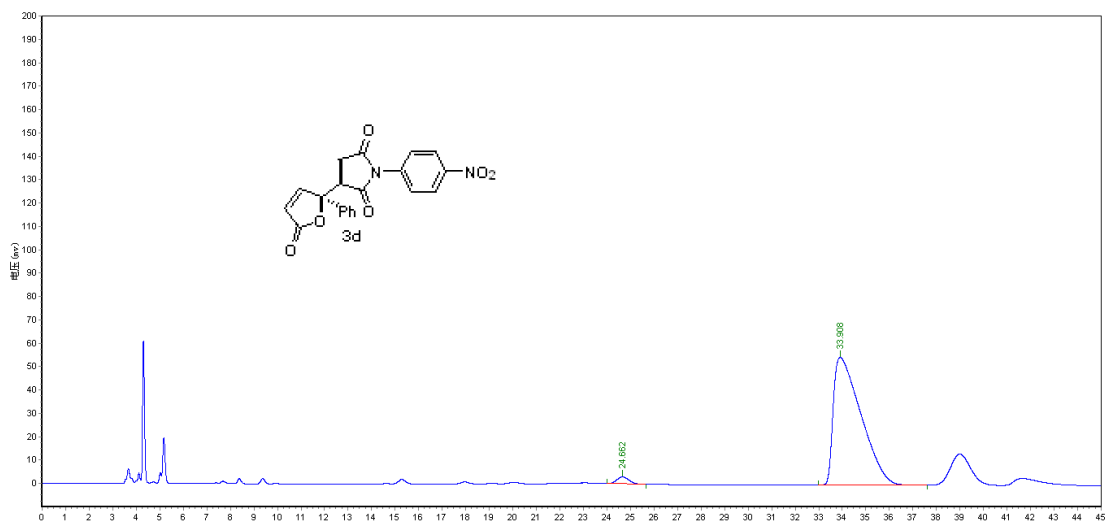
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	16.903	67446.188	1614178.000	30.1617
2	21.457	41208.969	1608164.375	30.0493
3	22.875	30470.871	1072916.125	20.0479
4	25.958	27383.795	1056493.375	19.7411



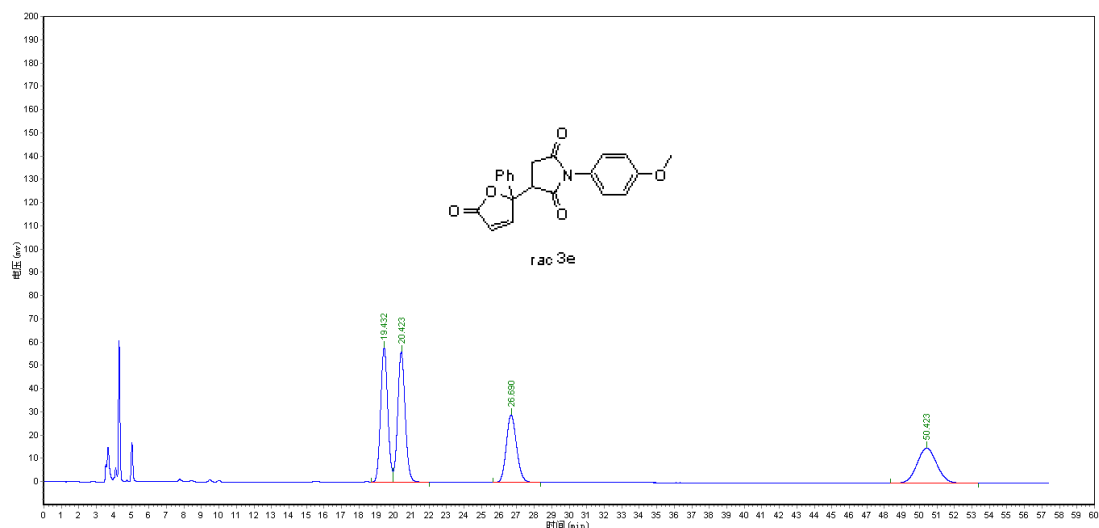
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	16.918	4491.180	107761.297	2.1234
2	21.057	95475.711	4967074.000	97.8765



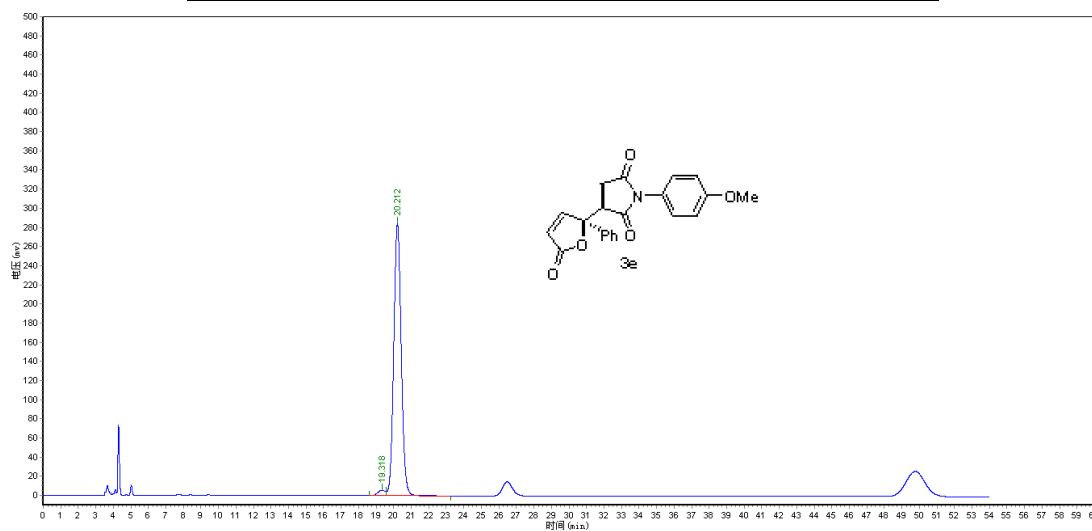
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	24.798	41886.059	1627868.250	28.0170
2	34.990	24176.246	1617652.375	27.8411
3	39.423	20623.900	1271841.375	21.8895
4	41.390	14689.401	1292931.500	22.2524



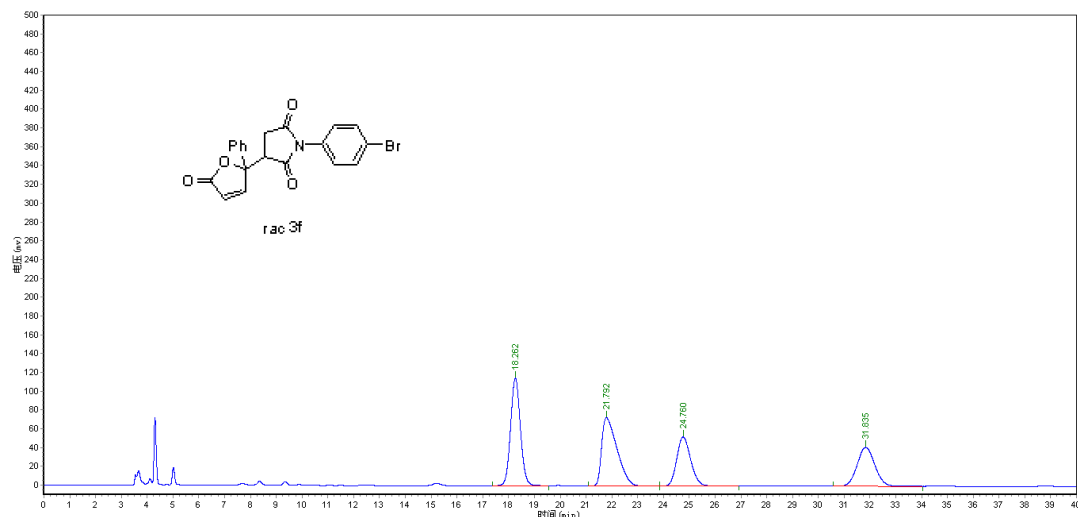
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	24.662	2932.684	105683.656	2.3138
2	33.908	54679.594	4461807.000	97.6862



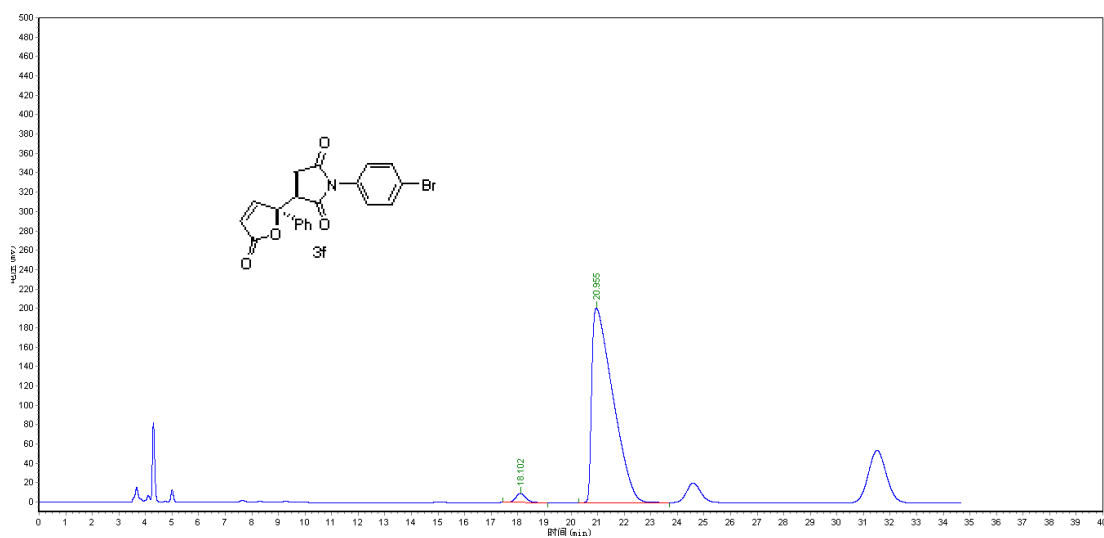
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	19.432	57761.852	1635921.500	28.9201
2	20.423	55882.164	1651876.000	29.2021
3	26.690	29064.914	1184007.875	20.9311
4	50.423	15070.583	1184890.500	20.9467



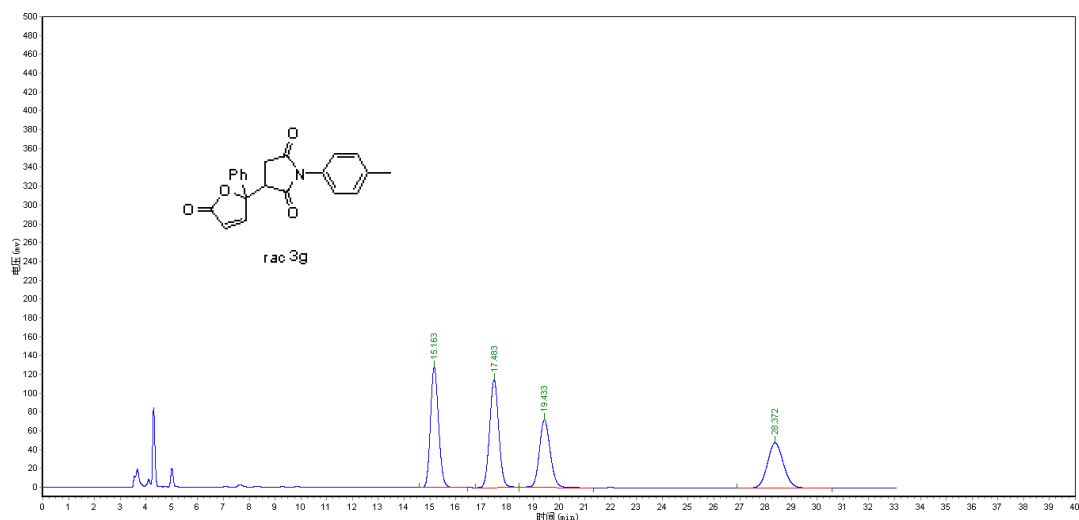
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	19.318	5826.944	170418.234	1.9786
2	20.212	284050.094	8442448.000	98.0214



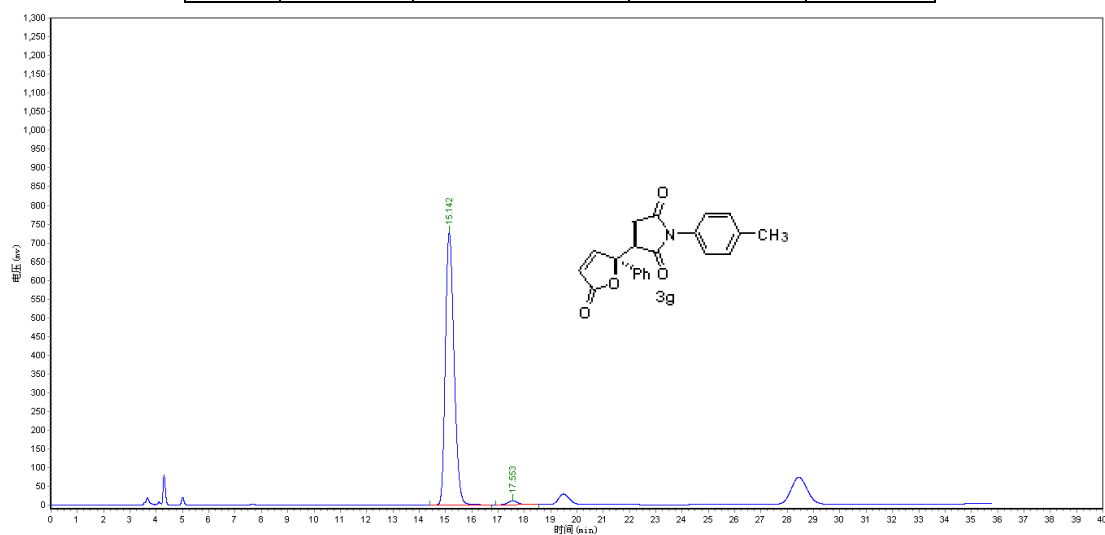
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	18.262	114452.703	3024875.500	30.4120
2	21.792	72564.633	2990599.250	30.0674
3	24.760	52331.043	1964496.375	19.7510
4	31.835	41344.438	1966348.500	19.7696



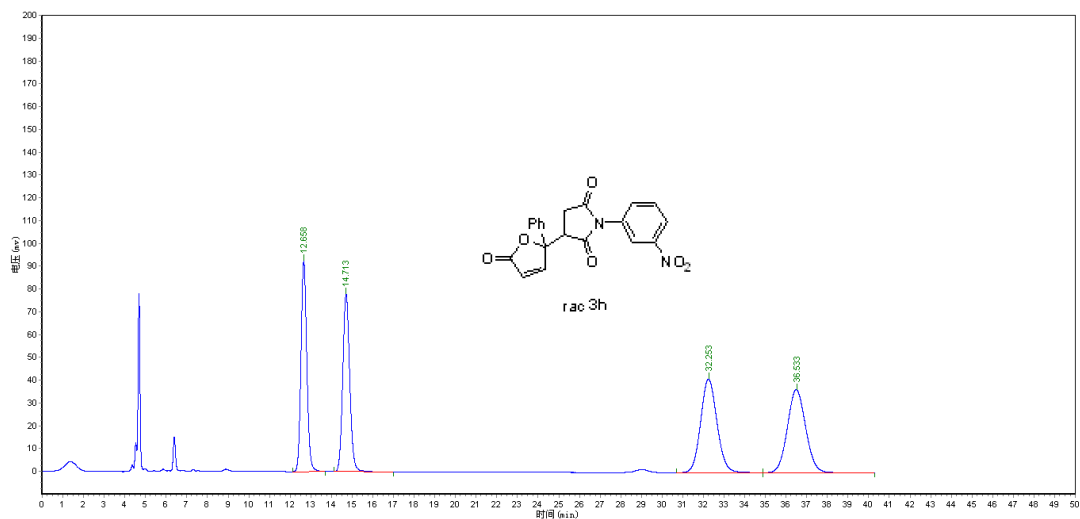
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	18.102	9226.181	244508.594	2.1636
2	20.955	200903.344	11056358.000	97.8364



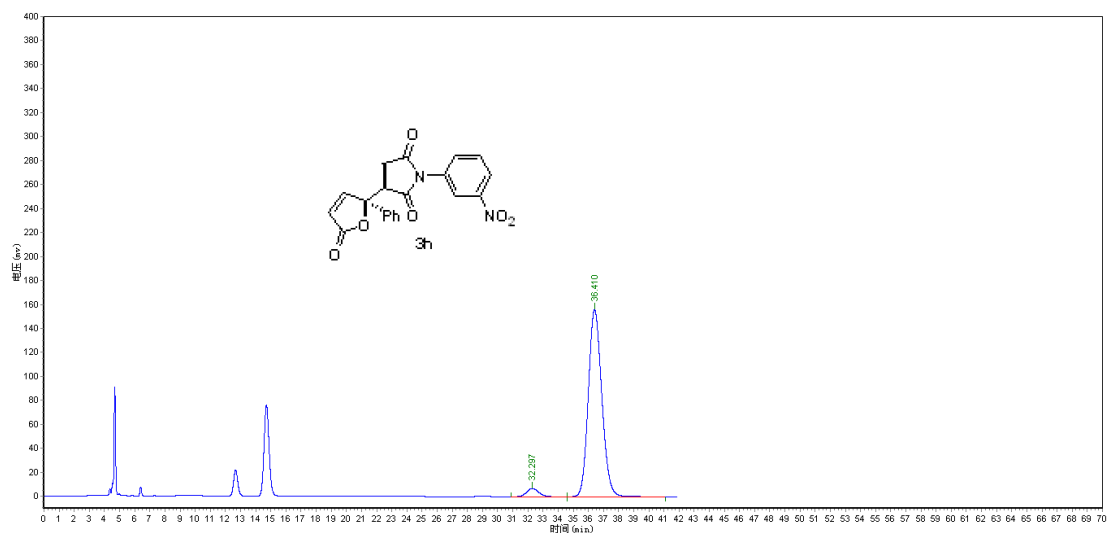
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	15.163	128059.516	2787174.750	28.8031
2	17.483	114241.711	2782915.250	28.7591
3	19.433	71556.125	2057388.375	21.2614
4	28.372	48012.992	2049166.625	21.1764



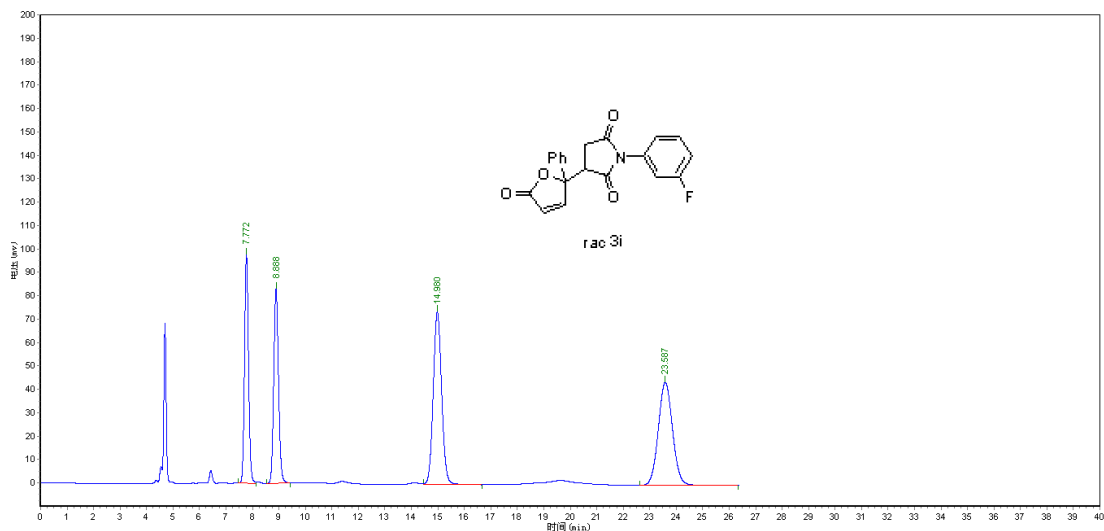
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	15.142	726830.813	16555297.000	98.4366
2	17.553	10837.622	262939.219	1.5634



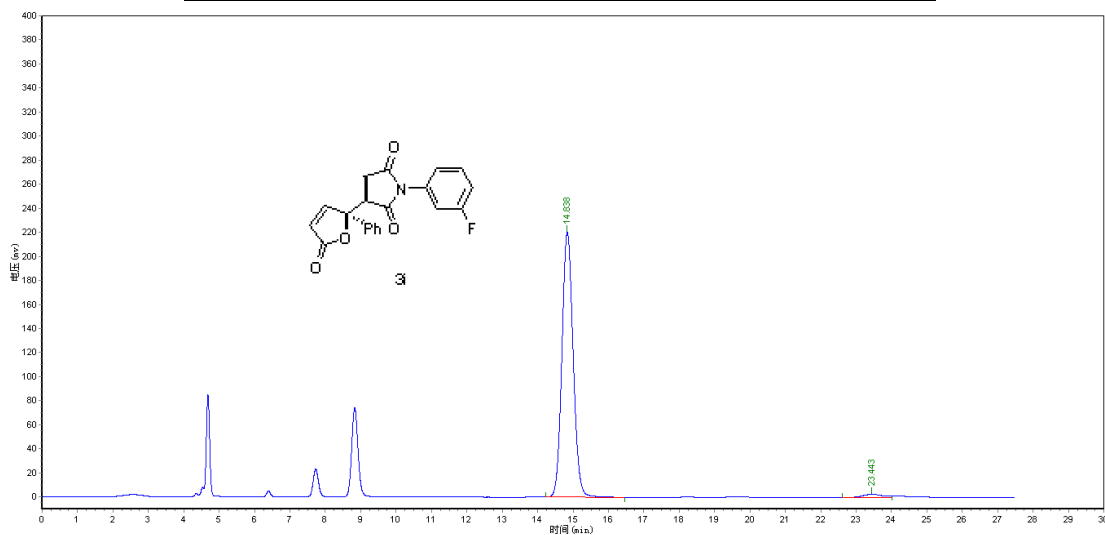
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	12.658	92224.664	1811916.875	22.2138
2	14.713	77898.031	1824431.000	22.3673
3	32.253	41036.988	2260634.000	27.7151
4	36.533	36368.492	2259718.250	27.7038



Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	32.297	6919.000	385162.500	3.8357
2	36.410	155893.703	9656291.000	96.1643

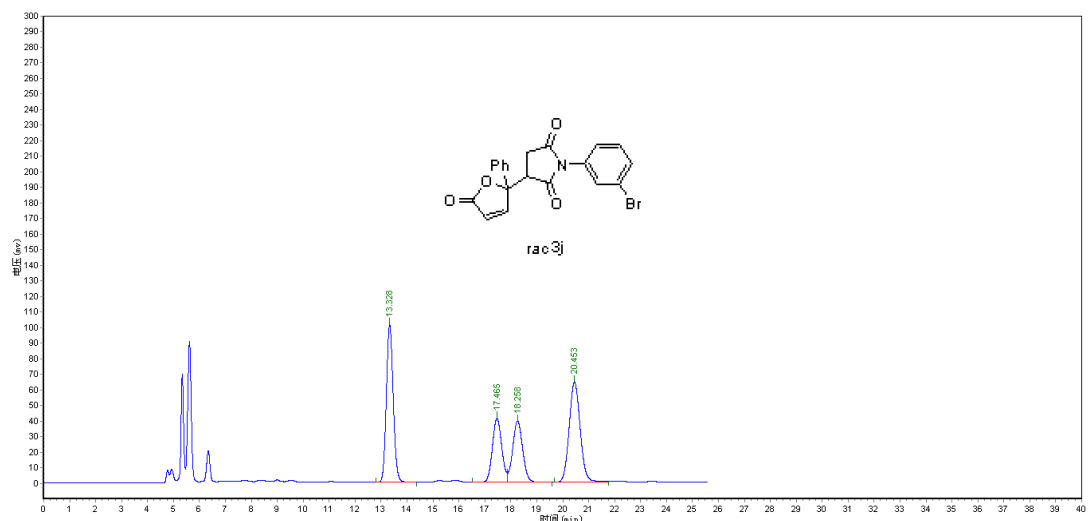


Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	7.772	97670.523	1028732.688	19.2422
2	8.888	83011.320	1038802.813	19.4306
3	14.980	73744.578	1635231.875	30.5866
4	23.587	43961.000	1643467.000	30.7406

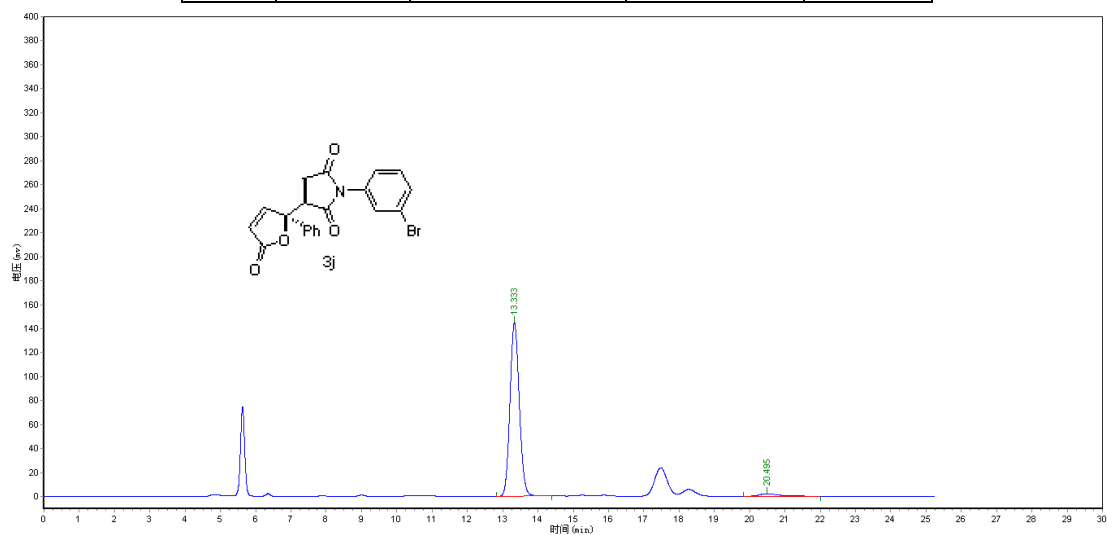


Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	14.838	220288.359	4851764.500	97.7737
2	23.443	2743.550	110472.367	2.2263

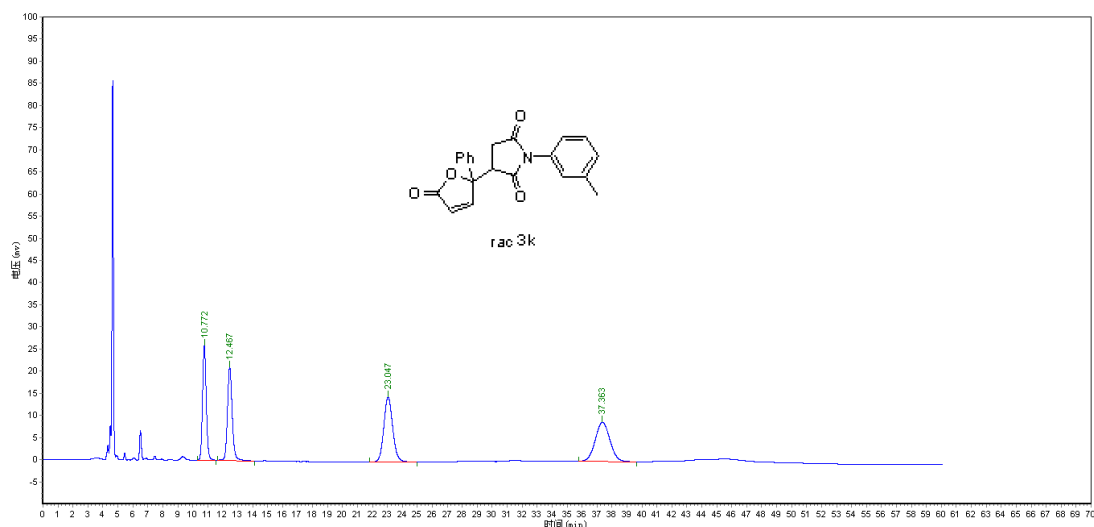




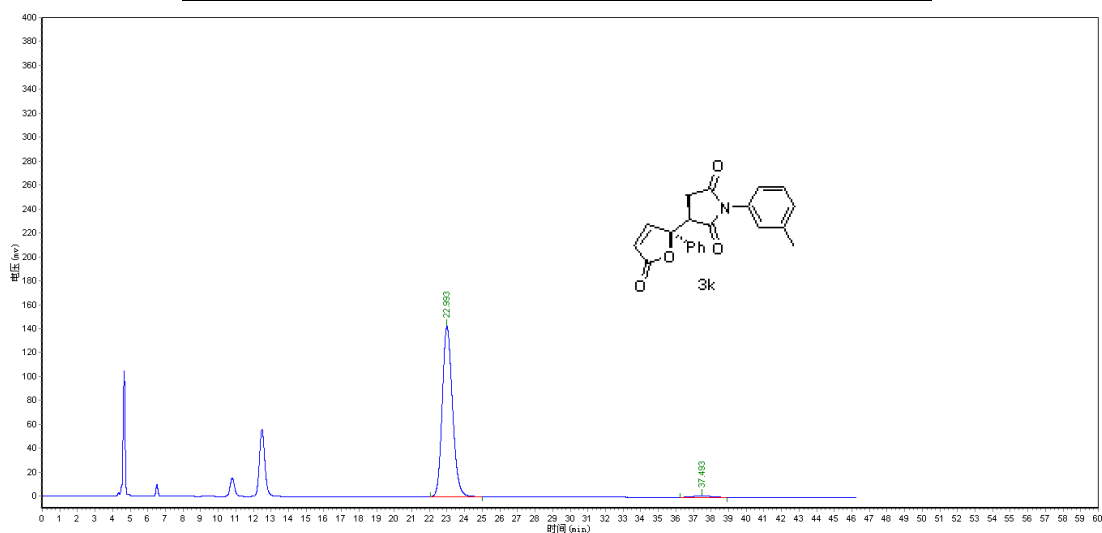
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	13.328	101027.859	1858826.750	31.7527
2	17.465	41067.301	1032279.625	17.6335
3	18.258	39402.367	1049159.625	17.9219
4	20.453	64232.703	1913813.000	32.6920



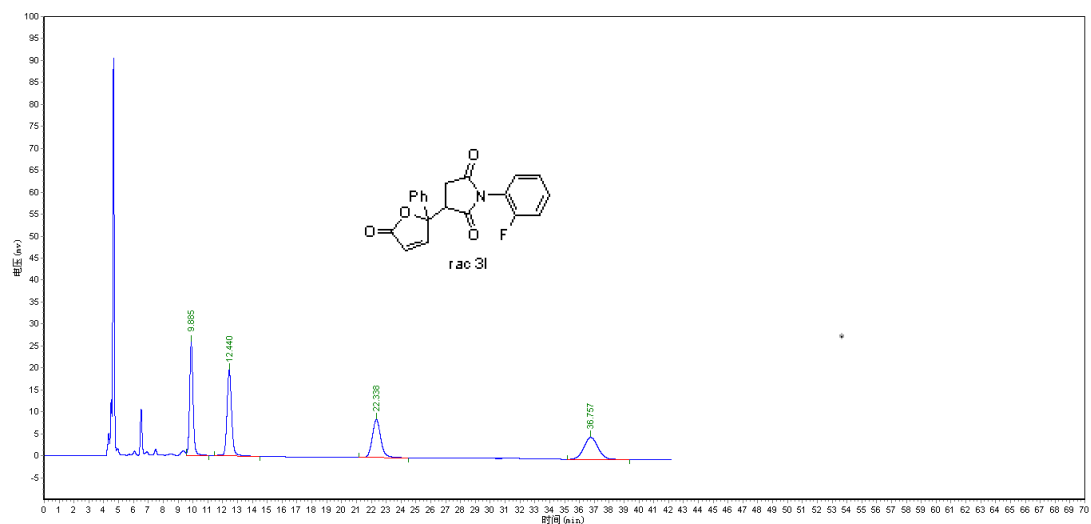
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	13.333	144632.984	2657440.250	96.8791
2	20.495	2169.279	85608.852	3.1209



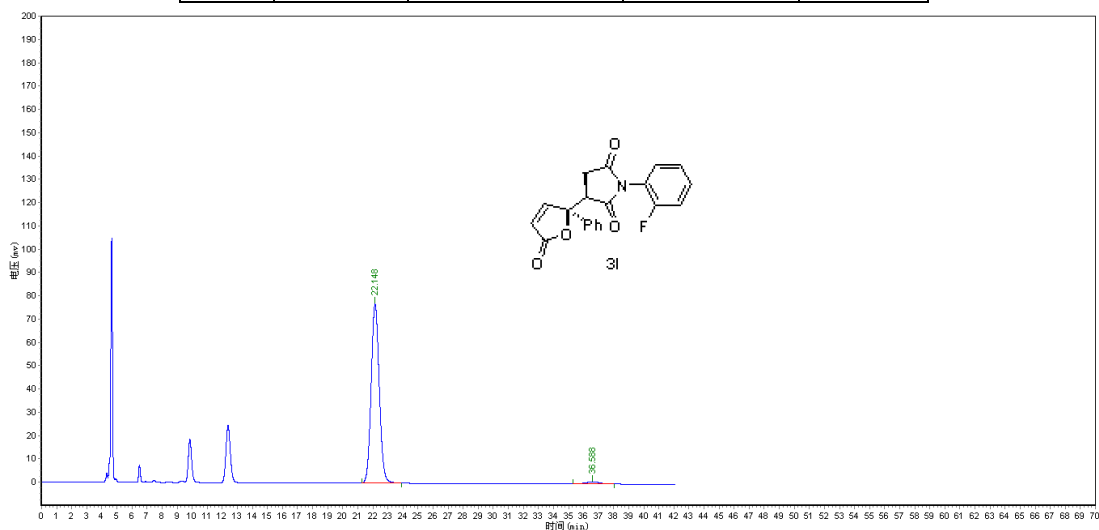
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	10.772	25790.639	450338.500	21.2231
2	12.467	21039.389	465095.813	21.9186
3	23.047	14664.769	607184.750	28.6148
4	37.363	8869.685	599303.750	28.2434



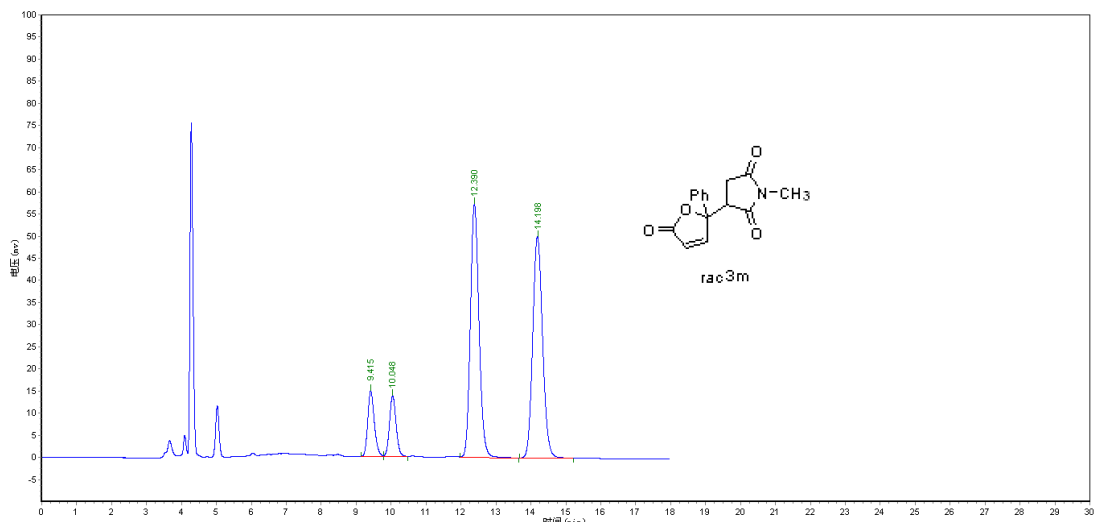
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	22.993	142279.734	5753646.500	98.5164
2	37.493	1309.790	86646.500	1.4836



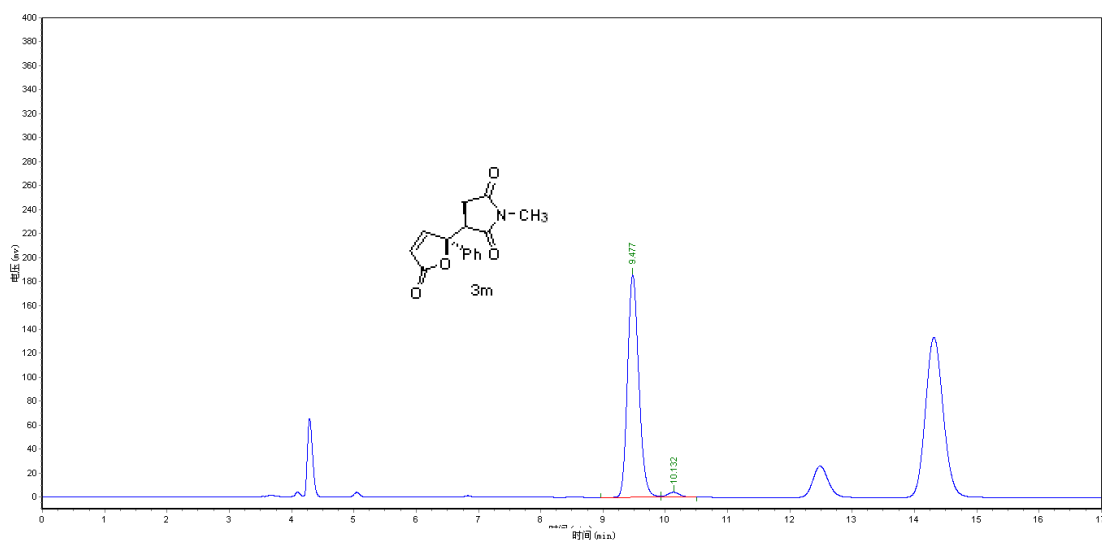
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	9.885	25732.828	413401.813	27.5238
2	12.440	19578.805	419018.906	27.8978
3	22.338	8664.123	339509.750	22.6041
4	36.757	4986.944	330049.188	21.9743



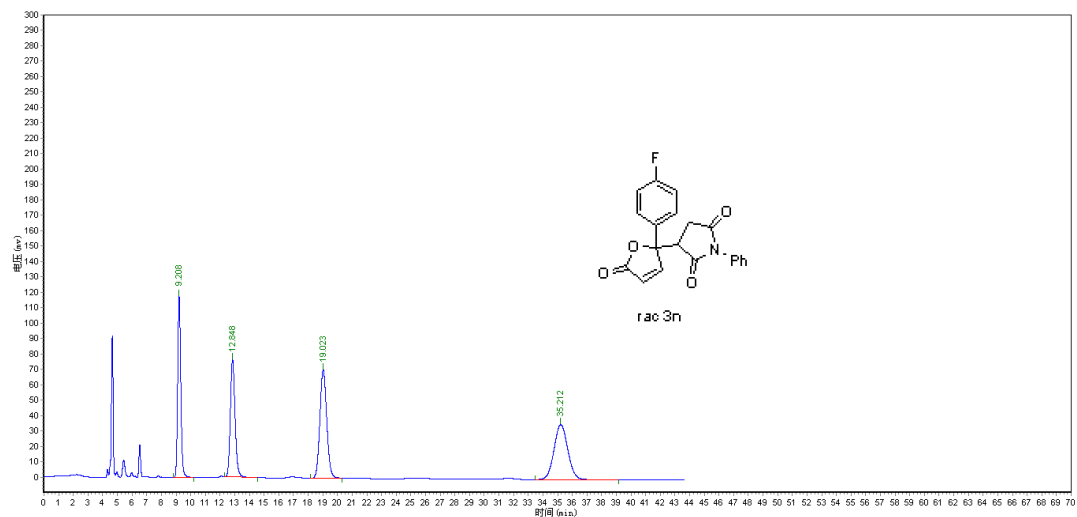
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	22.148	76768.422	2871967.750	97.9200
2	36.588	915.418	61007.301	2.0800



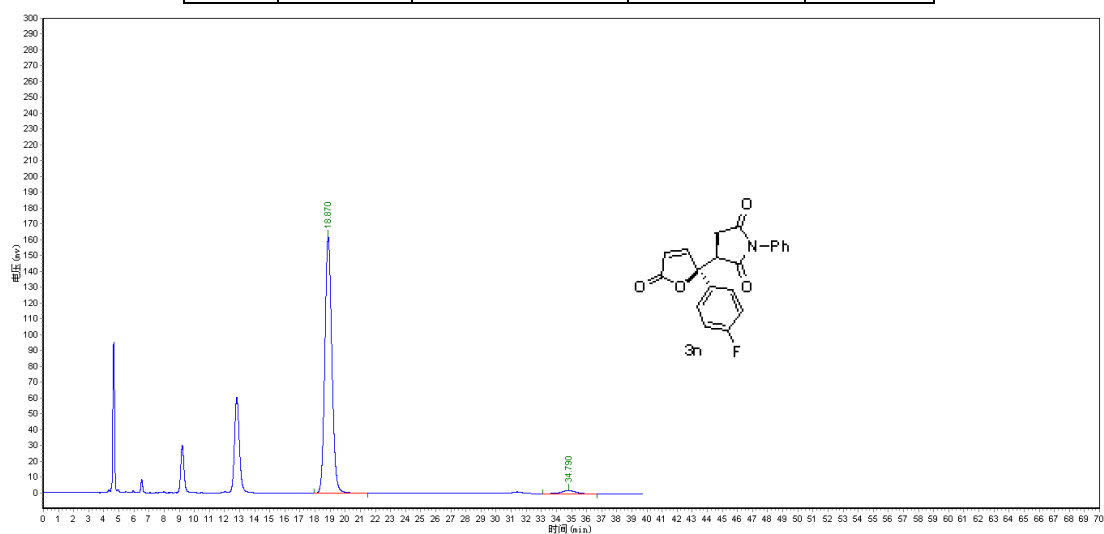
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	9.415	14727.787	192420.891	8.2399
2	10.048	13639.313	178425.609	7.6406
3	12.390	57144.816	980144.188	41.9722
4	14.198	50075.836	984233.188	42.1473



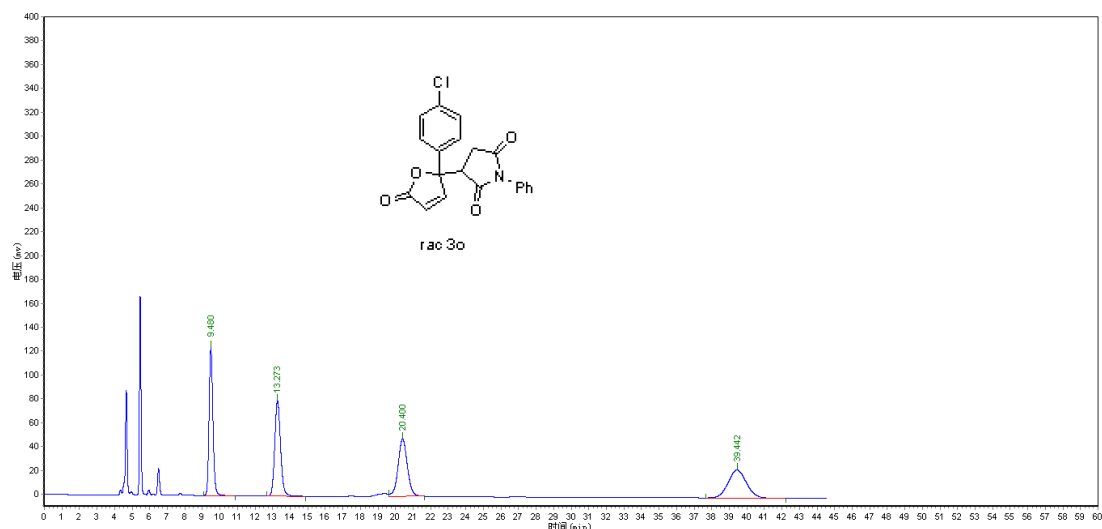
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	9.477	185365.203	2334369.750	97.5868
2	10.132	4098.399	57724.930	2.4132



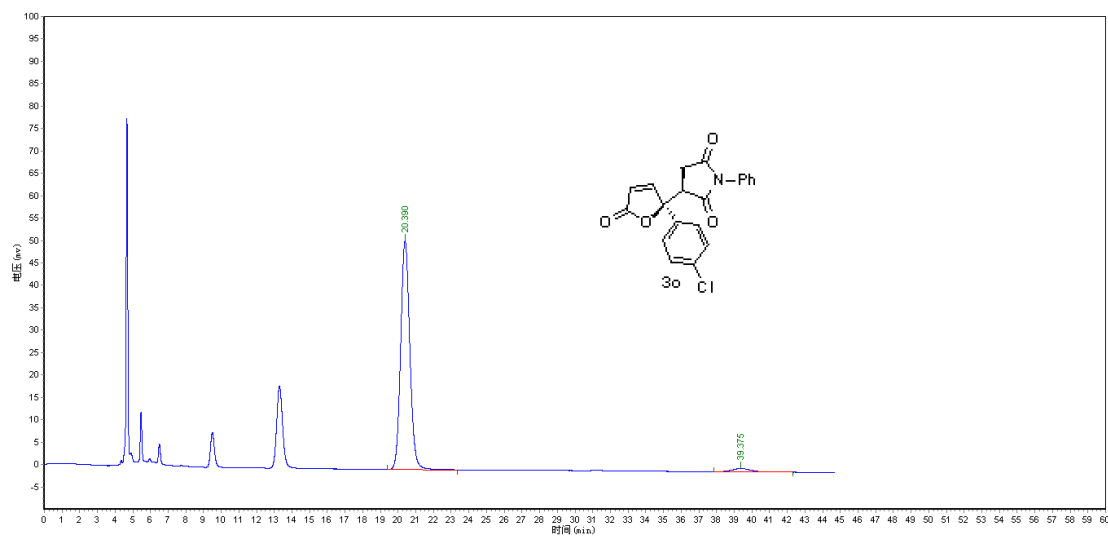
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	9.208	117397.227	1733921.125	21.4878
2	12.848	76436.258	1720065.875	21.3161
3	19.023	70366.297	2282811.500	28.2900
4	35.212	35826.762	2332523.750	28.9061



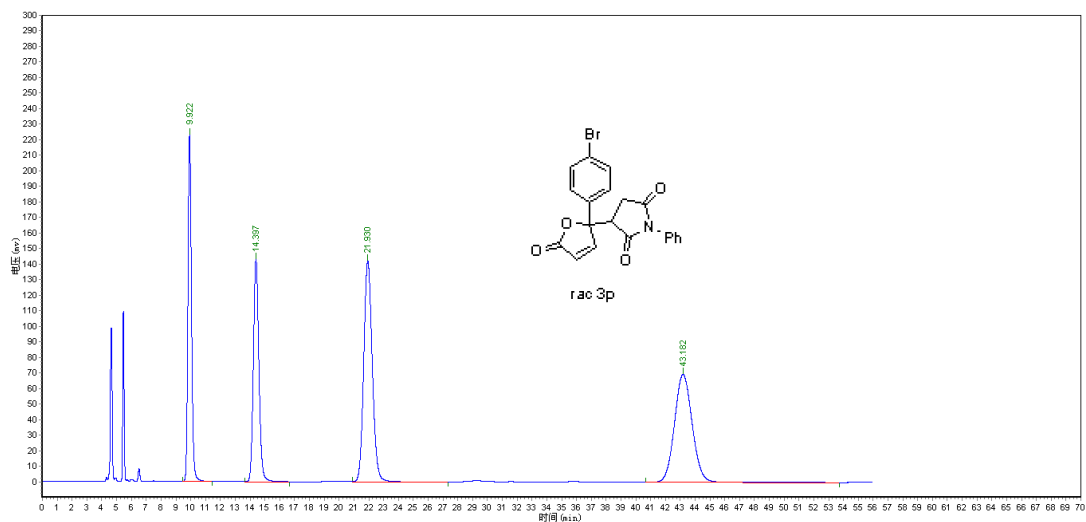
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	18.870	162153.719	5225613.000	97.6185
2	34.790	1942.891	127482.547	2.3815



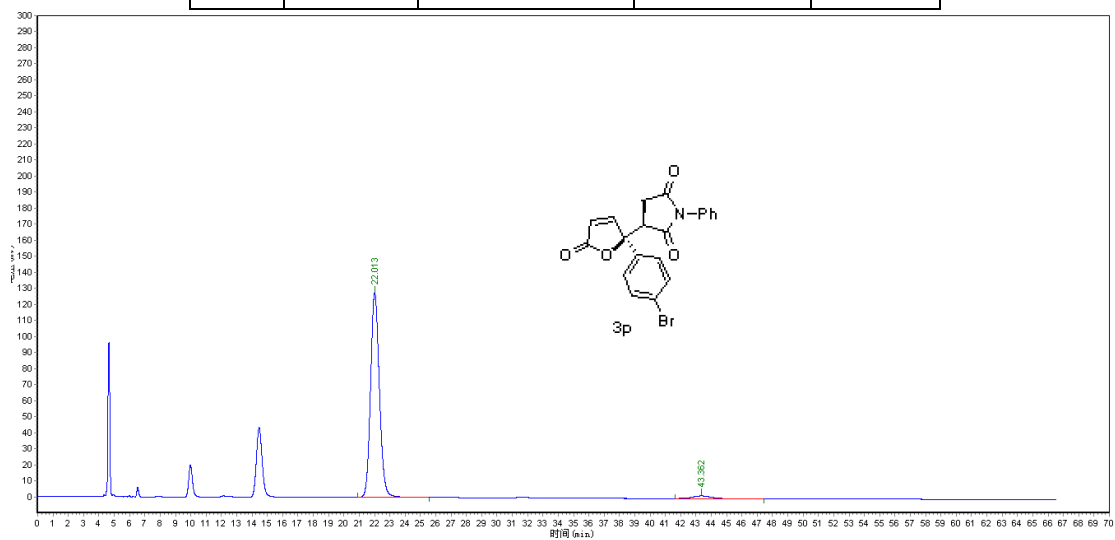
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	9.480	123814.117	1898169.500	26.3160
2	13.273	80028.648	1844499.125	25.5719
3	20.400	48119.168	1769619.875	24.5338
4	39.442	23359.359	1700698.000	23.5783



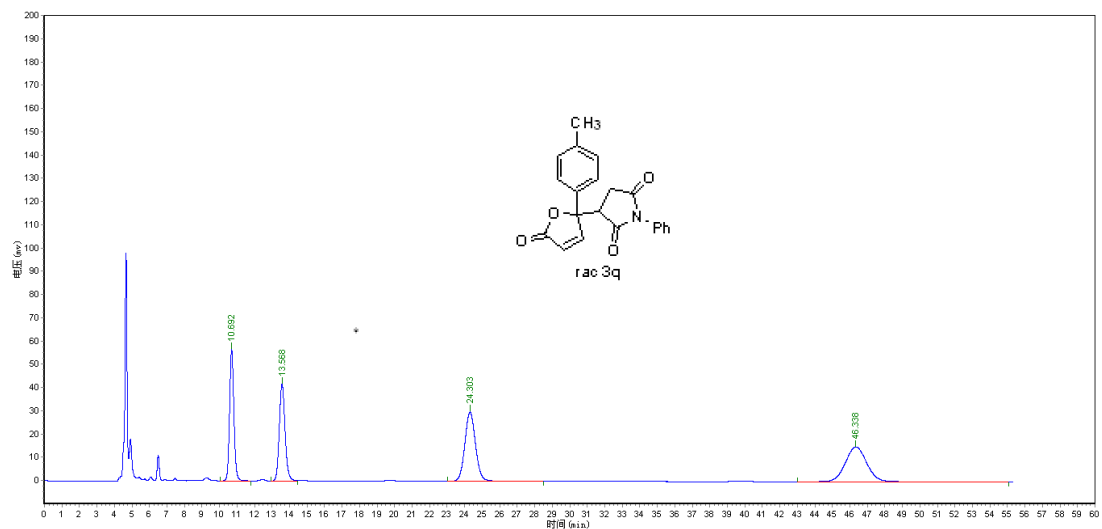
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	20.390	51037.648	1836498.125	97.1532
2	39.375	733.065	53814.211	2.8468



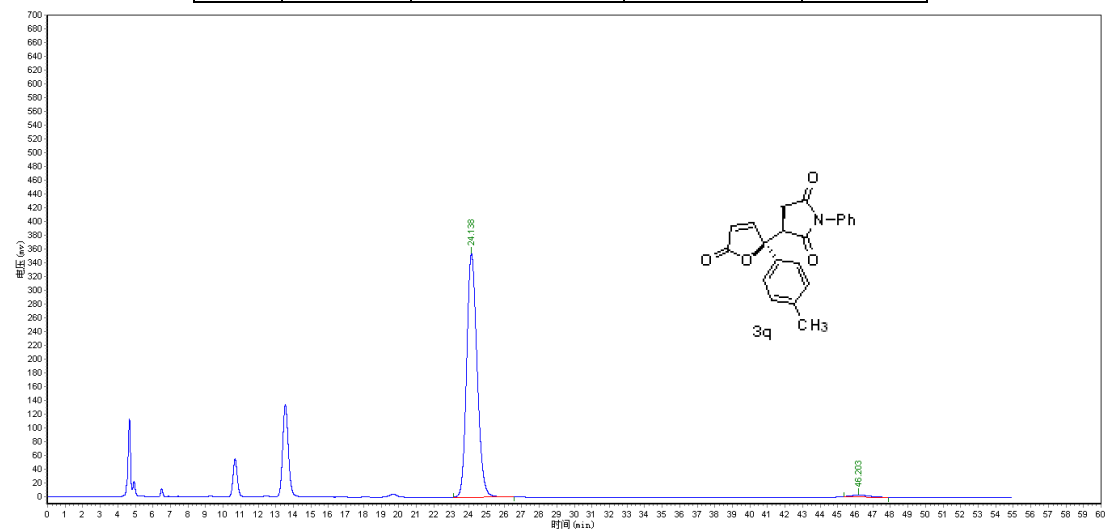
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	9.922	222978.734	3705097.250	19.6432
2	14.397	143080.266	3709828.250	19.6683
3	21.930	142281.781	5699361.500	30.2161
4	43.182	69428.164	5747727.500	30.4725



Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	22.013	127578.430	5107937.000	97.3259
2	43.362	1665.118	140344.688	2.6741

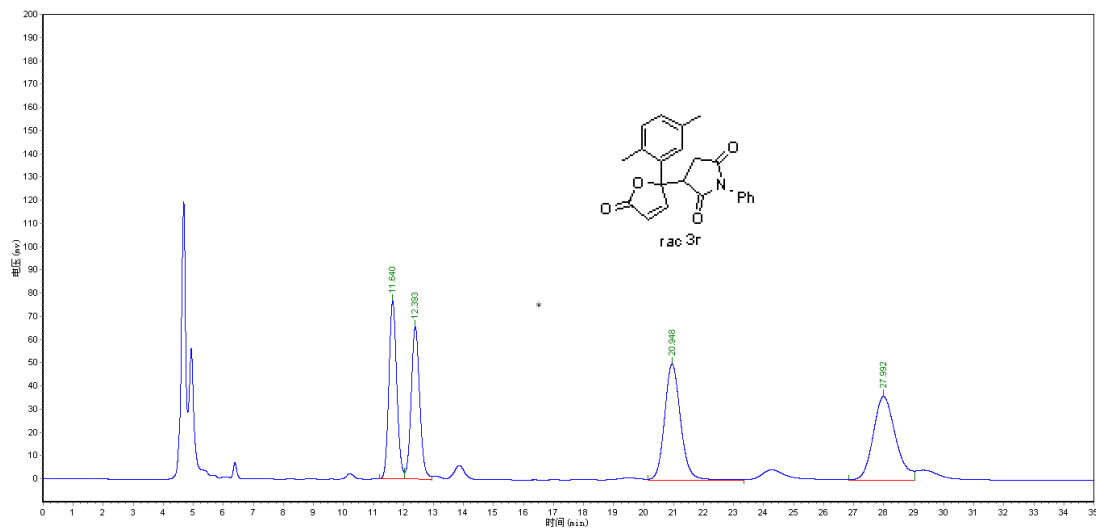


Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	10.692	56607.113	971988.938	21.6972
2	13.568	41793.234	962435.688	21.4840
3	24.303	29790.688	1263184.125	28.1974
4	46.338	14943.229	1282178.875	28.6214

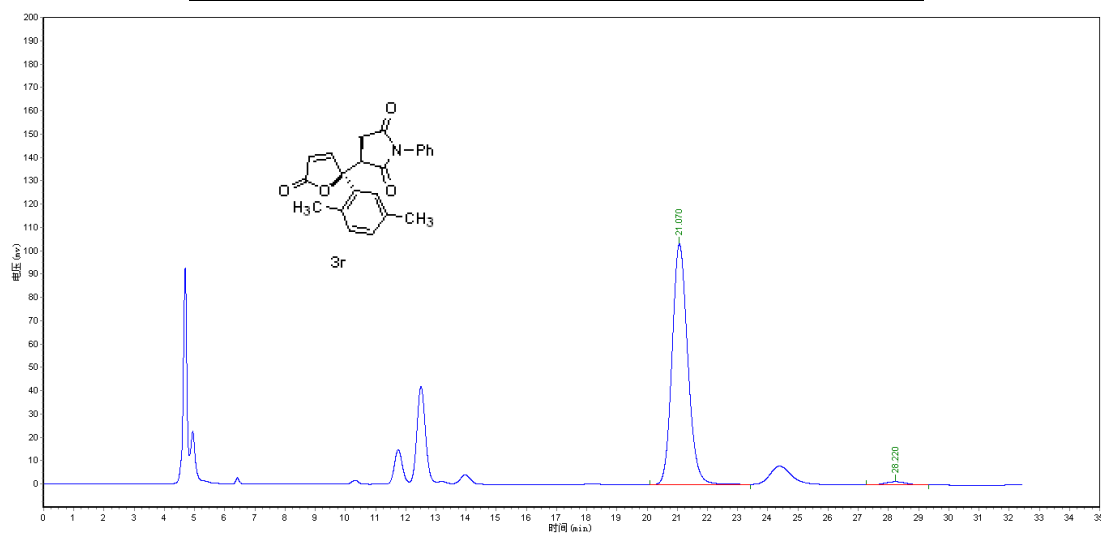


Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	24.138	353756.125	14585029.000	98.8712
2	46.203	2468.333	166508.406	1.1288

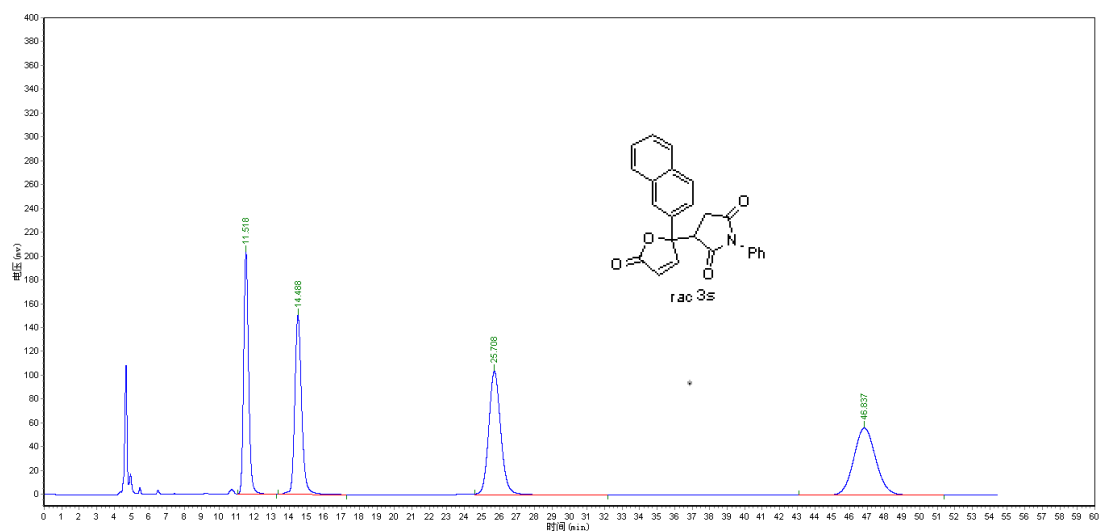




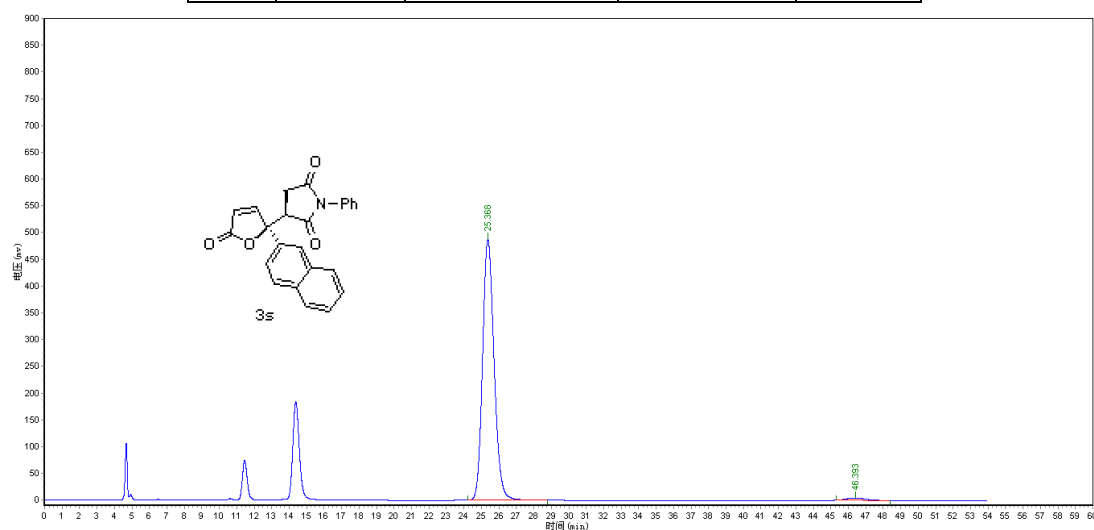
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	11.640	76490.922	1393198.625	21.7014
2	12.393	65625.461	1298067.125	20.2195
3	20.948	49990.965	1858089.750	28.9428
4	27.992	36108.949	1870508.375	29.1363



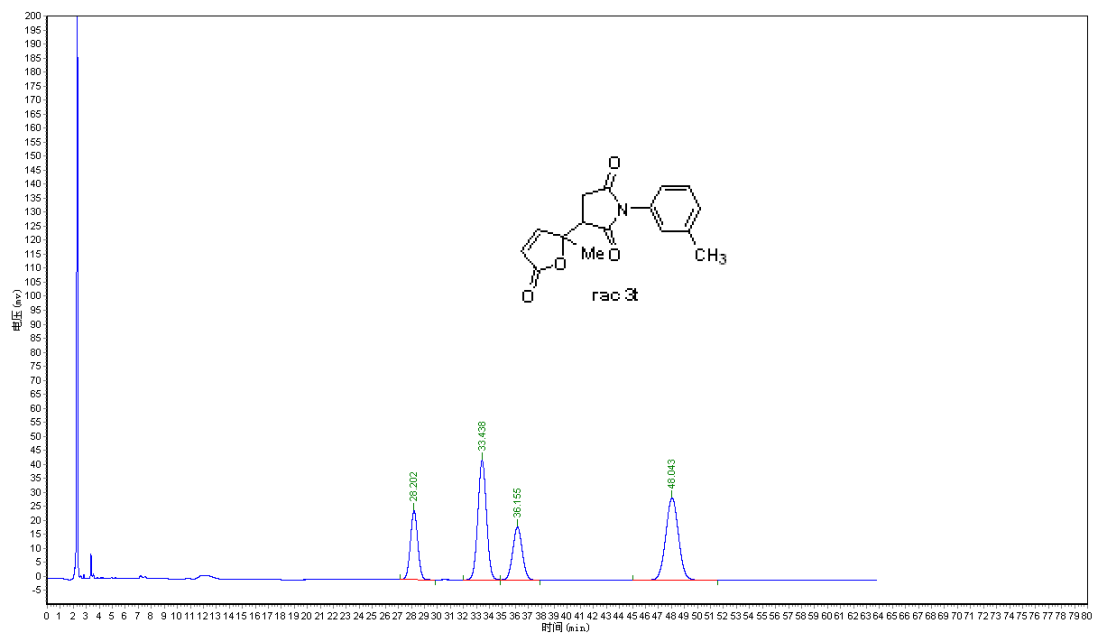
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	21.070	103217.664	3741532.750	98.2636
2	28.220	1386.738	66115.500	1.7364



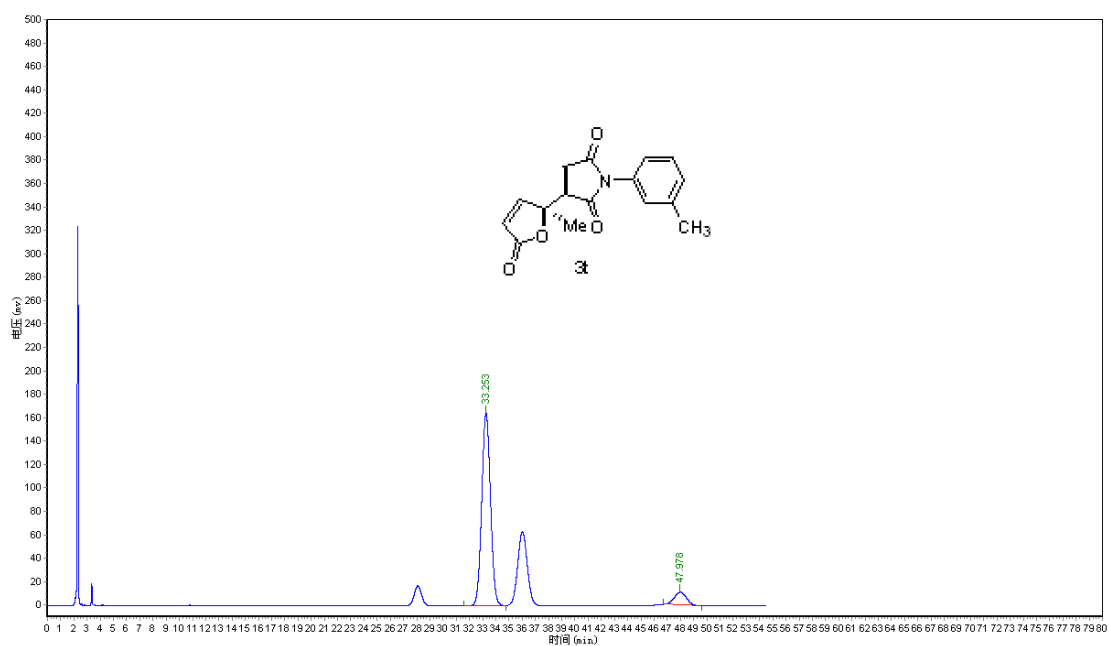
Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	11.518	203051.188	3994599.500	22.2269
2	14.488	150376.750	4083010.500	22.7188
3	25.708	103649.344	4959143.500	27.5938
4	46.837	56549.922	4935162.000	27.4604



Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	25.368	487294.719	22296036.000	98.5912
2	46.393	4155.056	318602.688	1.4088



Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	28.202	24514.580	960622.500	16.2466
2	33.438	42597.605	1975107.625	33.4042
3	36.155	18898.092	964426.375	16.3109
4	48.043	29433.535	2012599.750	34.0383



Peak	RT(min.)	Height(mV*sec)	Area(mV)	Area(%)
1	33.253	164512.313	7615249.000	91.5508
2	47.978	10884.428	702814.000	8.4493

### Copies of NMR spectra

