Design, Synthesis and Biological Evaluation of Novel Potent and Selective $\alpha_v\beta_3/\alpha_v\beta_5$ Integrin Dual Inhibitors With Improved Bioavailability. Selection of the Molecular Core.

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The purity of the final compounds was analyzed with a 218 PrepStar Varian HPLC system connected to a ProStar Varian UV detector and following the peaks at λ=254 nm. The flow was 1 ml/min and the gradient was from 5% acetonitrile-water (with 0.1% of trifluoroacetic acid), until 95% over a period of 23 minutes. The columns for the analysis were Betabasic C18 (5μ, 150Å, 150 X 4.6 mm) and Betabasic C8 (5μ, 150Å, 150 X 4.6 mm).

Method File : 219089-final001-2.mth
Sample ID : 219089-final

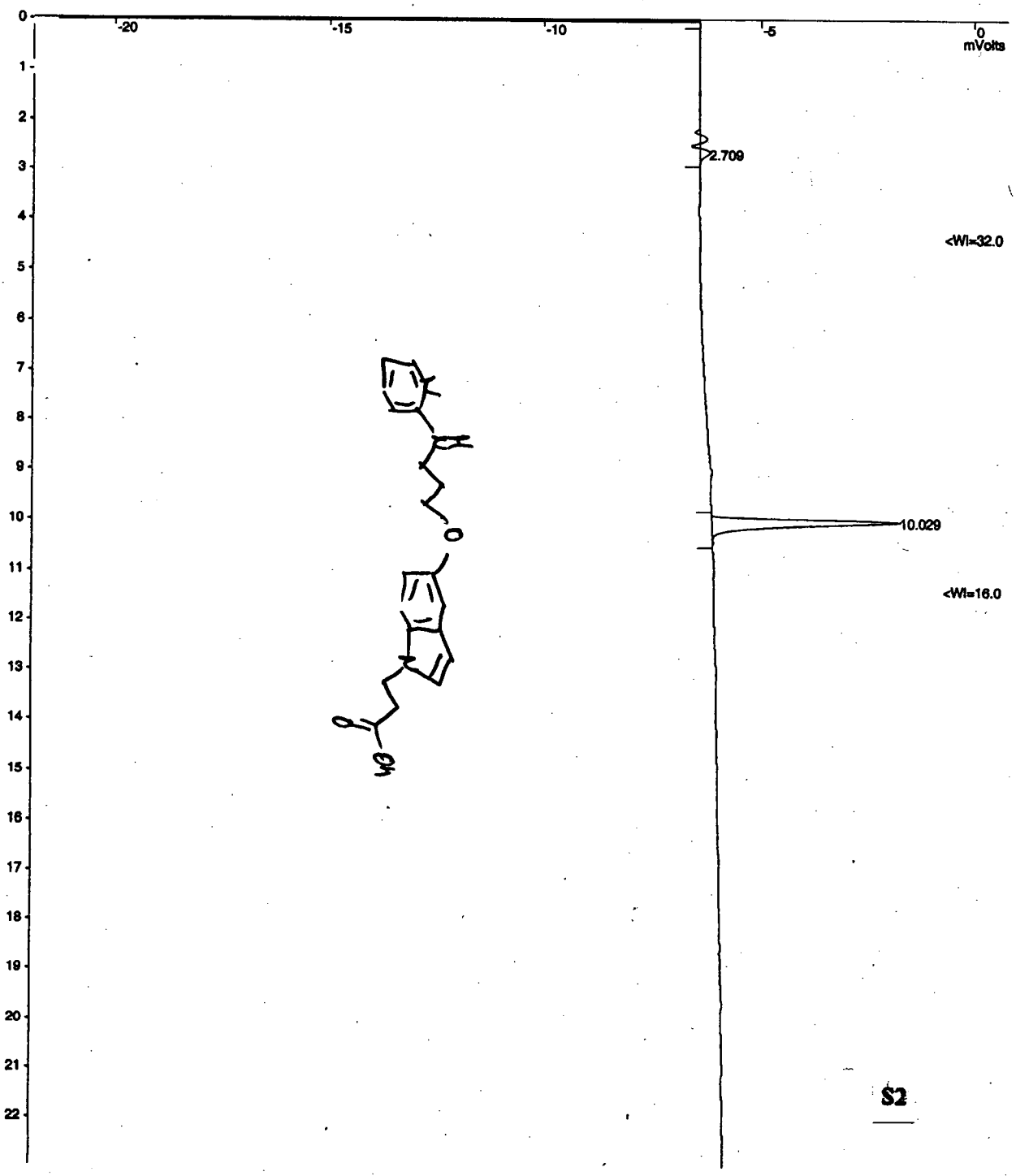
Injection Date: 8/18/2004 7:13 PM Calculation Date: 8/18/2004 8:01 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 2 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.86 cm/min Attenuation = 37 Zero Offset = 96%
Start Time = 0.000 min End Time = 22.990 min Min / Tick = 1.00



```
Title       :
Run File    : c:\star\data\kristi\219089-final001.run
Method File : 219089-final001-2.mth
Sample ID   : 219089-final

Injection Date: 8/18/2004 7:13 PM    Calculation Date: 8/18/2004 8:01 PM

Operator    :                        Detector Type: ProStar/Dynamax (2 Volts)
Workstation:                         Bus Address  : 24
Instrument : Varian Star #1          Sample Rate  : 5.00 Hz
Channel    : 2 = INTGR 1             Run Time     : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode         : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)
```

Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
1		3.5601	2.709	0.000	1379	BB	9.8	U
2		96.4399	10.029	0.000	37352	BB	7.7	
	Totals:	100.0000		0.000	38731			

```
Status Codes:
U - User-defined peak endpoint(s)

Total Unidentified Counts :      38731 counts

Detected Peaks: 2          Rejected Peaks: 0      Identified Peaks: 0

Multiplier: 1          Divisor: 1          Unidentified Peak Factor: 0

Baseline Offset: -6422 microVolts          LSB:     1 microVolts

Noise (used): 100 microVolts - fixed value
Noise (monitored before this run): 26672 microVolts

Manual injection

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```

Title :
Method File : 219089-c8-3002-2.mth
Sample ID : 219089-C8-3

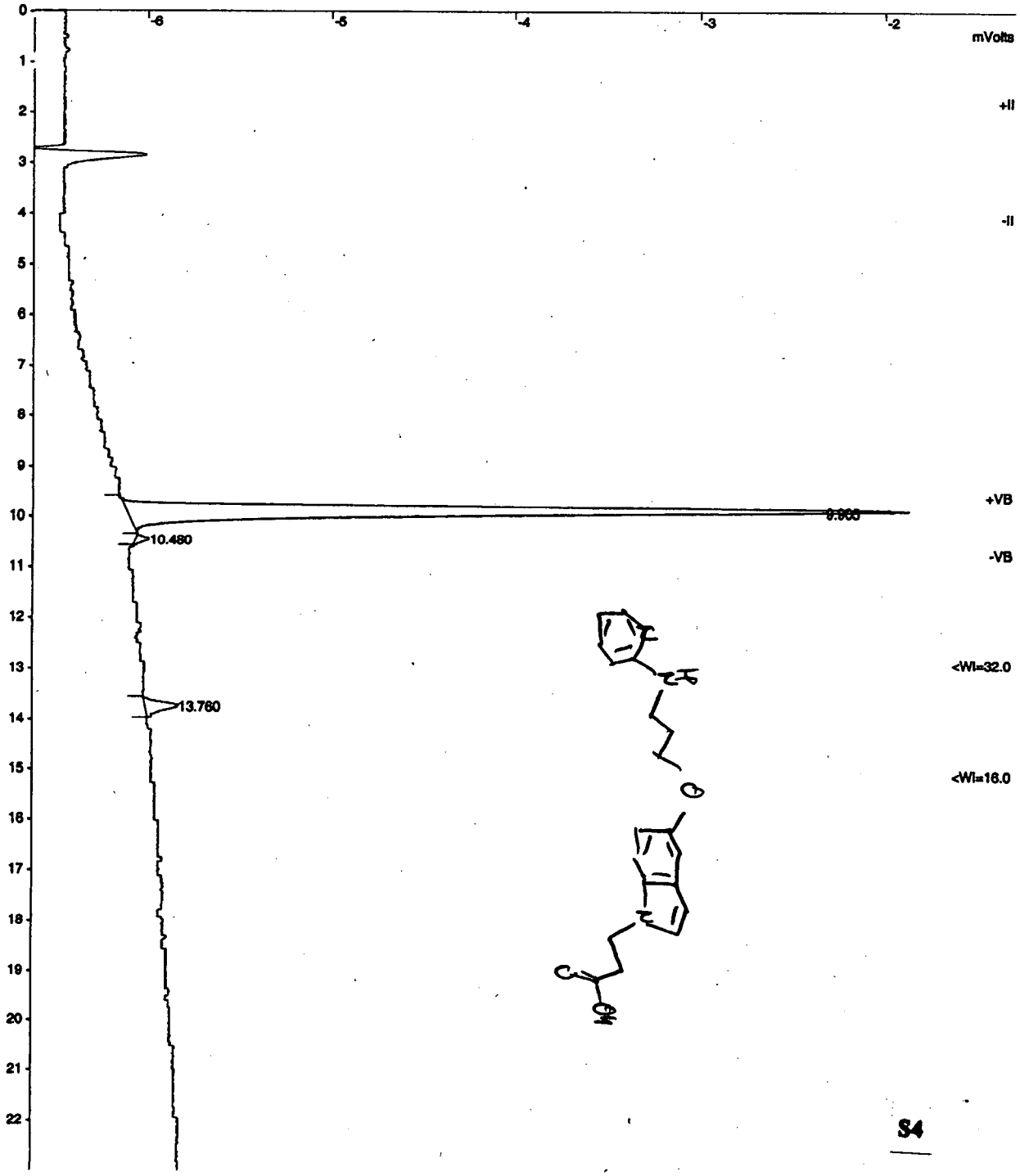
Injection Date: 8/20/2004 3:22 PM Calculation Date: 8/26/2004 2:57 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 2 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.86 cm/min Attenuation = 8 Zero Offset = 135%
Start Time = 0.000 min End Time = 22.990 min Min / Tick = 1.00



```
Title        :
Run File     : c:\star\data\kristi\219089-c8-3002.run
Method File  : 219089-c8-3002-2.mth
Sample ID    : 219089-C8-3

Injection Date: 8/20/2004 3:22 PM    Calculation Date: 8/26/2004 2:57 PM

Operator    :                        Detector Type: ProStar/Dynamax (2 Volts)
Workstation:                         Bus Address  : 24
Instrument : Varian Star #1          Sample Rate  : 5.00 Hz
Channel    : 2 = INTGR 1             Run Time     : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode         : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)
```

Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
1		94.8457	9.905	0.000	44672	BB	10.5	U
2		1.0795	10.480	0.000	508	BB	0.0	U
3		4.0748	13.760	0.000	1919	BB	10.6	U
	Totals:	100.0000		0.000	47099			

```
Status Codes:
U - User-defined peak endpoint(s)

Total Unidentified Counts :      47100 counts

Detected Peaks: 3          Rejected Peaks: 0      Identified Peaks: 0

Multiplier: 1          Divisor: 1          Unidentified Peak Factor: 0

Baseline Offset: -6449 microVolts          LSB:     1 microVolts

Noise (used): 25 microVolts - fixed value
Noise (monitored before this run): 26155 microVolts

Manual injection

*******************************************************************************
```

Title :
Method File : 219029-final001-2.mth
Sample ID : 219029-final

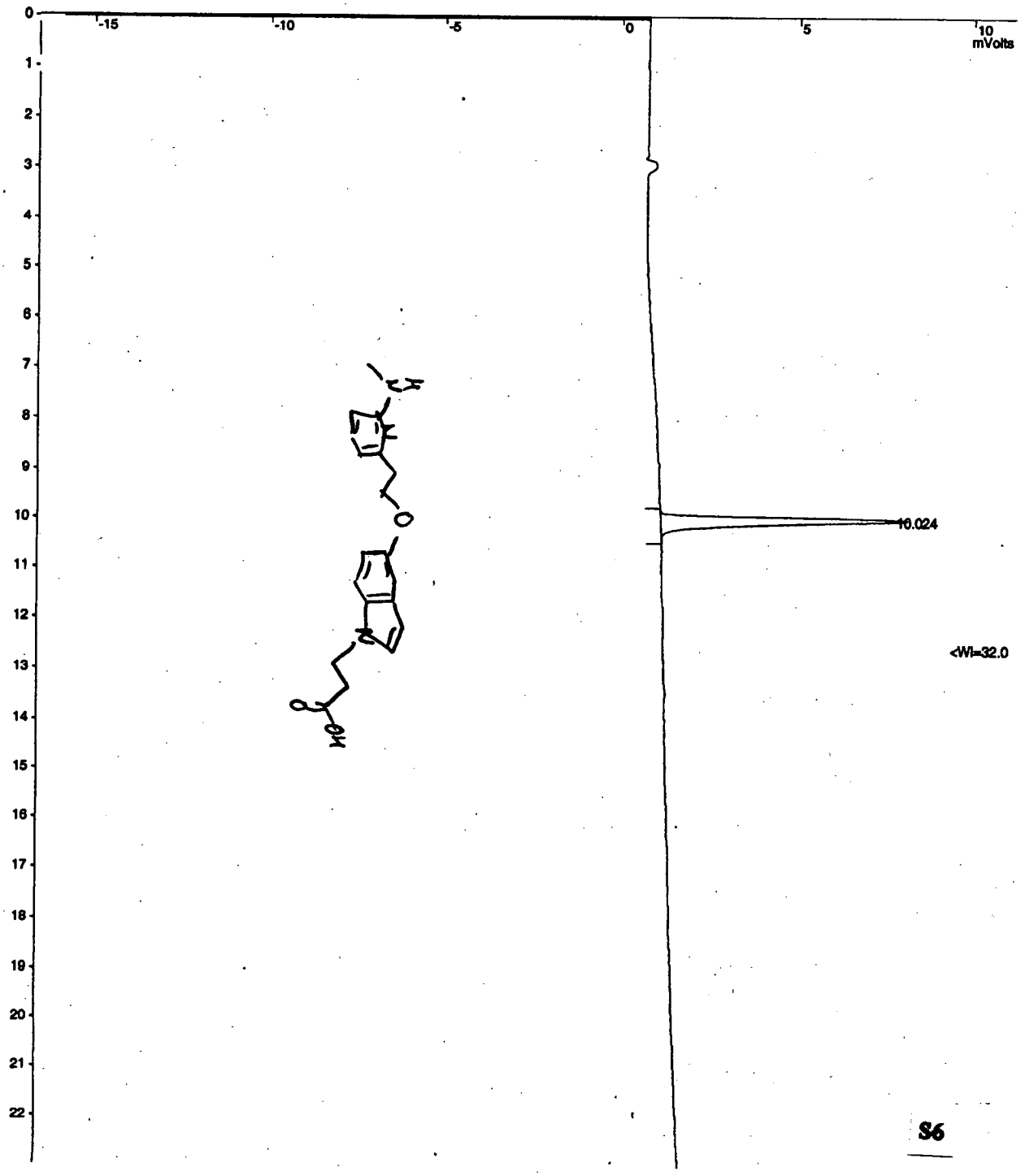
Injection Date: 8/18/2004 6:29 PM Calculation Date: 8/18/2004 7:24 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 1 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.987 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.87 cm/min Attenuation = 45 Zero Offset = 60%
Start Time = 0.000 min End Time = 22.987 min Min / Tick = 1.00



```
Title       :
Run File    : c:\star\data\kristi\219029-final001.run
Method File : 219029-final001-2.mth
Sample ID   : 219029-final

Injection Date: 8/18/2004 6:29 PM    Calculation Date: 8/18/2004 7:24 PM

Operator    :                        Detector Type: ProStar/Dynamax (2 Volts)
Workstation:                         Bus Address  : 24
Instrument : Varian Star #1          Sample Rate  : 5.00 Hz
Channel    : 1 = INTGR 1             Run Time     : 22.987 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode         : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)

                                  Ret.    Time                      Width
 Peak     Peak        Result      Time   Offset      Area    Sep.   1/2    Status
  No.     Name          ()        (min)  (min)     (counts)  Code  (sec)   Codes
 ---- ------------ ---------- ------- ------- ---------- ---- ----- ------
    1                100.0000   10.024   0.000      62521    BB    8.7
 ---- ------------ ========== ------- ======= ========== ---- ----- ------
      Totals:        100.0000            0.000      62521

Total Unidentified Counts :      62521 counts

Detected Peaks: 1            Rejected Peaks: 0      Identified Peaks: 0

Multiplier: 1          Divisor: 1          Unidentified Peak Factor: 0

Baseline Offset: 746 microVolts          LSB:     1 microVolts

Noise (used): 200 microVolts - fixed value
Noise (monitored before this run): 28733 microVolts

Manual injection

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```

Title :
Method File : 219029-c8-1001-2.mth
Sample ID : 219029-C8-1

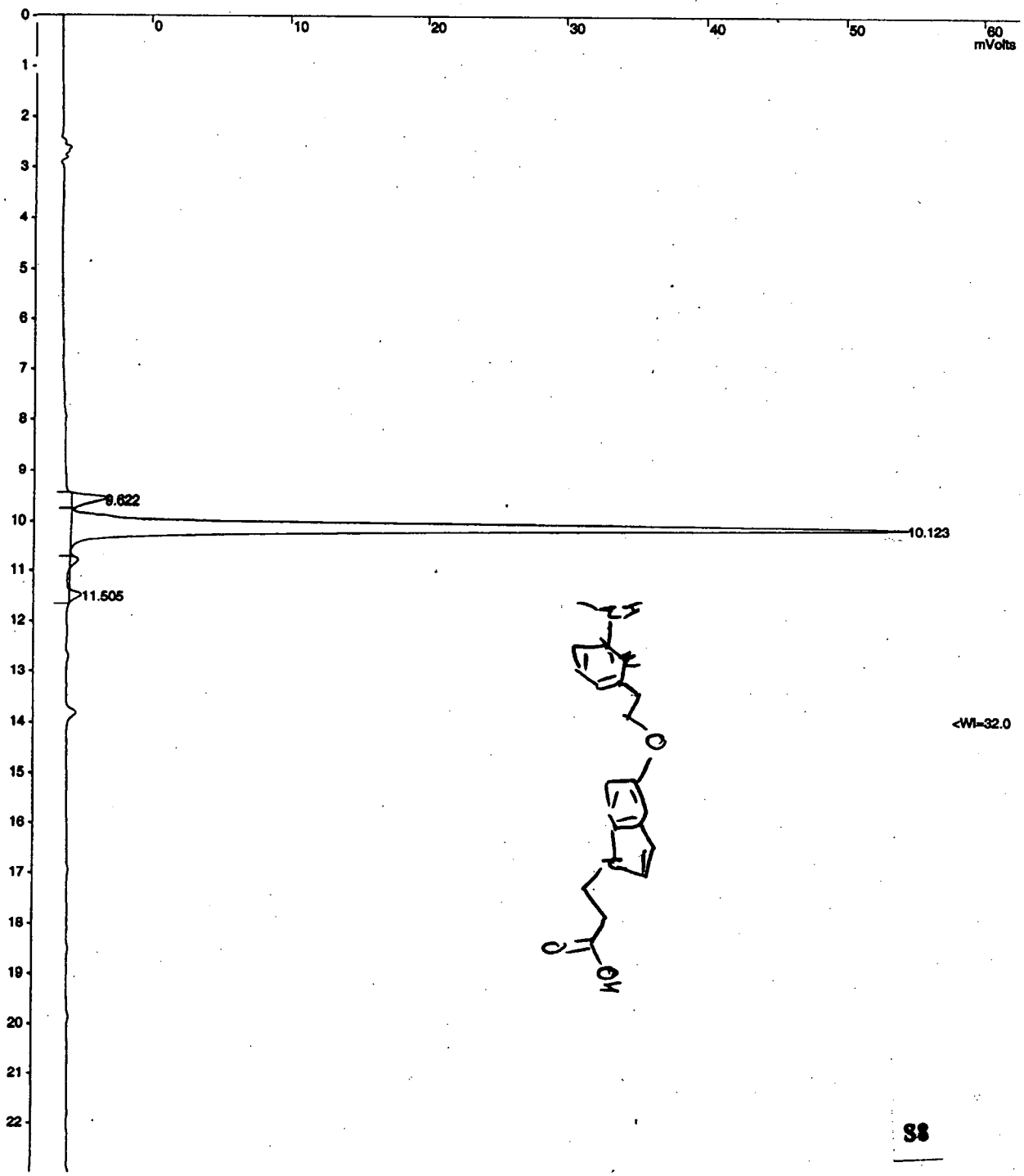
Injection Date: 8/20/2004 1:12 PM Calculation Date: 8/20/2004 2:14 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 2 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.987 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.87 cm/min Attenuation = 115 Zero Offset = 11%
Start Time = 0.000 min End Time = 22.987 min Min / Tick = 1.00



```
Title        :
Run File     : c:\star\data\kristi\219029-c8-1001.run
Method File  : 219029-c8-1001-2.mth
Sample ID    : 219029-C8-1

Injection Date: 8/20/2004 1:12 PM    Calculation Date: 8/20/2004 2:14 PM

Operator    :                        Detector Type: ProStar/Dynamax (2 Volts)
Workstation:                         Bus Address  : 24
Instrument : Varian Star #1          Sample Rate  : 5.00 Hz
Channel    : 2 = INTGR 1             Run Time     : 22.987 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode         : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)
```

Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
1		3.3281	9.622	0.000	23728	BV	10.3	U
2		95.4022	10.123	0.000	680182	VV	10.3	U
3		1.2697	11.505	0.000	9052	VB	11.1	U
	Totals:	100.0000		0.000	712962			

```
Status Codes:
U - User-defined peak endpoint(s)

Total Unidentified Counts :     712962 counts

Detected Peaks: 3        Rejected Peaks: 0      Identified Peaks: 0

Multiplier: 1          Divisor: 1          Unidentified Peak Factor: 0

Baseline Offset: -6416 microVolts          LSB:     1 microVolts

Noise (used): 400 microVolts - fixed value
Noise (monitored before this run): 26383 microVolts

Manual injection

*******************************************************************************
```

Title :
Method File : 219592-4001-2.mth
Sample ID : 219592-4

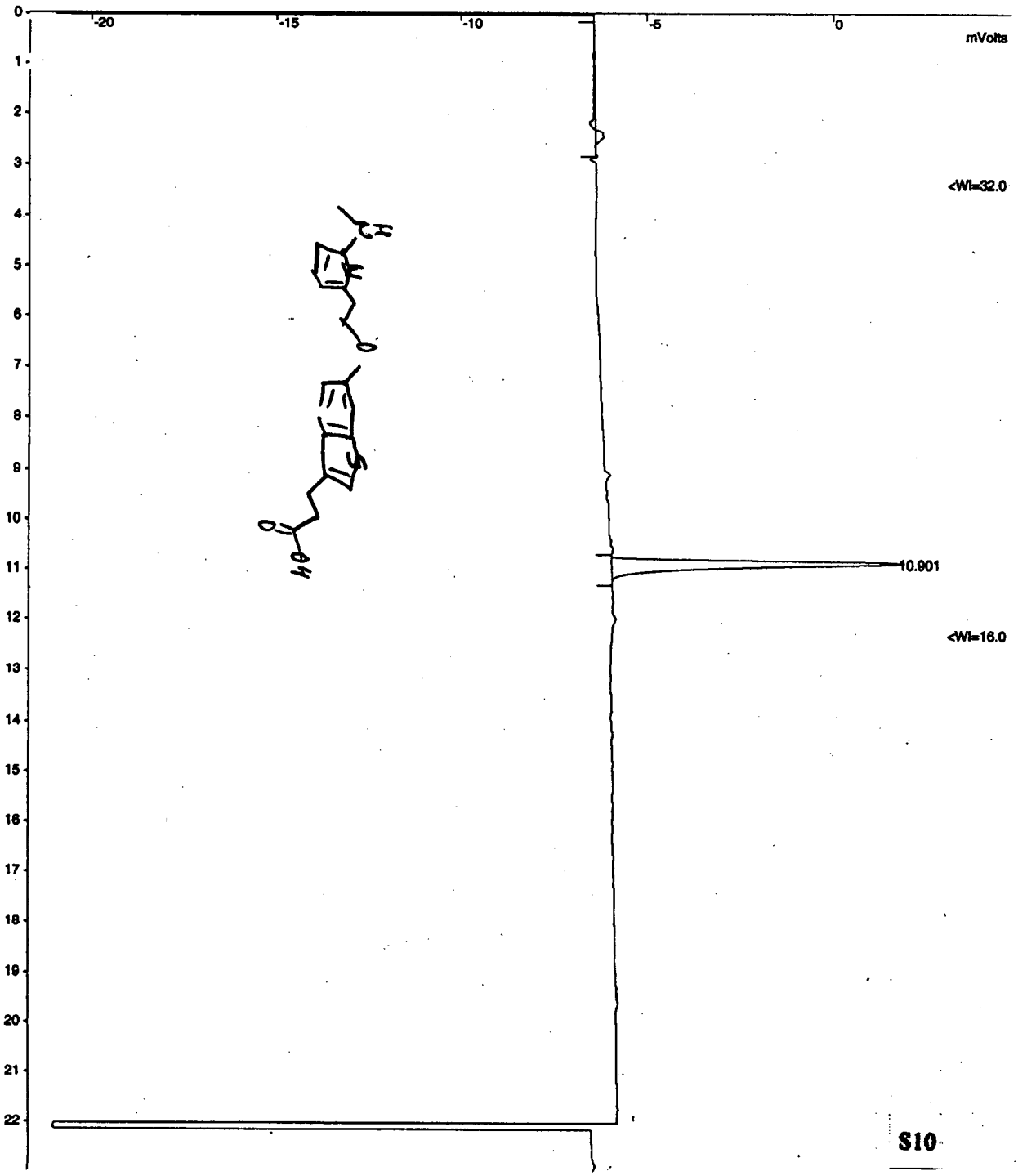
Injection Date: 8/18/2004 4:30 PM Calculation Date: 8/18/2004 7:52 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 2 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.86 cm/min Attenuation = 43 Zero Offset = 82%
Start Time = 0.000 min End Time = 22.990 min Min / Tick = 1.00



```
Title        :
Run File     : c:\star\data\kristi\219592-4001.run
Method File  : 219592-4001-2.mth
Sample ID    : 219592-4

Injection Date: 8/18/2004 4:30 PM    Calculation Date: 8/18/2004 7:52 PM

Operator    :                        Detector Type: ProStar/Dynamax (2 Volts)
Workstation:                         Bus Address  : 24
Instrument : Varian Star #1          Sample Rate  : 5.00 Hz
Channel     : 2 = INTGR 1            Run Time     : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode          : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)

                                  Ret.    Time                      Width
 Peak      Peak        Result     Time   Offset      Area    Sep.  1/2    Status
 No.       Name          ()       (min)  (min)     (counts) Code (sec)   Codes
 ---- ------------ ---------- ------- ------- ---------- ---- ----- ------
    1                 100.0000  10.901   0.000      67168    BB   7.8
 ---- ------------ ========== ------- ======= ========== ---- ----- ------
      Totals:         100.0000           0.000      67168

Total Unidentified Counts :       67168 counts

Detected Peaks: 2            Rejected Peaks: 1       Identified Peaks: 0

Multiplier: 1           Divisor: 1           Unidentified Peak Factor: 0

Baseline Offset: -6422 microVolts            LSB:      1 microVolts

Noise (used): 100 microVolts - fixed value
Noise (monitored before this run): 25915 microVolts

Manual injection

*****************************************************************************
```

Method File : 219592-c8-7001-2.mth
Sample ID : 219592-C8-7

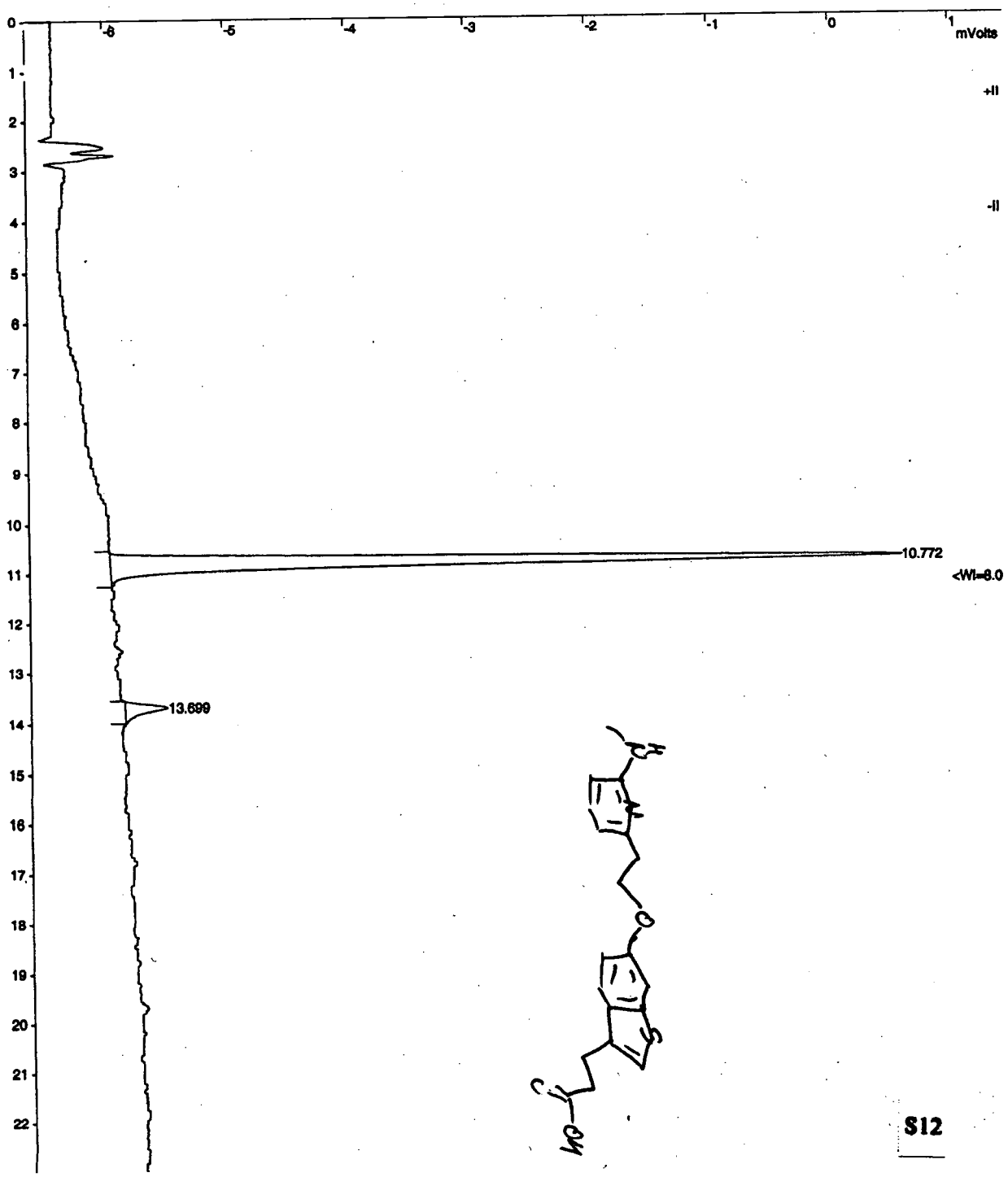
Injection Date: 8/24/2004 11:51 AM Calculation Date: 8/26/2004 2:33 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 2 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.86 cm/min Attenuation = 13 Zero Offset = 83%
Start Time = 0.000 min End Time = 22.990 min Min / Tick = 1.00



```
Title       :
Run File    : c:\star\data\kristi\219592-c8-7001.run
Method File : 219592-c8-7001-2.mth
Sample ID   : 219592-C8-7

Injection Date: 8/24/2004 11:51 AM    Calculation Date: 8/26/2004 2:33 PM

Operator    :                         Detector Type: ProStar/Dynamax (2 Volts)
Workstation:                          Bus Address  : 24
Instrument : Varian Star #1           Sample Rate  : 5.00 Hz
Channel    : 2 = INTGR 1              Run Time     : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode          : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent
```

Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
1		95.0662	10.772	0.000	72179	BB	10.2	U
2		4.9338	13.699	0.000	3746	BB	10.5	U
	Totals:	100.0000		0.000	75925			

```
Status Codes:
U - User-defined peak endpoint(s)

Total Unidentified Counts :      75925 counts

Detected Peaks: 2          Rejected Peaks: 0      Identified Peaks: 0

Multiplier: 1          Divisor: 1          Unidentified Peak Factor: 0

Baseline Offset: -6416 microVolts          LSB:     1 microVolts

Noise (used): 100 microVolts - fixed value
Noise (monitored before this run): 31148 microVolts

Manual injection

*******************************************************************************
```

Method File : 219605001-2.mth
Sample ID : 219605

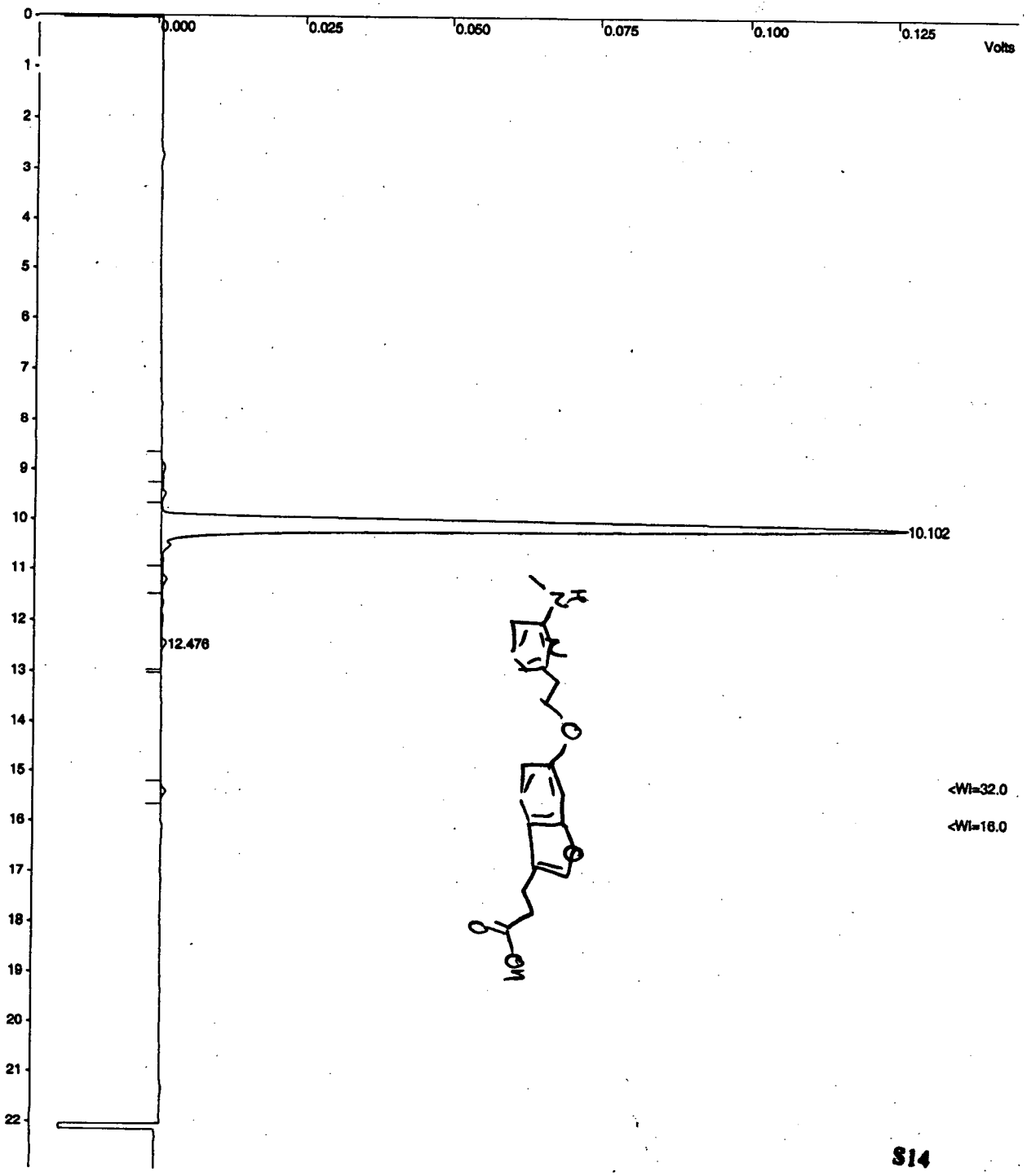
Injection Date: 8/17/2004 10:17 AM Calculation Date: 8/17/2004 5:24 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 1 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.983 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.87 cm/min Attenuation = 270 Zero Offset = 12%
Start Time = 0.000 min End Time = 22.983 min Min / Tick = 1.00



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Title :
Run File : c:\star\data\kristi\219605001.run
Method File : 219605001-2.mth
Sample ID : 219605

Injection Date: 8/17/2004 10:17 AM Calculation Date: 8/17/2004 5:24 PM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 1 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.983 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)

Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
1		99.2920	10.102	0.000	1636392	VB	12.4	
2		0.7080	12.476	0.000	11668	TF	0.0	
	Totals:	100.0000		0.000	1648060			

Total Unidentified Counts : 1648060 counts

Detected Peaks: 6 Rejected Peaks: 4 Identified Peaks: 0

Multiplier: 1 Divisor: 1 Unidentified Peak Factor: 0

Baseline Offset: 739 microVolts LSB: 1 microVolts

Noise (used): 200 microVolts - fixed value
Noise (monitored before this run): 29255 microVolts

Manual injection

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Method File : 219605-c8-1001-1.mth
Sample ID : 219605-C8-1

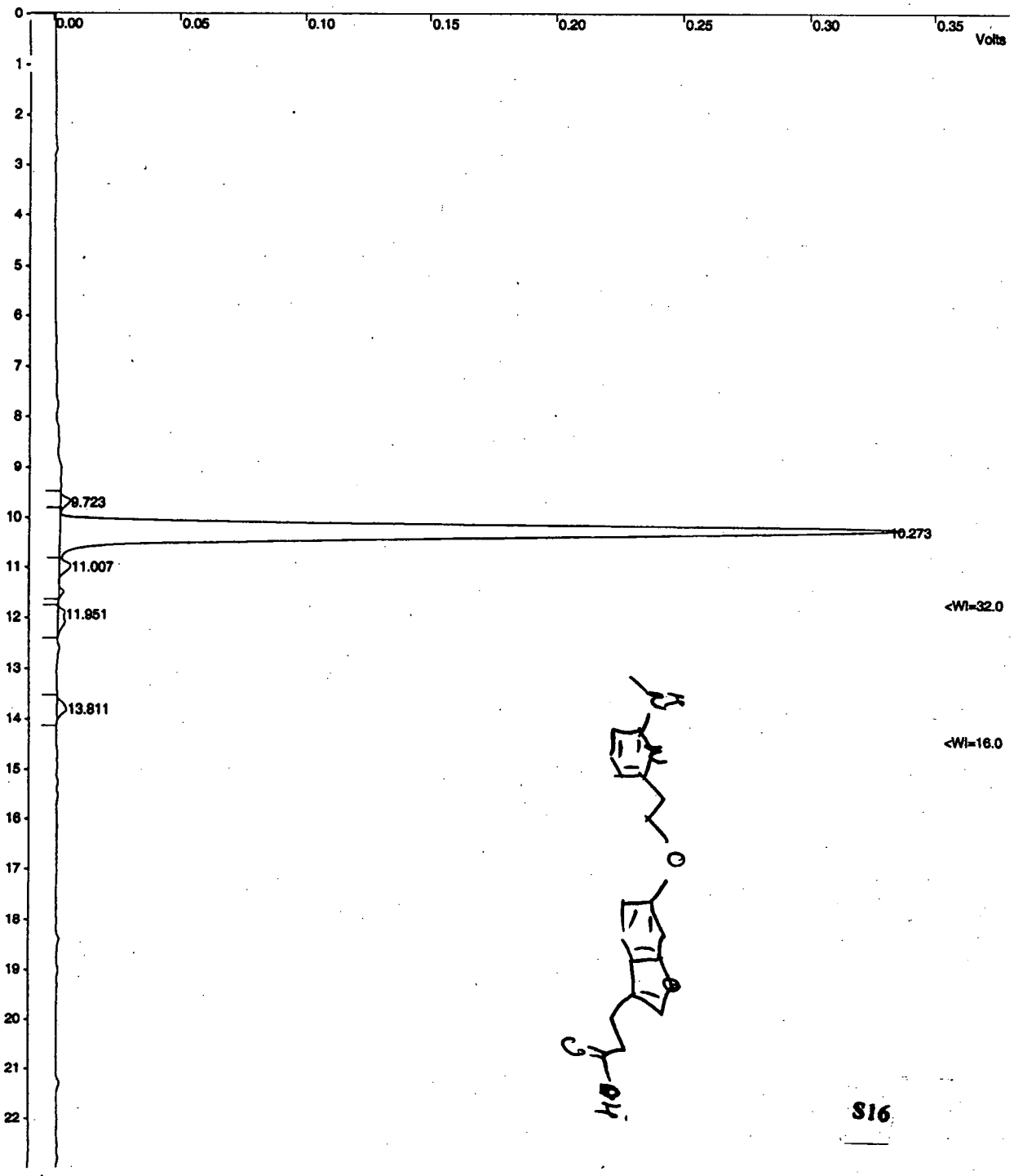
Injection Date: 8/20/2004 9:29 AM Calculation Date: 8/20/2004 11:07 AM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 1 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Chart Speed = 0.86 cm/min Attenuation = 637 Zero Offset = 2%
Start Time = 0.000 min End Time = 22.990 min Min / Tick = 1.00



Title :
Run File : c:\star\data\kristi\219605-c8-1001.run
Method File : 219605-c8-1001-1.mth
Sample ID : 219605-C8-1

Injection Date: 8/20/2004 9:29 AM Calculation Date: 8/20/2004 11:07 AM

Operator :
Workstation:
Instrument : Varian Star #1
Channel : 1 = INTGR 1

Detector Type: ProStar/Dynamax (2 Volts)
Bus Address : 24
Sample Rate : 5.00 Hz
Run Time : 22.990 min

** LC Workstation Version 6.30 ** 02812-37D0-AE7-0374 **

Run Mode : Analysis
Peak Measurement: Peak Area
Calculation Type: Percent (Normalized Results)

Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)	Sep. Code	Width 1/2 (sec)	Status Codes
1		0.6476	9.723	0.000	40051	BV	11.4	
2		96.3960	10.273	0.000	5962105	VV	17.3	
3		1.1062	11.007	0.000	68422	VB	11.6	
4		0.9908	11.951	0.000	61281	BB	22.5	
5		0.8594	13.811	0.000	53155	BB	13.7	
	Totals:	100.0000		0.000	6185014			

Total Unidentified Counts : 6185014 counts

Detected Peaks: 5 Rejected Peaks: 0 Identified Peaks: 0

Multiplier: 1 Divisor: 1 Unidentified Peak Factor: 0

Baseline Offset: 687 microVolts LSB: 1 microVolts

Noise (used): 700 microVolts - fixed value
Noise (monitored before this run): 29708 microVolts

Manual injection

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