Solvent Effects in the Nucleophilic Substitutions of Tetrahydropyran Acetals Promoted by Trimethylsilyl Trifluoromethanesulfonate: Trichloroethylene as Solvent for Stereoselective *C*- and *O*-Glycosylations

Joanna C. Kendale, Elizabeth M. Valentín, and K. A. Woerpel*

Department of Chemistry, New York University, New York, NY 10003, United States

Supporting Information

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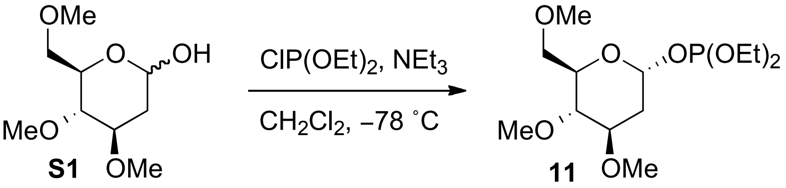
I. General Procedures

Solvents were dried by filtration through alumina according to the procedure by Grubbs, except otherwise noted.[1] Trichloroethylene was stored over molecular sieves (3 Å). Propionitrile was dried by distillation over CaH_2 and stored over 3 Å molecular sieves. All reagents and starting materials were purchased from commercial sources and, where appropriate, purified before use. Reactions were conducted in flame-dried flasks under an inert nitrogen atmosphere using standard Schlenk techniques. ^{1}H and ^{13}C NMR spectra were obtained at ambient temperature at 400, 500, or 600 MHz and 100, 125, or 150 MHz, respectively. Chemical shifts are reported in ppm and referenced downfield to tetramethylsilane for ^{1}H NMR spectra, or to the central peak in $CDCl_3$ (δ 77.23) for ^{13}C NMR spectra. The coupling constant values (*J*) are reported in Hertz (Hz), with the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, sext = sextet, m = multiplet. Analytical gas chromatography (GC) analyses were performed using a fused silica capillary column (30 m × 32 mm × 0.25µm) wall-coated with DB-1 (J & W Scientific) with helium as the carrier gas (25 psi column-head pressure). The chromatographic method was the following: start temperature = 150 °C; ramp 10 °C/min; final temperature = 250 °C. Chromatographic purifications were performed using standard forced flow (flash chromatography) in the indicated solvent system with 40-63 µm, 230-400 mesh silica gel. Acetals **1**, **4**, and **8** were prepared as previously described.[2-4] Nucleophiles **2** and **5** were prepared by reported methods.[5] Characterization of products obtained from the nucleophilic addition to acetals **1** and **8** were previously reported.[2,4]

II. Characterization of New Compounds

Previously unreported compounds were synthesized on a preparative scale. Characterization of these new compounds is described below.

3,4,6-Tri-*O*-methyl-2-deoxy-D-glucopyranosyl-diethyl phosphite 11[6-7]

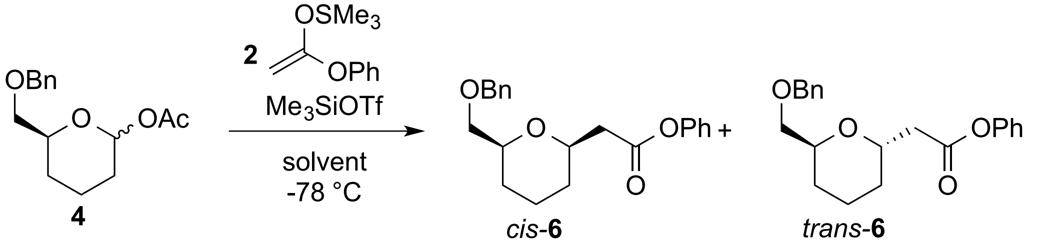


To a cooled (–78 °C) solution of **S1**[7] (0.11 g, 0.51 mmol) in CH_2Cl_2 (5.1 mL) was added NEt_3 (0.51 mL, 3.6 mmol) and diethyl chlorophosphite (0.15 mL, 1.0 mmol). After stirring for 30 minutes, ice was added to the reaction mixture and stirred at 0 °C for 1 h. The entire reaction mixture was poured into a flask containing a cooled (0 °C) mixture of EtOAc (50 mL), saturated $NaHCO_3$ (25 mL), and brine (25 mL). The phases were separated, and the aqueous phase was extracted with EtOAc (2 x 20 mL). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash chromatography of the crude mixture (50% EtOAc in hexanes, with 2% NEt_3) yielded 0.078 g (47%) of the product as a >95:5 mixture of anomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (ddd, *J* = 7.5, 3.4, 1.4 Hz, 1H), 3.92 (ddq, *J* = 7.1, 4.1, 0.8 Hz, 4H), 3.87 (ddq, *J* = 7.1, 4.4, 1.0 Hz), 3.80 (ddd, *J* = 9.9, 3.2, 2.2 Hz Hz, 1H), 3.69 – 3.60 (m, 2H), 3.55 (s, 3H), 3.53 (dd, *J* = 8.7, 1.8 Hz, 1H), 3.45 (s, 3H), 3.40 (s, 3H), 3.25 (dd, *J* = 9.7, 9.2 Hz, 1H), 2.22 (ddd, *J* = 13.0, 4.9, 1.4 Hz, 1H), 1.64 (ddd, *J* = 13.0, 11.5, 3.4 Hz, 1H), 1.26 (td, *J* = 7.1, 4.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 92.6 ($^2J_{CP}$ = 15.9 Hz), 79.8, 78.4, 71.9, 71.2, 60.6, 59.3, 58.40 ($^2J_{CP}$ = 10.9, 1.9 Hz), 57.5, 36.2 ($^3J_{CP}$ = 4.0 Hz), 17.0 ($^3J_{CP}$ = 5.0 Hz); IR (thin film) 2931, 2824, 1442, 1387, 1103, 1024, 900, 748 cm^{-1}; HRMS (TOF MS APCI+) *m / z* calcd for $C_{13}H_{28}O_7P$ $(M + H)^+$ 327.1567, found 327.1567.

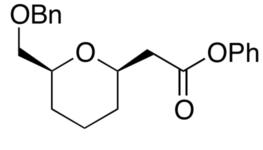
Standard procedure for nucleophilic additions

Me_3SiOTf (1.6 equiv) was slowly added to a cooled (–78 °C) 0.1 M solution of tetrahydropyran acetal (0.075–0.105 mmol, 1 equiv) and nucleophile (4 equiv) in the indicated solvent. The reaction mixture was stirred at –78 °C for 2 h. A cooled (–78 °C) solution of 1:1:1 $MeOH{:}Et_3N{:}CH_2Cl_2$ (2 mL) was then added to the reaction mixture, and the reaction was allowed to warm to room temperature. Saturated aqueous $NaHCO_3$ (2 mL) was added, and the mixture was extracted into CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Diastereomeric ratios of the crude oil were determined by gas chromatography and confirmed by ^1H NMR or ^{13}C NMR spectroscopy.[8] Cis- and trans- isomers were identified in ^1H NMR spectra by comparing to published spectroscopic data.[2,4,9-10]

Phenyl 2-[6-(benzyloxymethyl)-tetrahydro-2*H*-pyran-2-yl] acetate 6

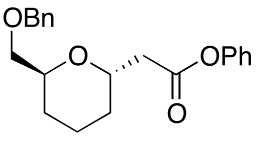


Following the standard procedure for nucleophilic additions, Me_3SiOTf (0.070 g, 0.32 mmol) was added dropwise to a cooled, –78 °C solution of acetal **4** (0.052 g, 0.20 mmol) and nucleophile **2** (0.17 g, 0.79 mmol) in trichloroethylene (2 mL) and stirred for 2 h. Purification of the crude mixture (48:52 cis/trans ratio) by flash chromatography (10% EtOAc in hexanes) yielded 0.032 g pure of *cis*-**6** and 0.034 g of *trans*-**6**, for a combined 86% yield.



cis-**6**

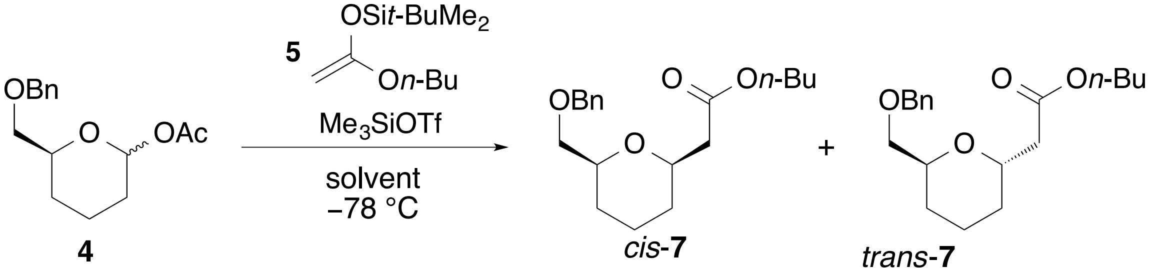
cis-**6**: ^1H NMR (500, $CDCl_3$) δ 7.35 – 7.25 (m, 7H), 7.21 – 7.16 (m, 1H), 7.08 – 7.04 (m, 2 H), 4.60 (d, J = 12.2 Hz, 1H), 4.56 (d, J = 12.2 Hz, 1H), 3.94 (dddd, J = 9.9, 7.8, 5.6, 2.0 Hz, 1H), 3.67 (dddd, J = 10.5, 6.1, 4.2, 2.0 Hz, 1 H), 3.53 (dd, J = 10.3, 6.1 Hz, 1H), 3.45 (dd, J = 10.3, 4.2 Hz, 1H), 2.81 (dd, J = 14.9, 7.8 Hz, 1H), 2.67 (dd, J = 14.9, 5.6 Hz, 1H), 1.93 – 1.87 (m, 1H), 1.75 (dddd, J = 12.6, 7.6, 5.6, 2.0 Hz, 1H), 1.65 – 1.60 (m, 1H), 1.60 – 1.55 (m, 1H), 1.40 – 1.32 (m, 1H), 1.32 – 1.24 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 150.9, 138.6, 129.6, 128.5, 127.9, 127.7, 125.9, 121.9, 77.6, 74.7, 73.9, 73.5, 42.0, 31.3, 27.9, 23.3; IR (thin film) 2934, 2851, 1758, 1734, 1088, 800 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{21}H_{24}NaO_4$ $(M + Na)^+$ 363.1567, found, 363.1545. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H; 7.11. Found: C, 74.04; H, 7.02.



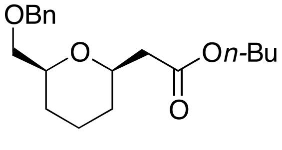
trans-**6**

trans-**6**, characterized as an 11:1 mixture with the cis isomer: ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 7H), 7.20 (m, 1H), 7.10 – 7.06 (m, 2H), 4.58 (d, J = 12.1 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.44 (dtd, *J* = 8.6, 5.8, 4.3 Hz, 1H), 4.04 (dddd, *J* = 7.0, 6.1, 5.2, 3.6 Hz, 1H), 3.62 (dd, *J* = 10.0, 6.1 Hz, 1H), 3.52 (dd, *J* = 10.0, 5.2 Hz, 1H), 2.98 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.68 (dd, *J* = 14.6, 5.8 Hz, 1H), 1.85 (ddt, *J* = 8.9, 6.5, 5.0 Hz, 1H), 1.74 – 1.68 (m, 3H), 1.57 – 1.52 (m, 1H), 1.52 – 1.47 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 150.9, 138.5, 129.5, 128.5, 127.8, 127.7, 125.9, 121.8, 73.5, 71.9, 70.6, 69.3, 39.0, 29.6, 27.0, 18.5; IR (thin film) 2933, 1756, 1493, 1454, 1150, 1025, 799 cm^{-1}. HRMS (TOF MS ES+) *m / z* calcd for $C_{21}H_{24}NaO_4$ $(M + Na)^+$ 363.1567, found, 363.1559. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.24; H, 7.12.

_n_-Butyl 2-[6-(benzyloxymethyl)-tetrahydro-2_H_-pyran-2-yl] acetate 7

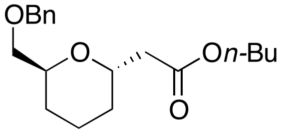


Following the standard procedure for nucleophilic additions, Me_3SiOTf (0.040 g, 0.18 mmol) was added dropwise to a cooled, –78 °C solution of acetal **4** (0.031 g, 0.11 mmol) and nucleophile **2** (0.10 g, 0.45 mmol) in propionitrile (1 mL) and stirred for 2 h. Purification of the crude mixture (40:60 mixture of cis- and trans- isomers) by flash chromatography (10% EtOAc in hexanes) yielded 0.010 g of *cis*-**7** and 0.011 g of *trans*-**7**, for a combined 57% yield.



cis-**7**

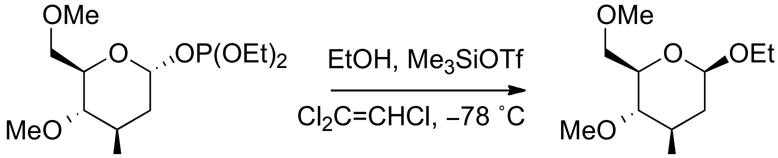
cis-**7**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 5H), 4.58 (d, *J* = 12.2 Hz, 1H), 4.54 (d, *J* = 12.2 Hz, 1H), 4.07 (t, *J* = 6.7 Hz, 2H), 3.80 (dddd, *J* = 11.2, 7.1, 6.2, 2.0 Hz, 1H), 3.60 (dddd, *J* = 11.6, 5.7, 4.6, 2.1 Hz, 1H), 3.48 (dd, *J* = 10.2, 5.7 Hz, 1H), 3.41 (dd, *J* = 10.2, 4.6 Hz, 1H), 2.60 (dd, *J* = 15.0, 7.1 Hz, 1H), 2.40 (dd, *J* = 15.0, 6.2 Hz, 1H), 1.91 – 1.82 (m, 1H), 1.69 – 1.63 (m, 1H), 1.64 – 1.55 (m, 3H), 1.55 – 1.50 (m, 1H), 1.36 (tq, *J* = 9.4, 7.4 Hz, 2H), 1.31 – 1.19 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 138.7, 128.5, 127.9, 127.7, 74.7, 73.7, 73.5, 64.5, 42.0, 30.9, 28.1, 19.3, 13.9; IR (thin film) 2934, 2862, 1735, 1454, 1089, 737 cm^{-1}; HRMS (TOF MS ES+) *m / z* calcd for $C_{19}H_{28}KO_4$ $(M + K)^+$ 359.1619, found, 359.1629.



trans-**7**

trans-**7**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.27 (dtd, *J* = 7.8, 6.4, 4.3 Hz, 1H), 4.07 (t, *J* = 6.7 Hz, 2H), 3.94 (dddd, *J* = 9.1, 5.9, 5.6, 3.4 Hz, 1H), 3.56, (dd, *J* = 9.9, 5.9 Hz, 1H) 3.48 (dd, *J* = 9.9, 5.6 Hz, 1H), 2.71 (dd, *J* = 14.6, 7.8 Hz, 1H), 2.46 (dd, *J* = 14.6, 6.4 Hz, 1H), 1.79 – 1.69 (m, 1H), 1.69 – 1.62 (m, 3 H), 1.61 – 1.57 (m, 2H), 1.54 – 1.45 (m, 1H), 1.46 – 1.39 (m, 1H), 1.37 (sext, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 138.6, 128.5, 127.8, 127.7, 73.5, 71.8, 70.6, 69.3, 64.6, 39.0, 30.9, 29.4, 27.0, 19.3, 18.5, 13.9; IR (thin film) 2934, 2868, 1732, 1097, 1048, 736, 698 cm^{-1}; HRMS (TOF MS ES+) *m / z* calcd for $C_{19}H_{28}KO_4$ (M + K)$^+$ 359.1619; found, 359.1609.

(2*R*,3*S*,4*R*,6*R*)-6-Ethoxy-3,4-dimethoxy-2-(methoxymethyl)tetrahydro-2*H*-pyran 12



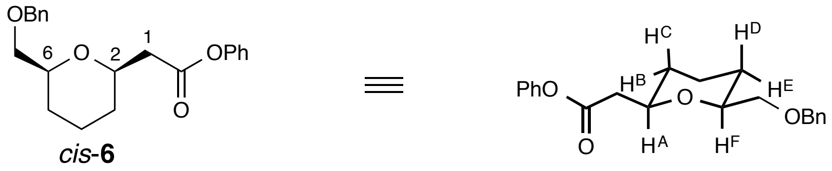
11 **12β**

Following the standard procedure for nucleophilic additions, Me_3SiOTf (0.16 g, 0.74 mmol) was added dropwise to a cooled (–78 °C) solution of **11** (0.20 g, 0.61 mmol) and EtOH (0.056 g, 1.23 mmol) in trichloroethylene (6.1 mL). Purification by flash chromatography (50% EtOAc in hexanes) yielded 0.10 g (82%) of **12β** in a 90:10 ratio. This ratio of products is not consistent with the ratio expected by a thermodynamically controlled reaction, which favors the α product. Characterization data matched the reported literature values.[9]

III. Stereochemical Proofs of Nucleophilic Substitution Products

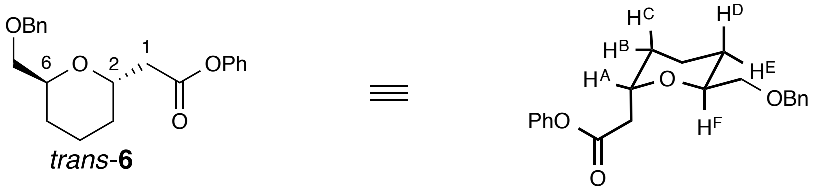
The stereochemical configuration of products **6** and **7** was determined by ^{1}H NMR spectroscopy and compared with known compounds.[3,10] Diagnostic coupling constants of $^3J > 9$ Hz were observed for axial hydrogens (H^A–H^C; H^F–H^D). The observed downfield chemical shift displacements of the 1,5-trans products relative to the 1,5-cis products for H^A and H^F is consistent with observed chemical shifts in the 1,5-allyl substituted tetrahydropyrans.[3,10] The ^{13}C NMR spectrum shows a characteristic chemical shift δ of about 42 ppm for C1 in the 1,5-cis products **6** and **7**, compared to a δ of ~39 ppm for their 1,5-trans counterparts.

Figure S1. Diagnostic ^{1}H-^{1}H coupling constants for *cis*-**6**



H^A: δ 3.94 ppm; J = 9.9 Hz (ax^A–ax^C), 2.0 Hz (ax^A–eq^B)
H^F: δ 3.67 ppm; J = 10.5 Hz (ax^F–ax^D), 2.0 Hz (ax^F–eq^E)

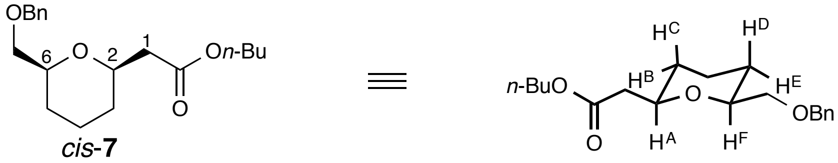
Figure S2. Diagnostic ^{1}H-^{1}H coupling constants for *trans*-**6**



H^A: δ 4.44 ppm; J = 5.7 Hz (eq^A–ax^C), 4.3 Hz (eq^A–eq^B)
H^F: δ 3.67 ppm; J = 7.0 Hz (ax^F–ax^D), 3.6 Hz (ax^F–eq^E)

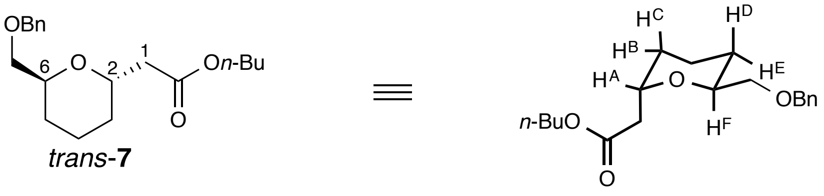
Note: These coupling constants reflect the fact that two conformers of similar energy are present.

Figure S3. Diagnostic ^{1}H-^{1}H coupling constants for *cis*-**7**



H^A: δ 3.80 ppm; J = 11.2 Hz (ax^A–ax^C), 2.0 Hz (ax^A–eq^B)
H^F: δ 3.60 ppm; J = 11.6 Hz (ax^F–ax^D), 2.1 Hz (ax^F–eq^E)

Figure S4. Diagnostic ^{1}H-^{1}H coupling constants for *trans*-**7**



H^A: δ 4.27 ppm; J = 6.0 Hz (eq^A–ax^C), 4.3 Hz (eq^A–eq^B)
H^F: δ 3.94 ppm; J = 9.1 Hz (ax^F–ax^D), 3.4 Hz (ax^F–eq^E)

Note: These coupling constants reflect the fact that two conformers of similar energy are present.

IV. Correlation Between Selected Solvent Parameters and S_N2 Selectivity

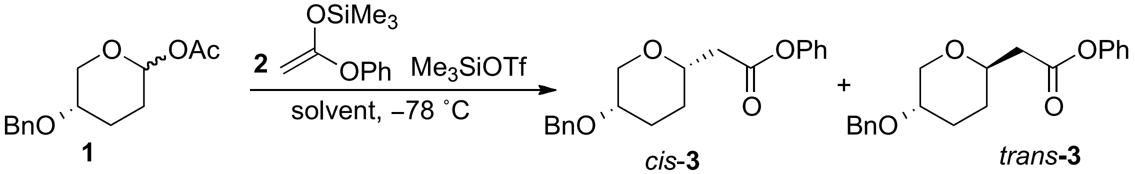


Table S1: Influence of solvent in S_N2 selectivity for the reaction between tetrahydropyran acetal **1** and nucleophile **2**

Order of selectivity	Solvent	ε (F/m)[a]	μ, (D)[b]	$E_T(30)$ (kcal/mol)[c]	cis : trans ratio	% S_N2 product *cis*-**3**
1	$Cl_2C{=}CHCl$	3.4	0.8	35.9	10.11 : 1	91
2	PhMe	2.38	0.37	33.9	7.33 : 1	88
3	CS_2	2.6	0	32.8	3.55 : 1	78
4	CH_2Cl_2	8.93	1.6	40.7	3.00 : 1	75
5	Et_2O	4.33	1.15	34.5	1.86 : 1	65
6	THF	7.58	1.75	37.4	1.22 : 1	55
7	EtOAc	6.02	1.78	38.1	1 : 1.70	37
8	EtCN	27.7	4.05	43.6	1 : 3.76	21
9	$H_2C{=}CCN$	37.5	3.87	46.7	1 : 4.88	17

[a] Dielectric constant.[11] [b] Dipole moment.[12] [c] Empirical solvent polarity parameter.[13]

No direct correlation was found between the different solvent parameters (dipole moment, dielectric constant, etc.) and selectivity towards the S_N2 product. This observation is consistent with Mayr's conclusions that none of the common solvent polarity parameters accurately predict relative ionizing power of aprotic solvents.[14] The closest correlation ($R^2 = 0.79$) was observed for the dipole moment.

Figure S5: Plot of the log (cis/trans product ratios) against dielectric constant

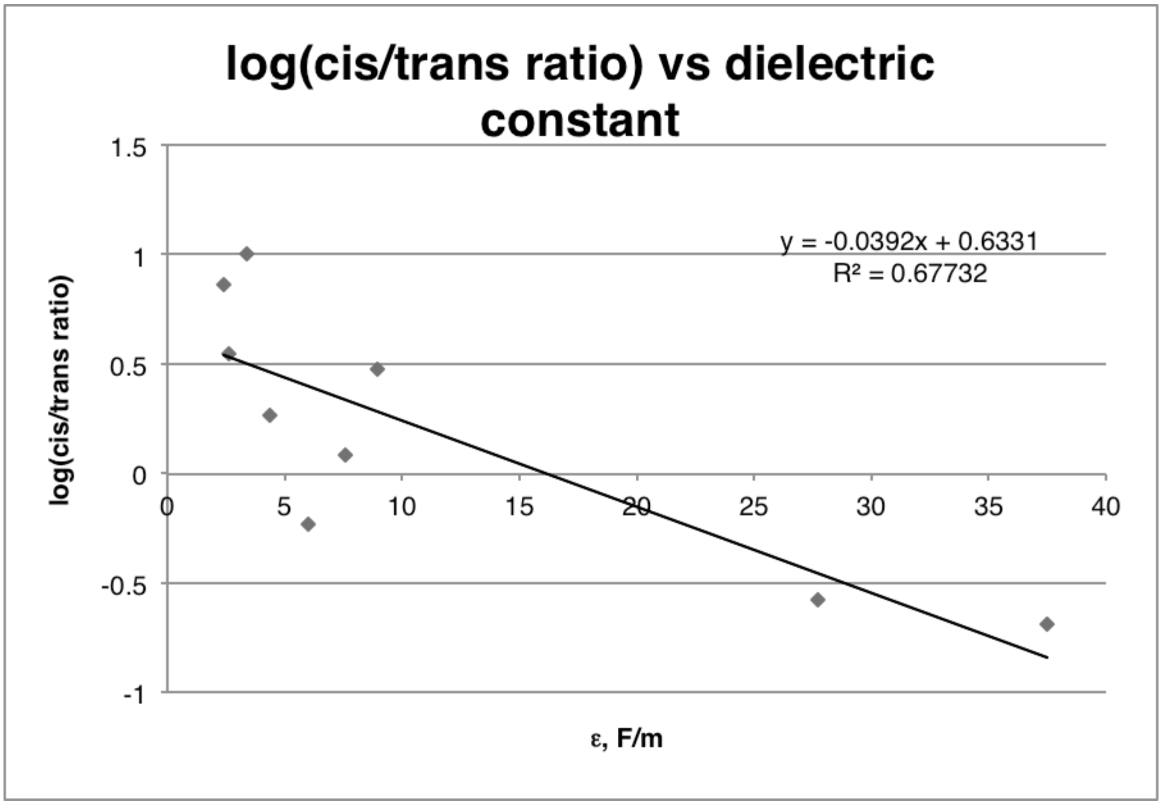


Figure S6: Plot of the log (cis/trans product ratios) against dipole moment

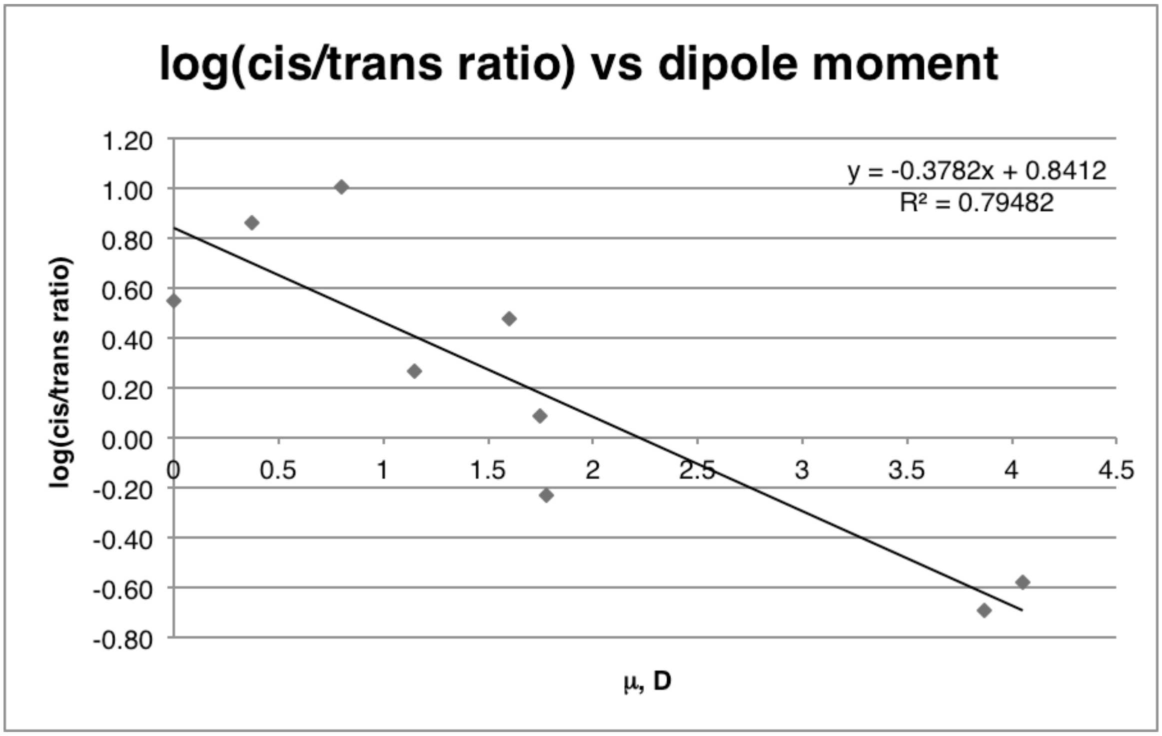
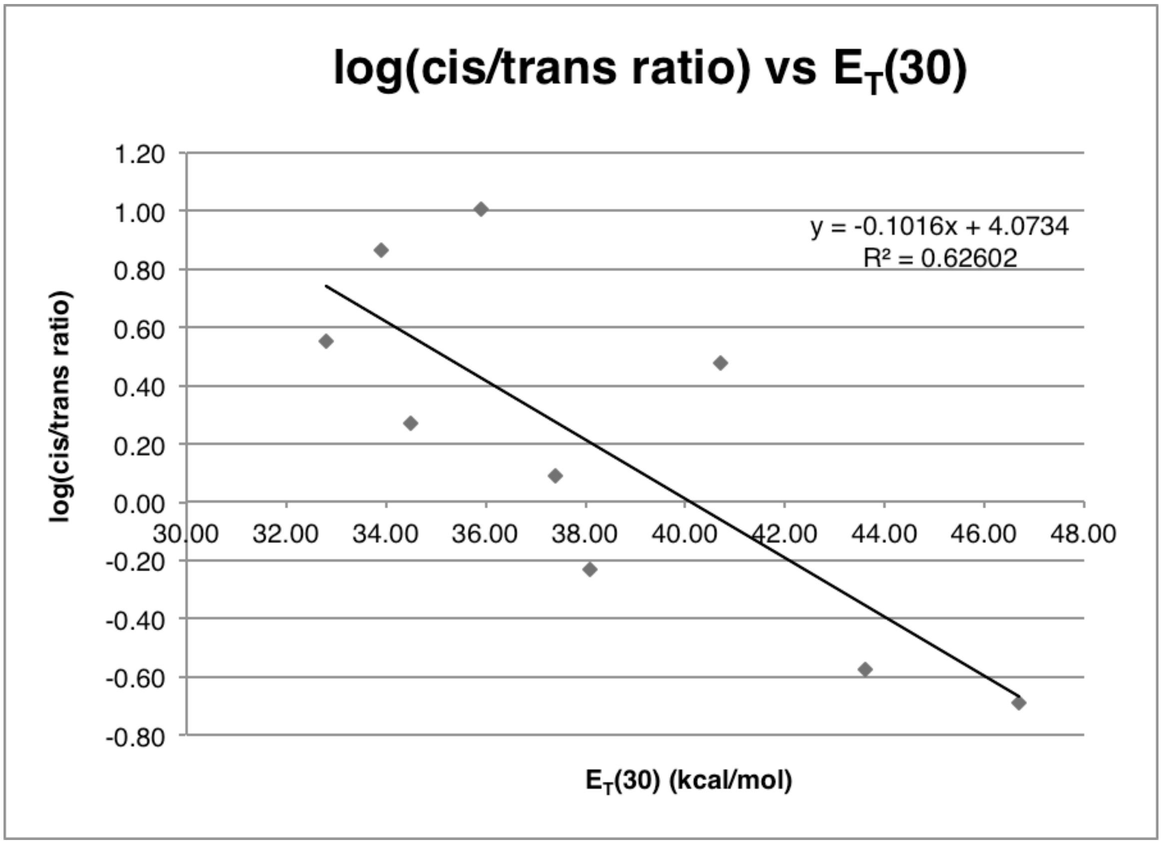
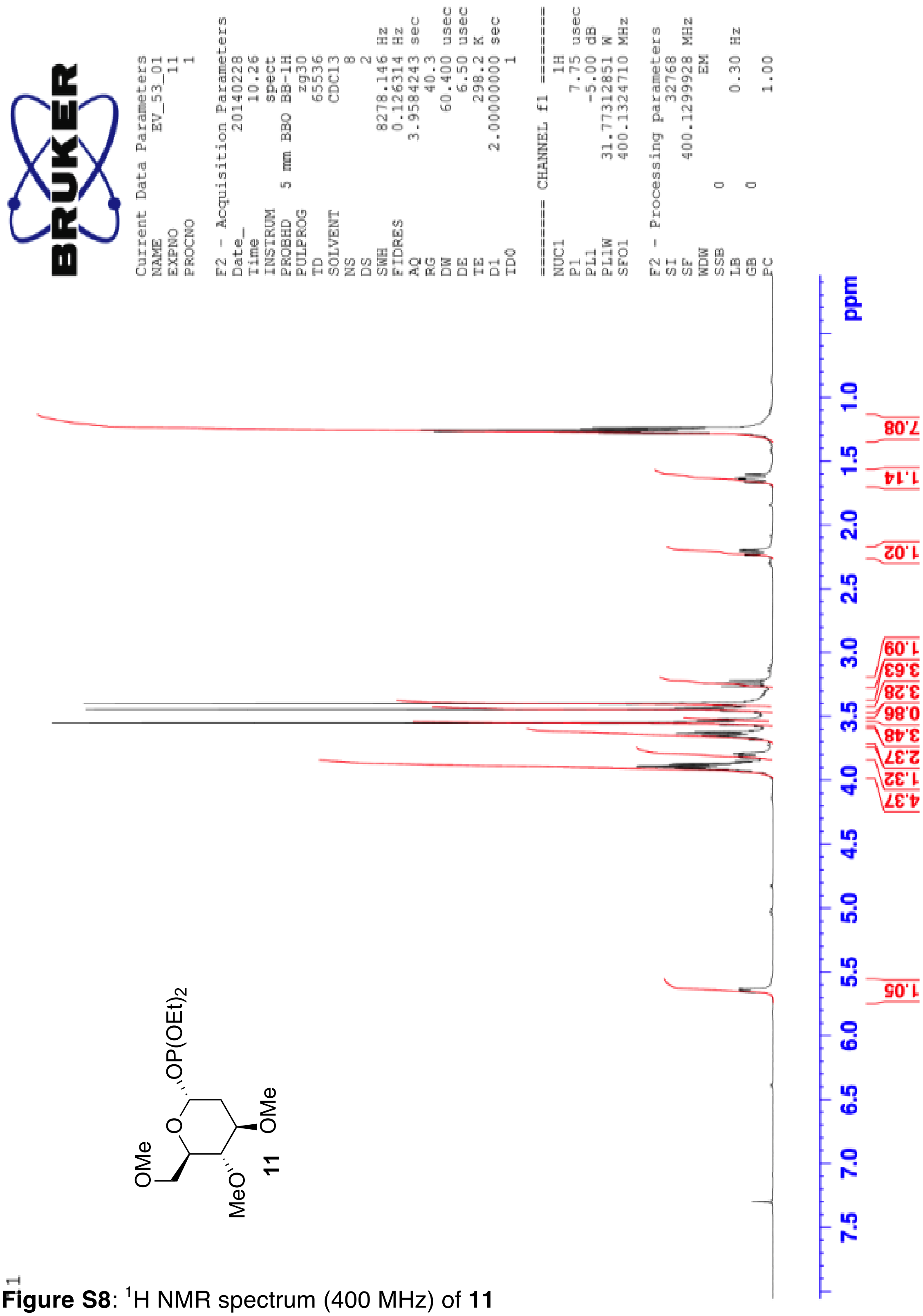


Figure S7: Plot of the log (cis/trans product ratios) against the empirical solvent polarity parameter $E_T(30)$



V. Selected NMR Spectra



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PROCNO               1

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DS                   2
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FIDRES        0.126314 Hz
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DW              60.400 usec
DE                6.50 usec
TE               298.2 K
D1          2.00000000 sec
TD0                  1

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GB                   0
PC                1.00
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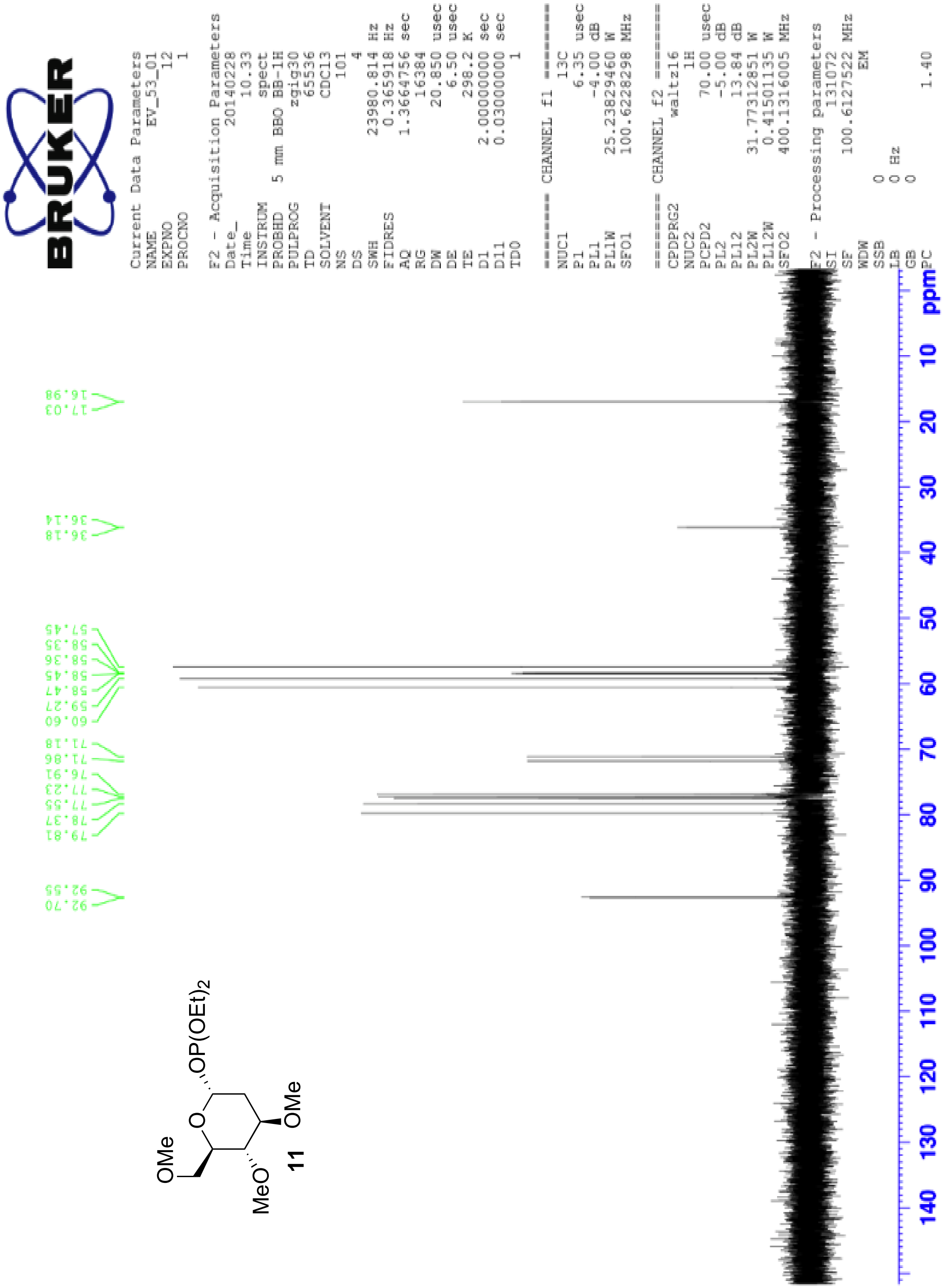
11

Figure S8: ^{1}H NMR spectrum (400 MHz) of **11**



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PROCNO                 1

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TD                 65536
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NS                   101
DS                     4
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FIDRES          0.365918 Hz
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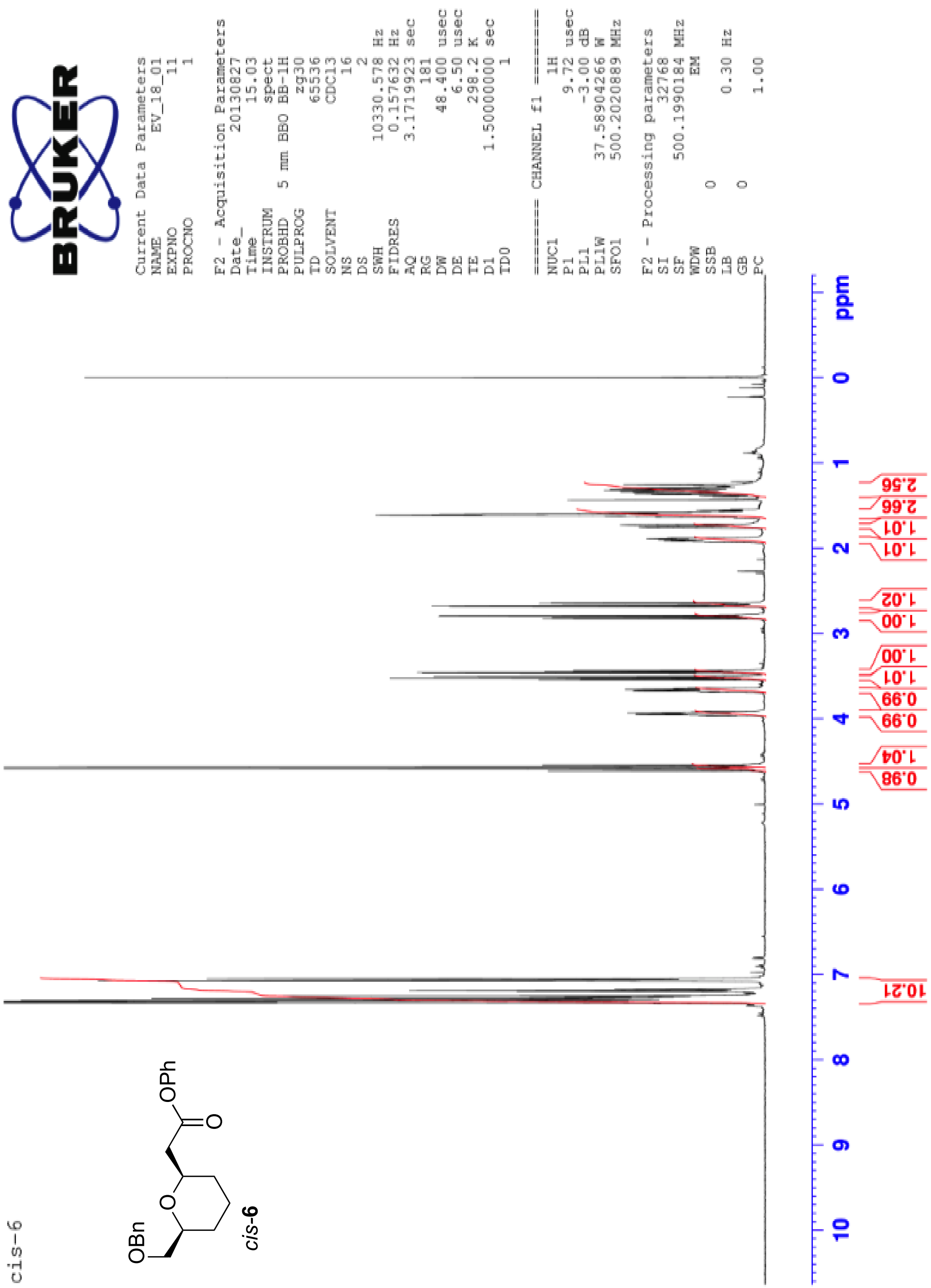
DW                20.850 usec
DE                  6.50 usec
TE                 298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  6.35 usec
PL1                -4.00 dB
PL1W         25.23829460 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              70.00 usec
PL2                -5.00 dB
PL12               13.84 dB
PL2W         31.77312851 W
PL12W         0.41501135 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                131072
SF           100.6127522 MHz
WDW                   EM
SSB      0
LB       0 Hz
GB       0
PC                  1.40
```

Figure S9: ^{13}C NMR spectrum (100 MHz) of **11**



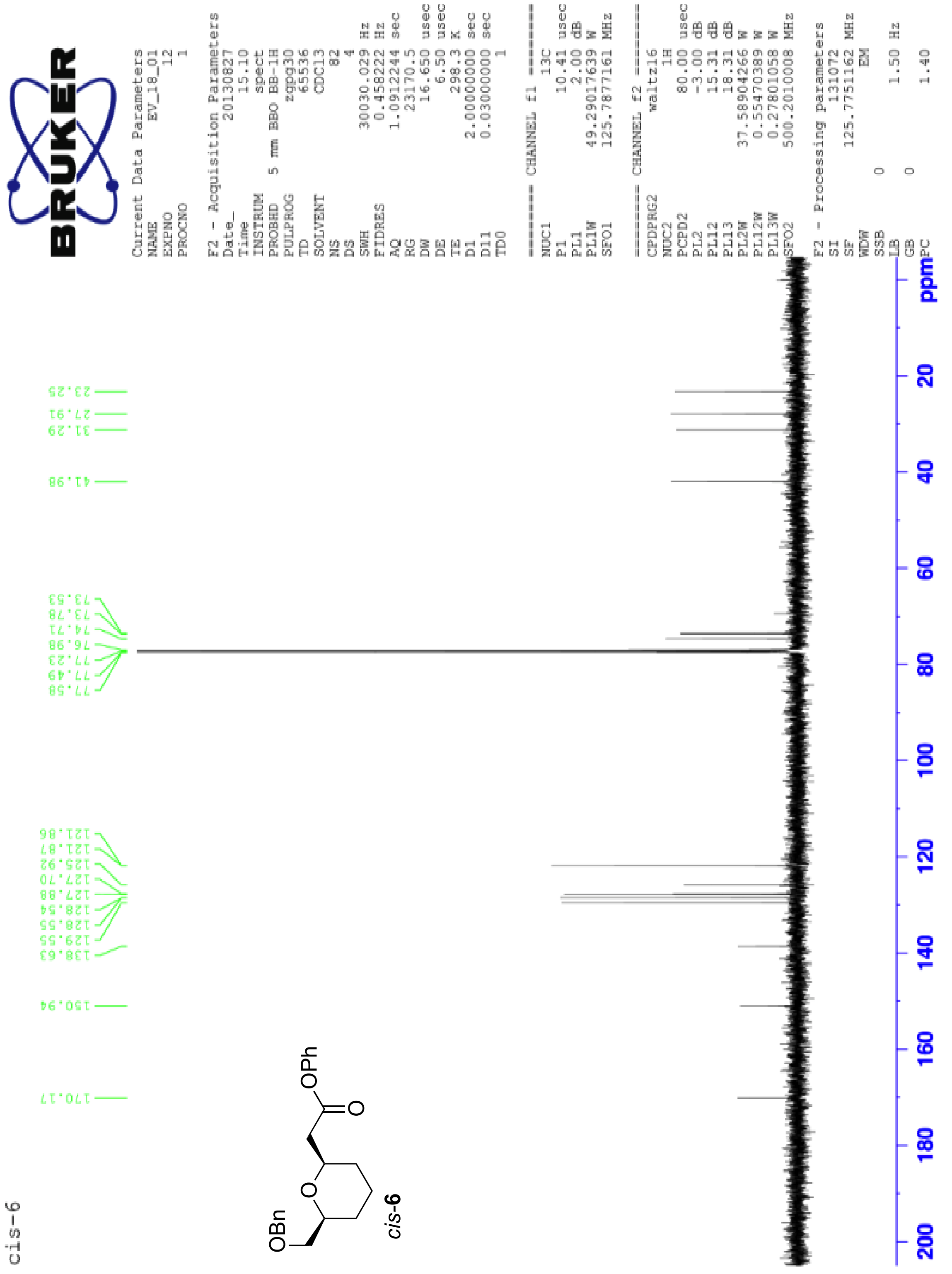
```
Current Data Parameters
NAME          EV_18_01
EXPNO               11
PROCNO               1

F2 - Acquisition Parameters
Date_         20130827
Time             15.03
INSTRUM          spect
PROBHD   5 mm BBO BB-1H
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH          10330.578 Hz
FIDRES        0.157632 Hz
AQ           3.1719923 sec
RG                 181
DW              48.400 usec
DE                6.50 usec
TE               298.2 K
D1          1.50000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1                9.72 usec
PL1              -3.00 dB
PL1W       37.58904266 W
SFO1       500.2020889 MHz

F2 - Processing parameters
SI               32768
SF         500.1990184 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

Figure S10: ^{1}H NMR spectrum (500 MHz) of *cis*-**6**



```
Current Data Parameters
NAME          EV_18_01
EXPNO               12
PROCNO               1

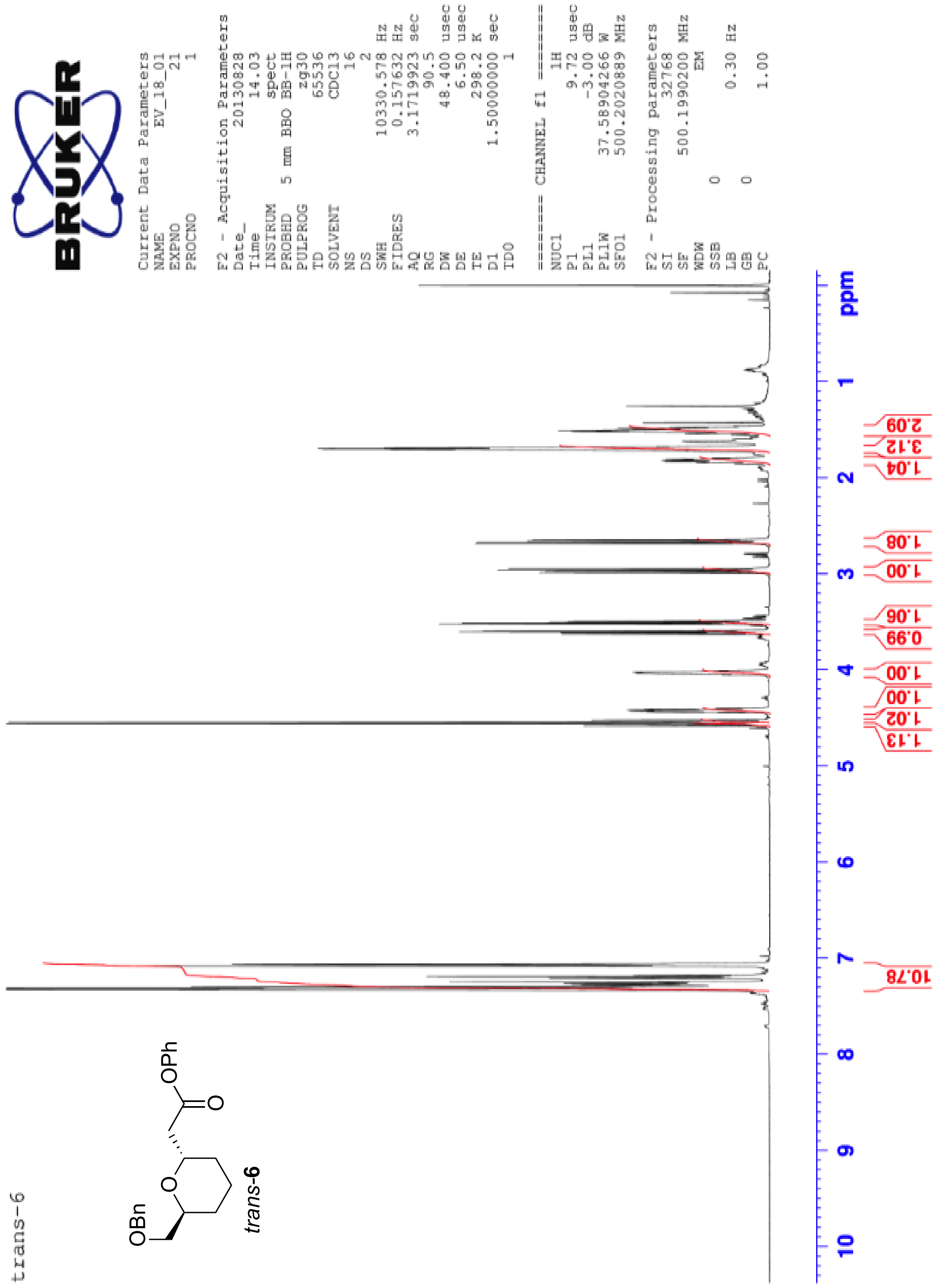
F2 - Acquisition Parameters
Date_         20130827
Time             15.10
INSTRUM          spect
PROBHD   5 mm BBO BB-1H
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS                  82
DS                   4
SWH          30030.029 Hz
FIDRES        0.458222 Hz
AQ           1.0912244 sec
RG             23170.5
DW              16.650 usec
DE                6.50 usec
TE               298.3 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1               13C
P1               10.41 usec
PL1               2.00 dB
PL1W       49.29017639 W
SFO1       125.7877161 MHz

======== CHANNEL f2 ========
CPDPRG2        waltz16
NUC2                1H
PCPD2            80.00 usec
PL2              -3.00 dB
PL12             15.31 dB
PL13             18.31 dB
PL2W       37.58904266 W
PL12W       0.55470389 W
PL13W       0.27801058 W
SFO2       500.2010008 MHz

F2 - Processing parameters
SI              131072
SF         125.7751162 MHz
WDW                 EM
SSB      0
LB                1.50 Hz
GB       0
PC                1.40
```

Figure S11: ^{13}C NMR spectrum (125 MHz) of *cis*-**6**



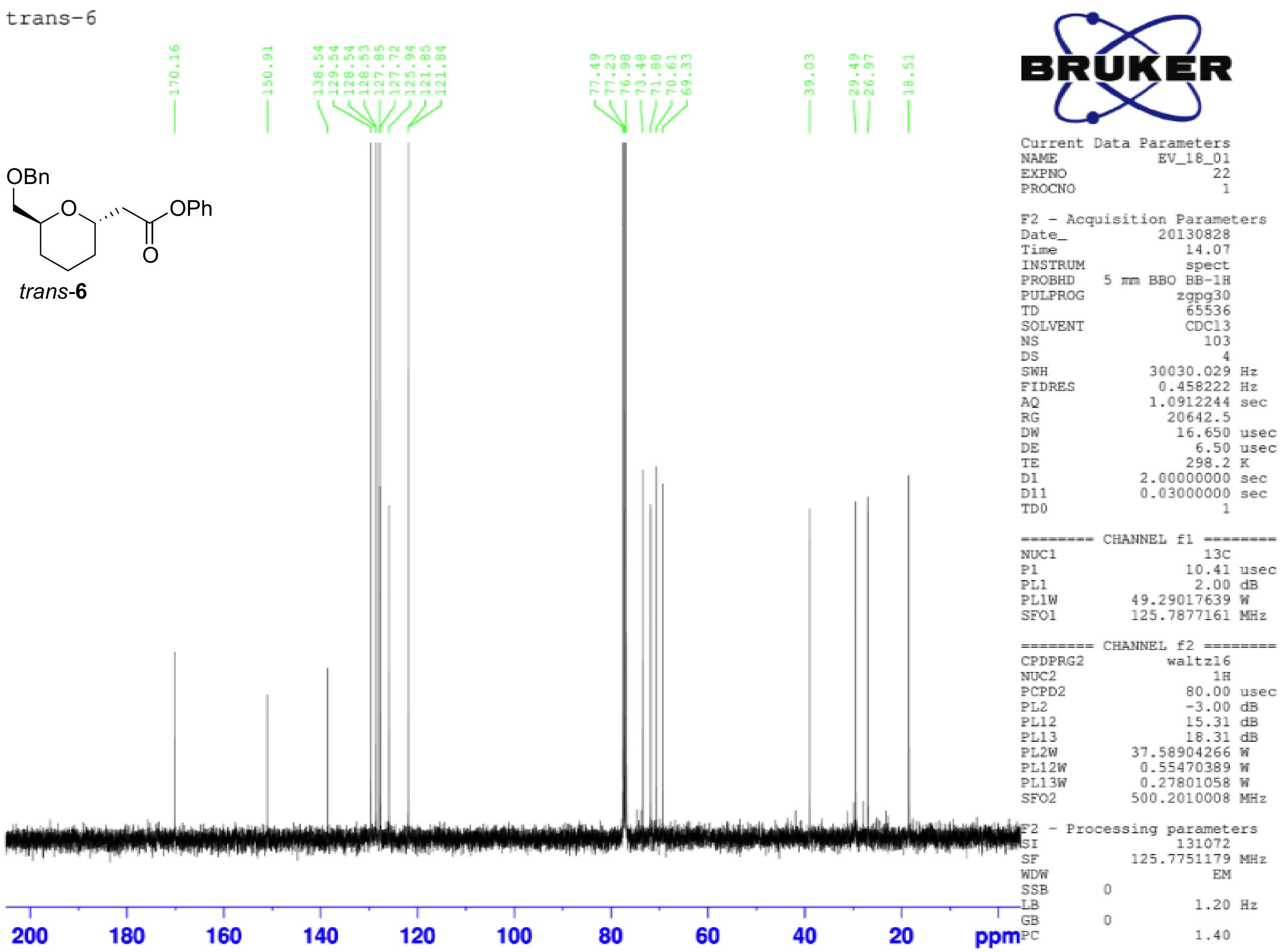
```
Current Data Parameters
NAME            EV_18_01
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130828
Time               14.03
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                  90.5
DW                48.400 usec
DE                  6.50 usec
TE                 298.2 K
D1            1.50000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.72 usec
PL1                -3.00 dB
PL1W         37.58904266 W
SFO1         500.2020889 MHz

F2 - Processing parameters
SI                 32768
SF           500.1990200 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Figure S12: ^{1}H NMR spectrum (500 MHz) of *trans*-**6**



```
Current Data Parameters
NAME             EV_18_01
EXPNO                  22
PROCNO                  1

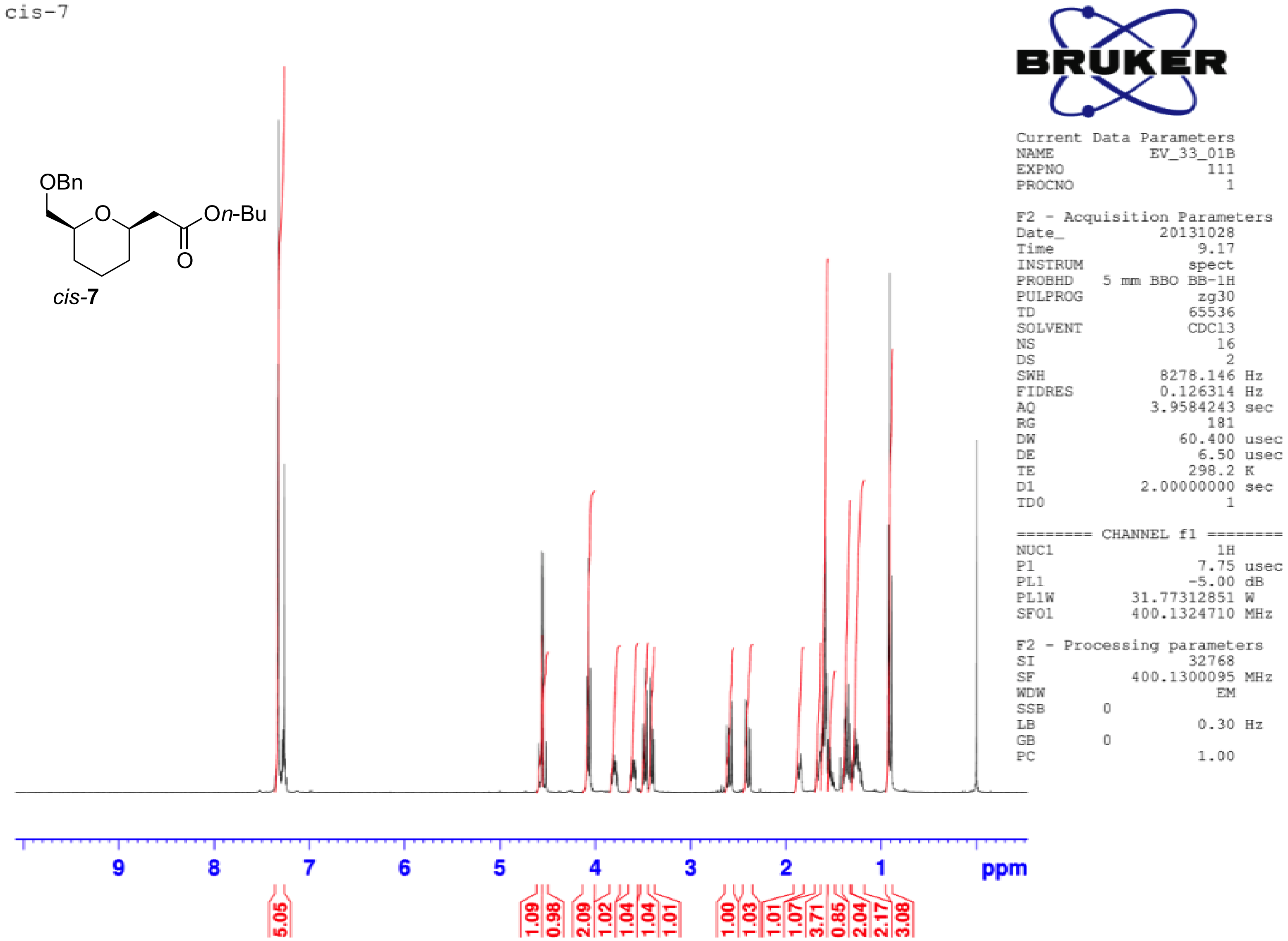
F2 - Acquisition Parameters
Date_            20130828
Time                14.07
INSTRUM             spect
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   103
DS                     4
SWH            30030.029 Hz
FIDRES          0.458222 Hz
AQ             1.0912244 sec
RG               20642.5
DW                16.650 usec
DE                  6.50 usec
TE                 298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 10.41 usec
PL1                 2.00 dB
PL1W         49.29017639 W
SFO1         125.7877161 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                -3.00 dB
PL12               15.31 dB
PL13               18.31 dB
PL2W         37.58904266 W
PL12W         0.55470389 W
PL13W         0.27801058 W
SFO2         500.2010008 MHz

F2 - Processing parameters
SI                131072
SF           125.7751179 MHz
WDW                   EM
SSB      0
LB                  1.20 Hz
GB       0
PC                  1.40
```

Figure S13: ^{13}C NMR spectrum (125 MHz) of *trans*-**6**



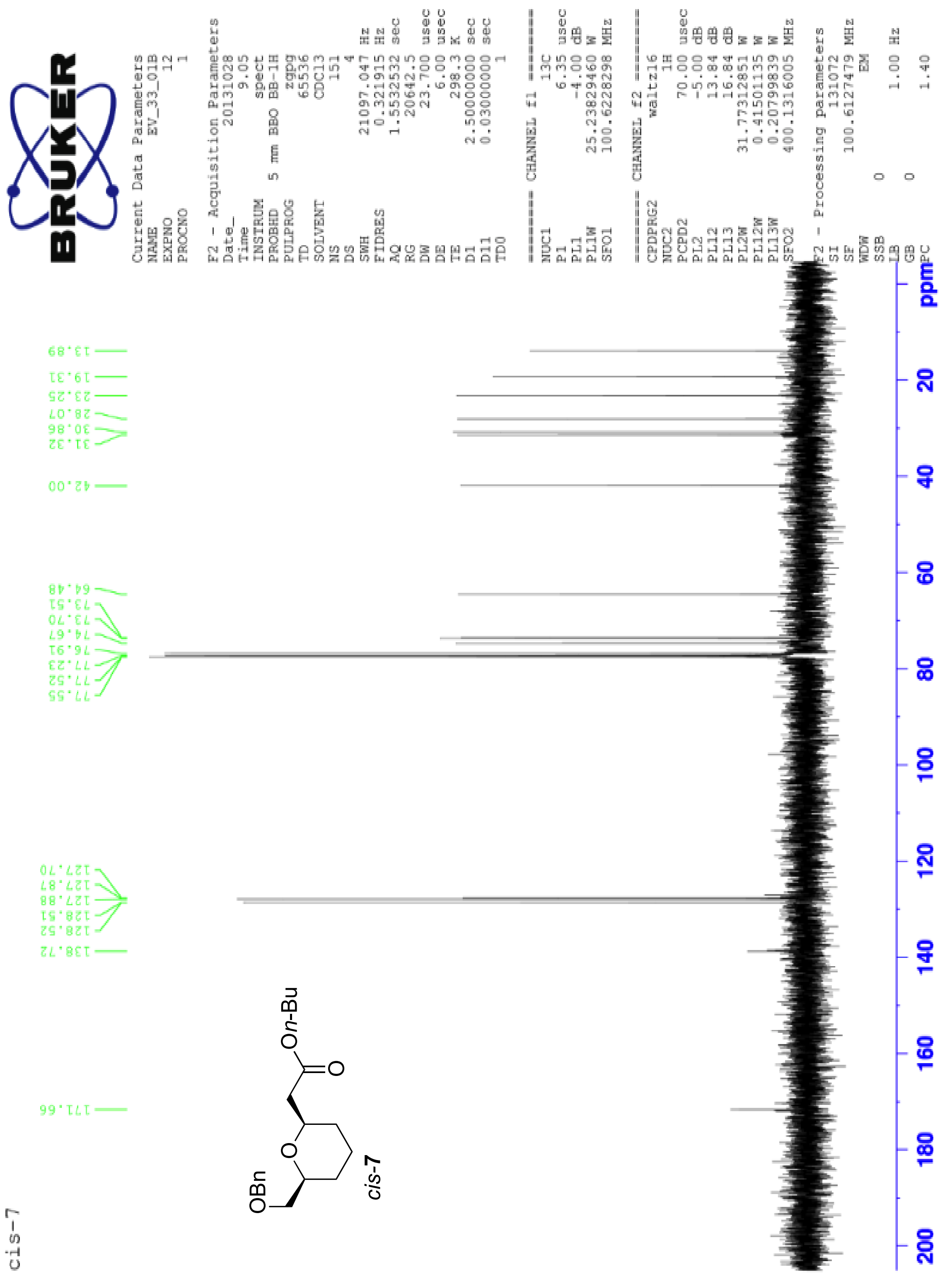
```
Current Data Parameters
NAME             EV_33_01B
EXPNO                  111
PROCNO                   1

F2 - Acquisition Parameters
Date_             20131028
Time                  9.17
INSTRUM              spect
PROBHD   5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ               3.9584243 sec
RG                     181
DW                  60.400 usec
DE                    6.50 usec
TE                   298.2 K
D1              2.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                    7.75 usec
PL1                  -5.00 dB
PL1W           31.77312851 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF             400.1300095 MHz
WDW                     EM
SSB      0
LB                    0.30 Hz
GB       0
PC                    1.00
```

Figure S14: ^{1}H NMR spectrum (400 MHz) of *cis*-**7**



```
Current Data Parameters
NAME        EV_33_01B
EXPNO              12
PROCNO              1

F2 - Acquisition Parameters
Date_        20131028
Time             9.05
INSTRUM         spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg
TD              65536
SOLVENT         CDCl3
NS                151
DS                  4
SWH         21097.047 Hz
FIDRES       0.321915 Hz
AQ          1.5532532 sec
RG            20642.5
DW             23.700 usec
DE               6.00 usec
TE              298.3 K
D1         2.50000000 sec
D11        0.03000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1              13C
P1               6.35 usec
PL1             -4.00 dB
PL1W      25.23829460 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2       waltz16
NUC2               1H
PCPD2           70.00 usec
PL2             -5.00 dB
PL12            13.84 dB
PL13            16.84 dB
PL2W      31.77312851 W
PL12W      0.41501135 W
PL13W      0.20799839 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI             131072
SF        100.6127479 MHz
WDW                EM
SSB      0
LB               1.00 Hz
GB       0
PC               1.40
```

Figure S15: ^{13}C NMR spectrum (100 MHz) of *cis*-**7**

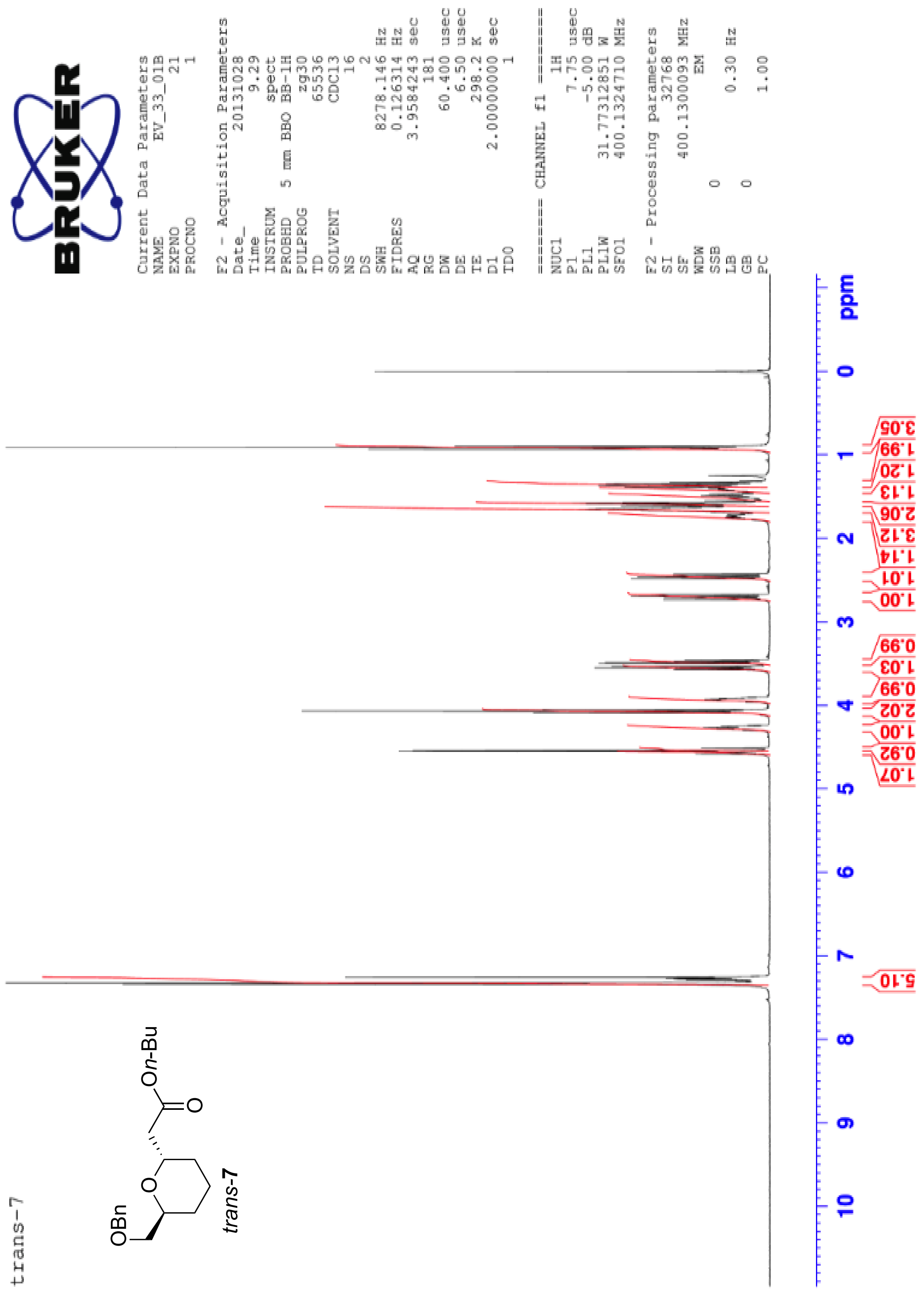
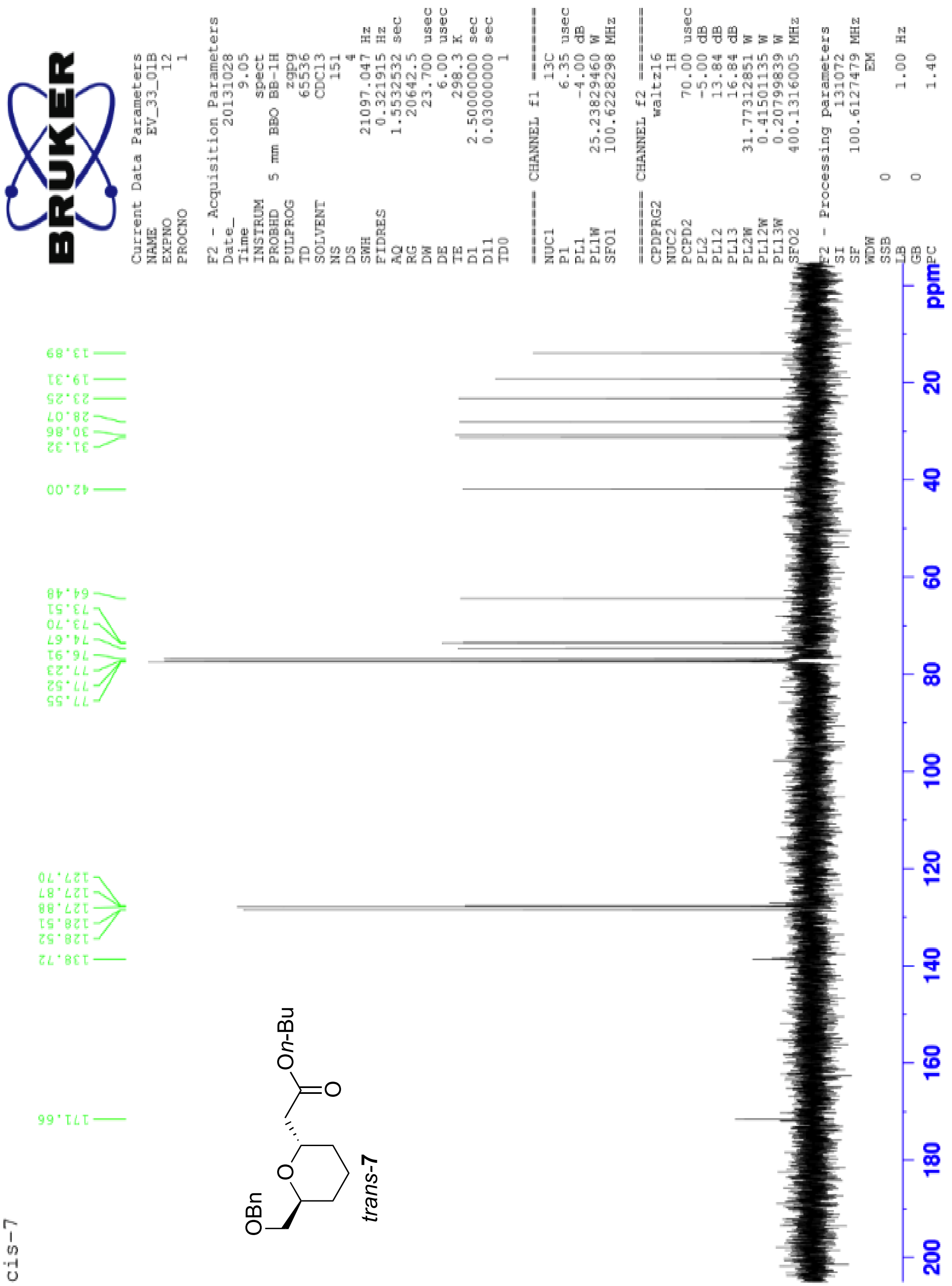


Figure S16: ^{1}H NMR spectrum (400 MHz) of *trans*-**7**



```
Current Data Parameters
NAME          EV_33_01B
EXPNO                12
PROCNO                1

F2 - Acquisition Parameters
Date_          20131028
Time               9.05
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG            zgpg
TD                65536
SOLVENT           CDCl3
NS                  151
DS                    4
SWH        21097.047 Hz
FIDRES      0.321915 Hz
AQ        1.5532532 sec
RG              20642.5
DW           23.700 usec
DE             6.00 usec
TE              298.3 K
D1       2.50000000 sec
D11      0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1             6.35 usec
PL1            -4.00 dB
PL1W       25.23829460 W
SFO1     100.6228298 MHz

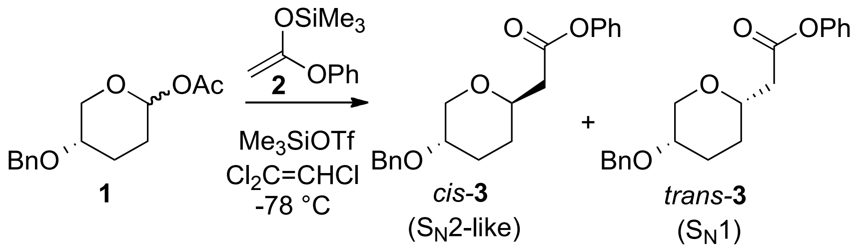
======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2         70.00 usec
PL2            -5.00 dB
PL12           13.84 dB
PL13           16.84 dB
PL2W       31.77312851 W
PL12W       0.41501135 W
PL13W       0.20799839 W
SFO2     400.1316005 MHz

F2 - Processing parameters
SI               131072
SF       100.6127479 MHz
WDW                  EM
SSB      0
LB              1.00 Hz
GB       0
PC                 1.40
```

Figure S17: ^{13}C NMR spectrum (100 MHz) of *trans*-**7**

VI. Determination of Diastereoselectivity of Selected Compounds

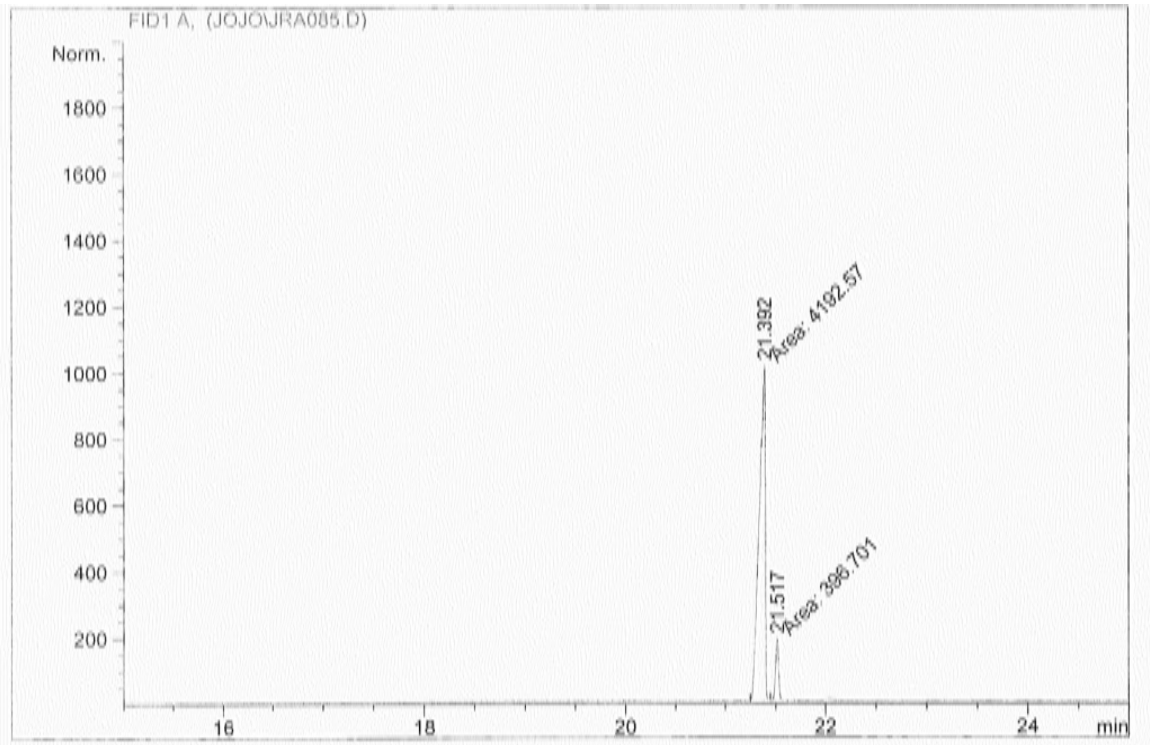
Figure S18: GC spectrum for Table 1, Entry 4



1

cis-**3** (S_N2-like)

trans-**3** (S_N1)



```
=====================================================================
                        Area Percent Report
=====================================================================

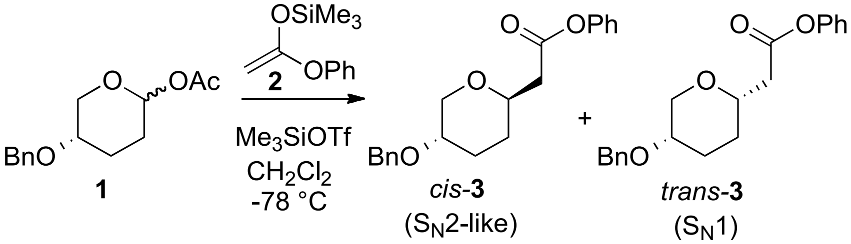
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

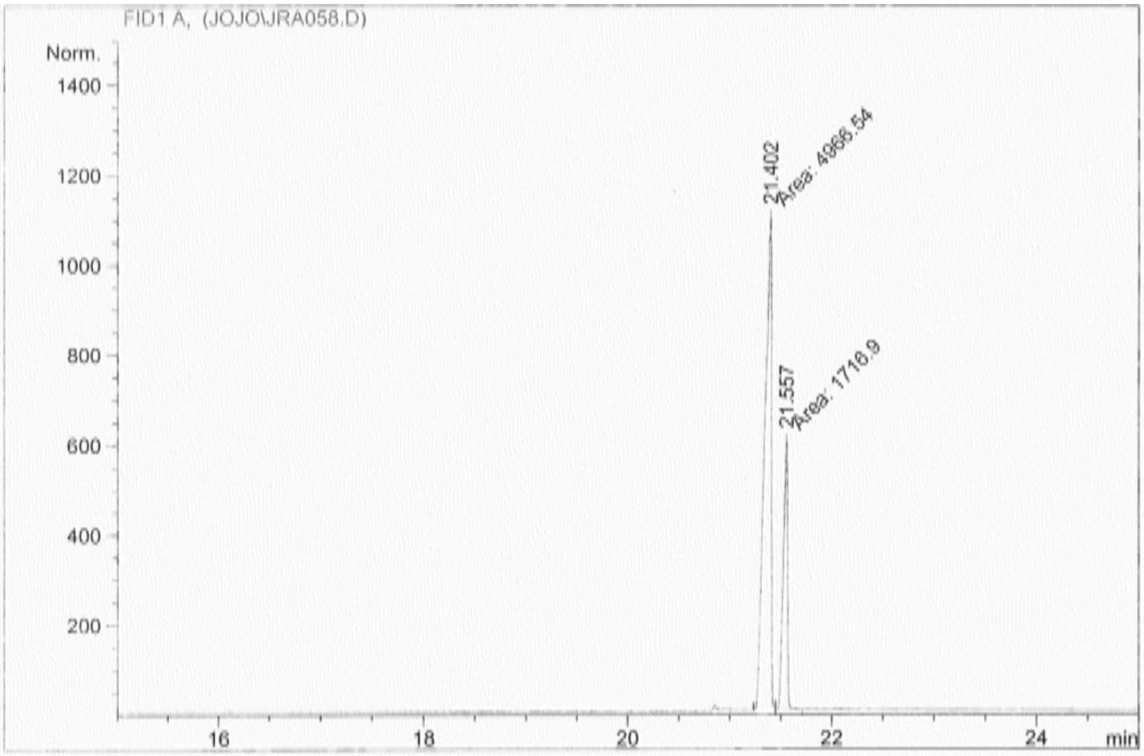

Signal 1: FID1 A,

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [pA*s]        [pA]         %
----|-------|----|-------|----------|----------|--------|
   1  21.392 MF    0.0692 4192.56934 1010.49298 91.35591
   2  21.517 FM    0.0353  396.70062  187.27995  8.64409

Totals :                  4589.26996 1197.77293
```

Figure S19: GC spectrum for Table 1, Entry 6





```
=====================================================================
                         Area Percent Report
=====================================================================

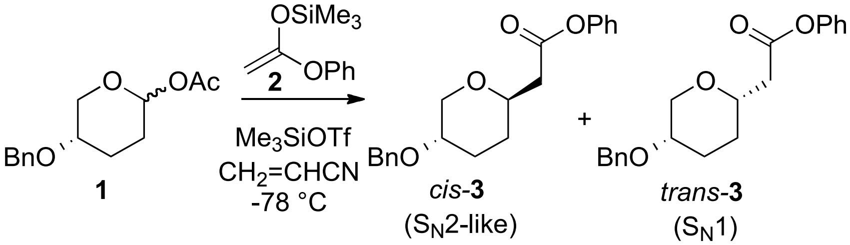
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

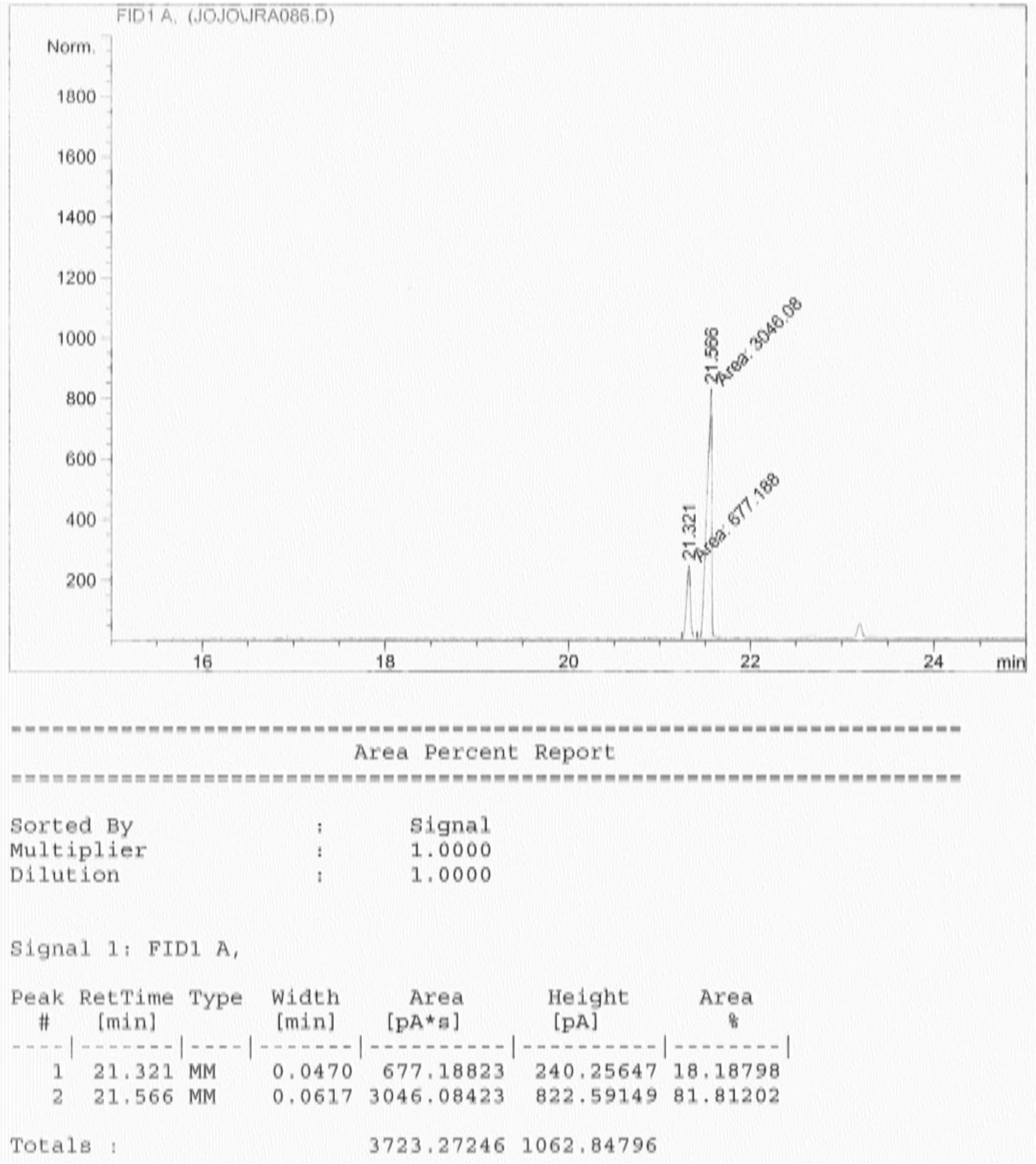

Signal 1: FID1 A,

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [pA*s]       [pA]         %
----|-------|----|-------|----------|----------|--------|
   1  21.402 MM    0.0745 4966.54102 1110.44775 74.31116
   2  21.557 MM    0.0466 1716.89832  613.65430 25.68884

Totals :                  6683.43933 1724.10205
```

Figure S20: GC spectrum for Table 1, Entry 10





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=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  21.321 MM    0.0470  677.18823  240.25647 18.18798
   2  21.566 MM    0.0617 3046.08423  822.59149 81.81202

Totals :                  3723.27246 1062.84796
```
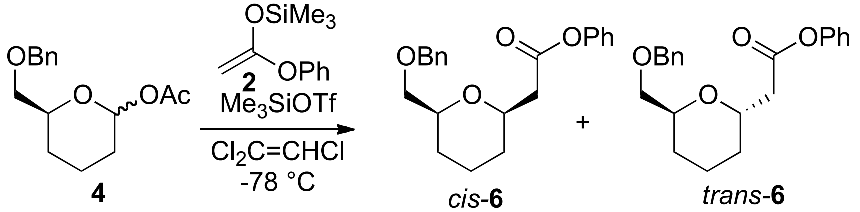
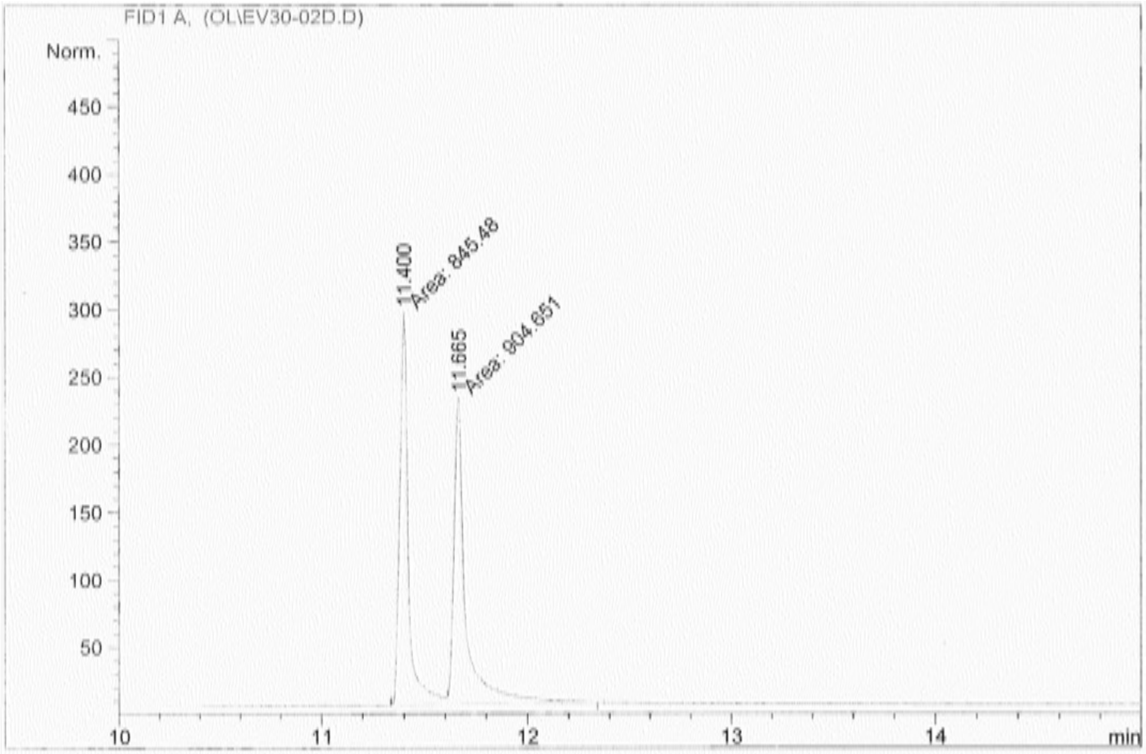
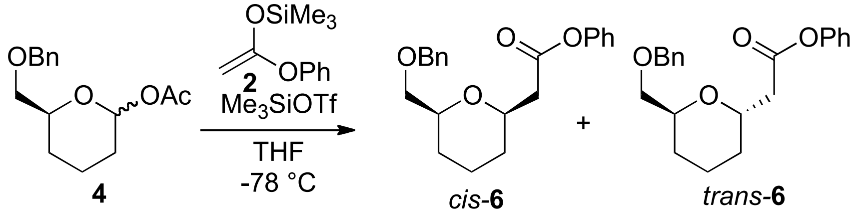

Figure S21: GC spectrum for Table 2, Entry 2

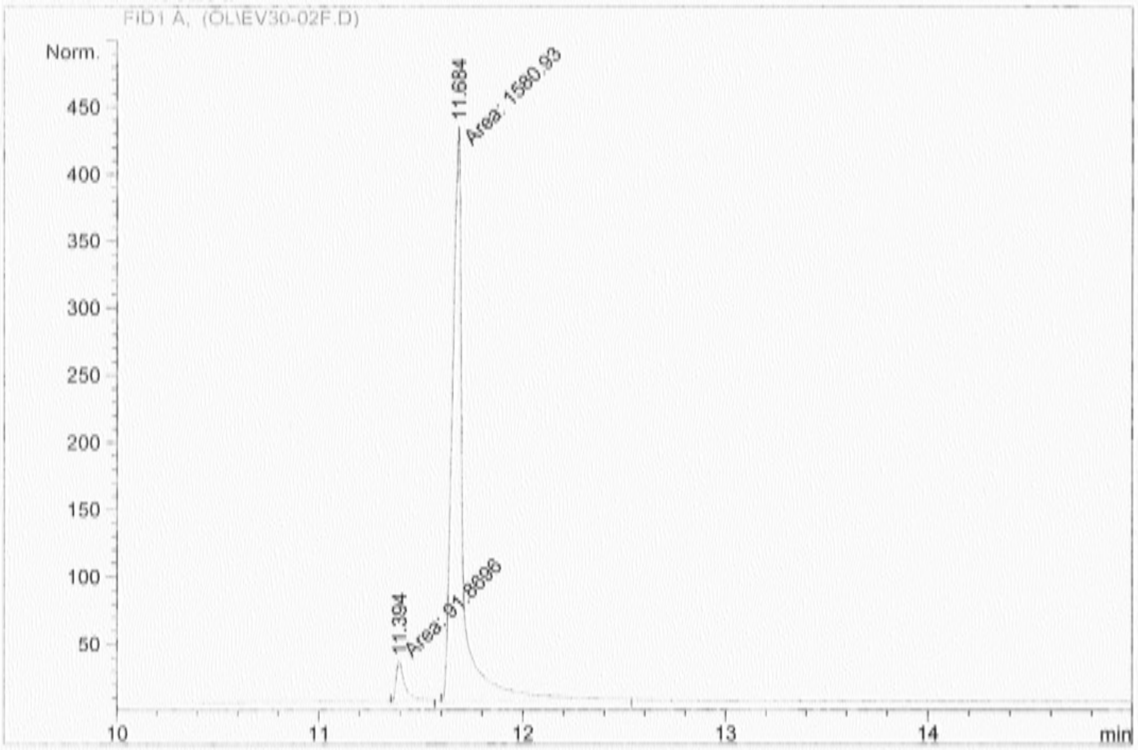




```
=====================================================================
                       Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [pA*s]       [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  11.400 MF     0.0485  845.48047  290.50101 48.30954
   2  11.665 FM     0.0666  904.65118  226.55608 51.69046

Totals :                   1750.13165  517.05708
```

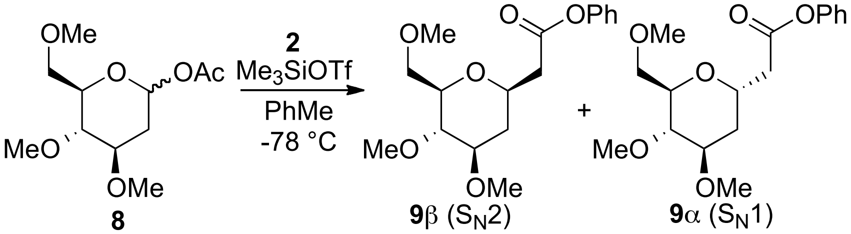
Figure S22: GC spectrum for Table 2, Entry 5

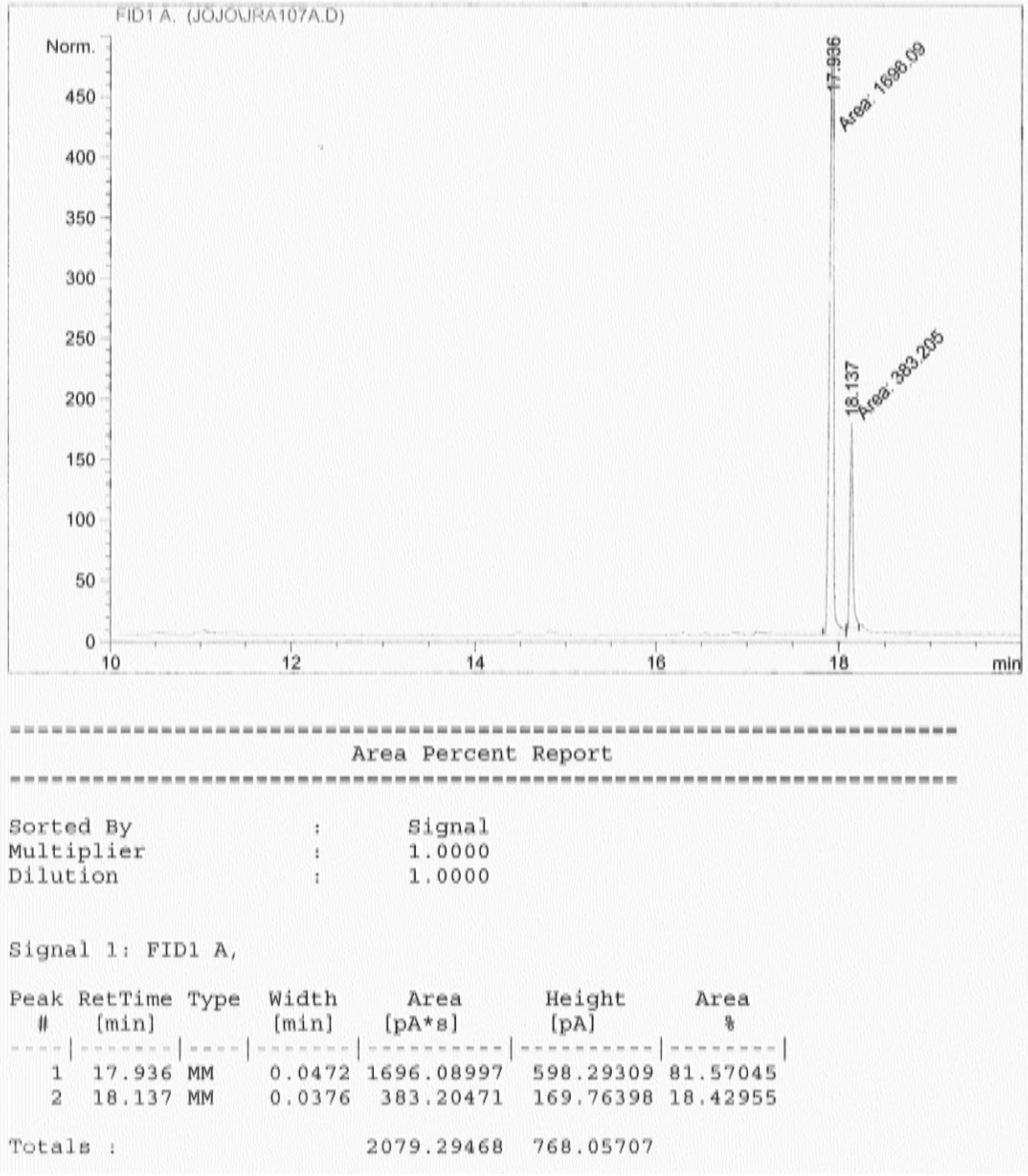




```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  11.394 MM    0.0503   91.86956   30.46175  5.49195
   2  11.684 MM    0.0614 1580.93494  428.97388 94.50805

Totals :                  1672.80450  459.43563
```

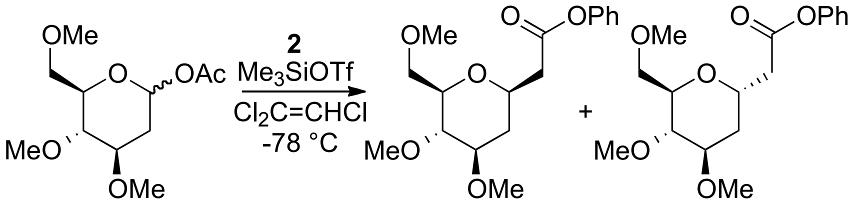
Figure S23: GC spectrum for Table 3, Entry 2



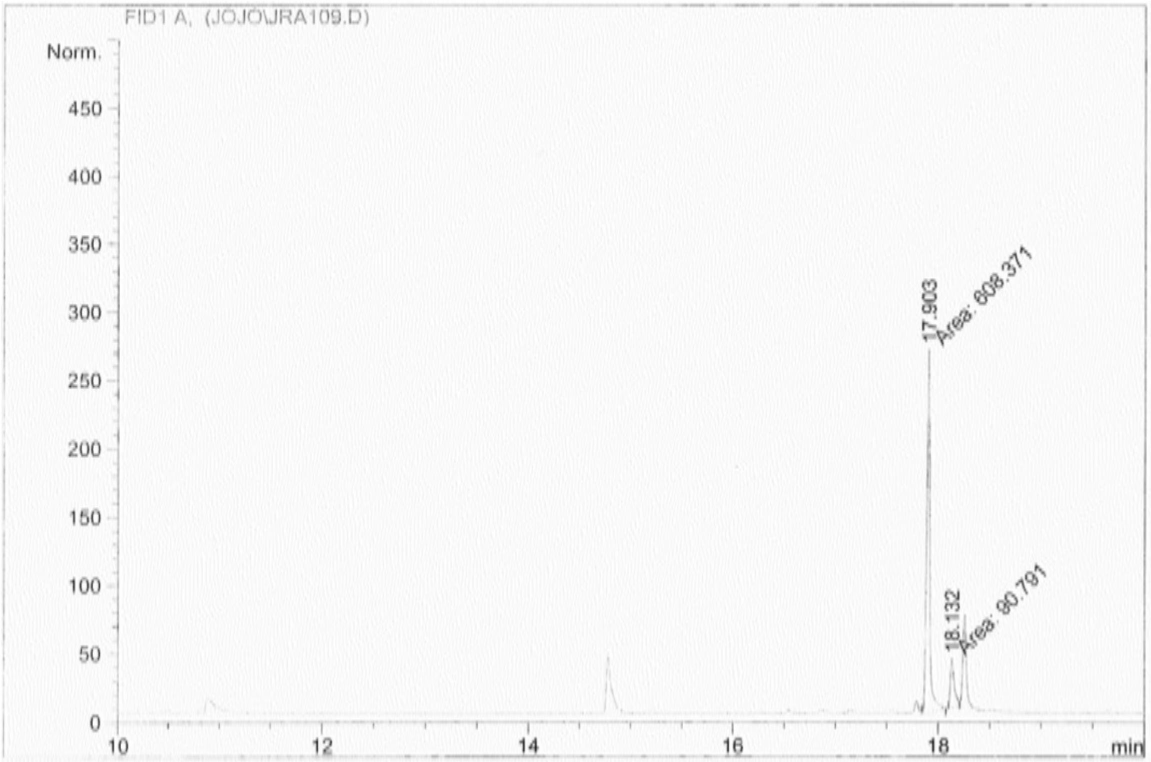


```
=====================================================================
                       Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [pA*s]       [pA]         %
----|-------|----|-------|----------|----------|--------|
   1  17.936 MM    0.0472 1696.08997  598.29309 81.57045
   2  18.137 MM    0.0376  383.20471  169.76398 18.42955

Totals :                  2079.29468  768.05707
```

Figure S24: GC spectrum for Table 3, Entry 3

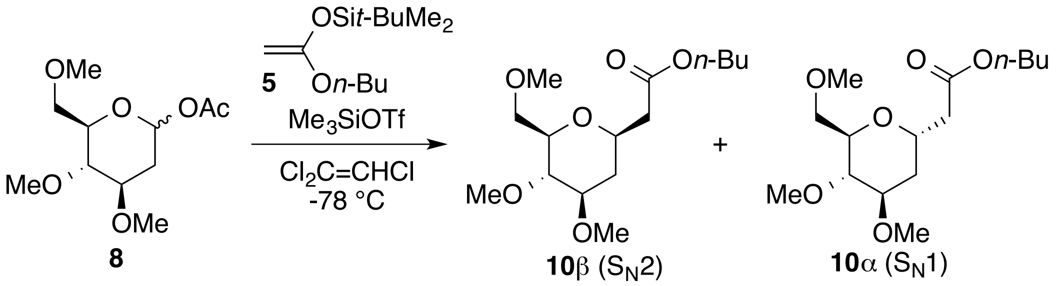


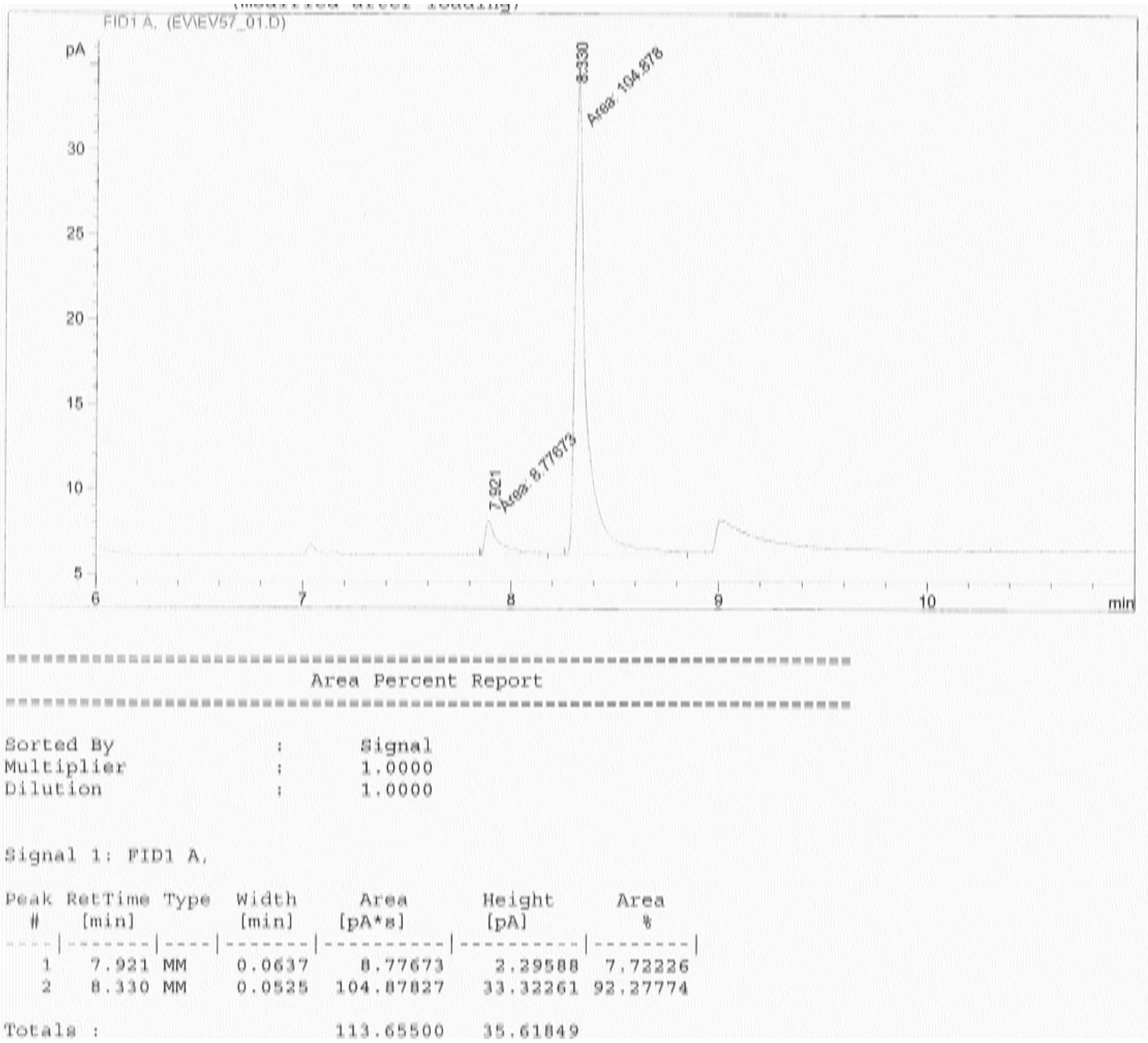
8 **9**β (S_N2) **9**α (S_N1)



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [pA*s]        [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  17.903 MM    0.0381  608.37109  266.02127 87.01431
   2  18.132 MM    0.0419   90.79105   36.10112 12.98569

Totals :                   699.16214  302.12239
```

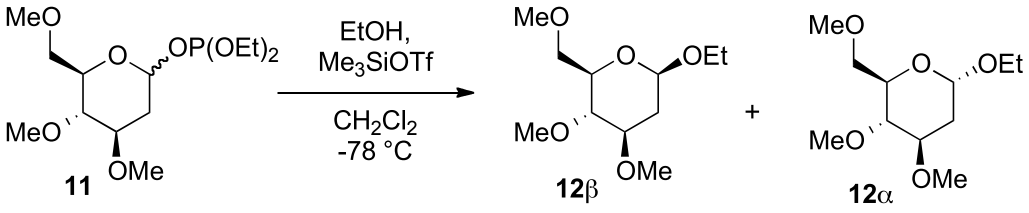
Figure S25: GC spectrum for Scheme 5, with trichloroethylene as solvent

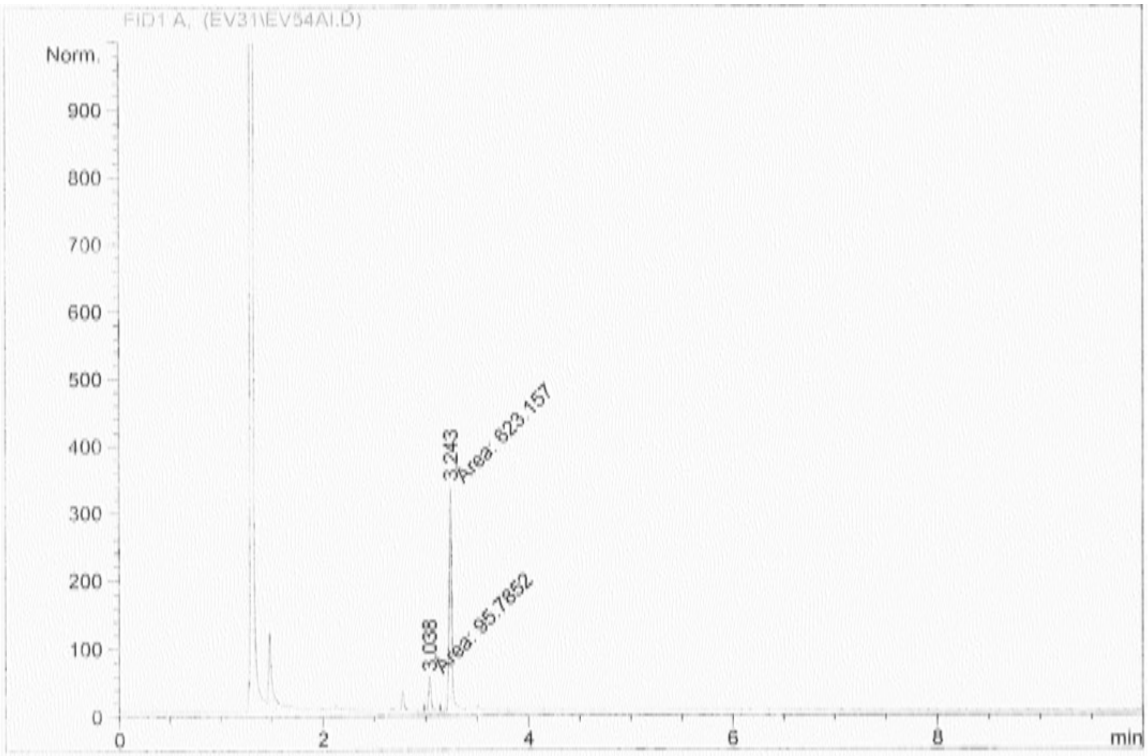




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]         %
----|-------|----|-------|----------|----------|--------|
   1   7.921 MM    0.0637    8.77673    2.29588  7.72226
   2   8.330 MM    0.0525  104.87827   33.32261 92.27774

Totals :                   113.65500   35.61849
```

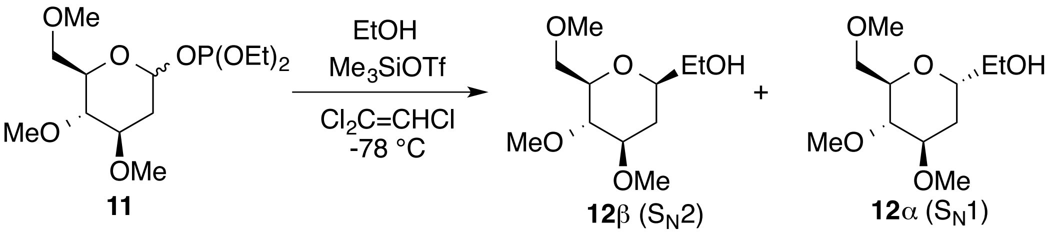
Figure S26: GC spectrum for Scheme 6, with dichloromethane as solvent





```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1   3.038 MM    0.0312   95.78522   51.21309 13.32308
   2   3.243 MM    0.0313  623.15674  331.40598 86.67692
```

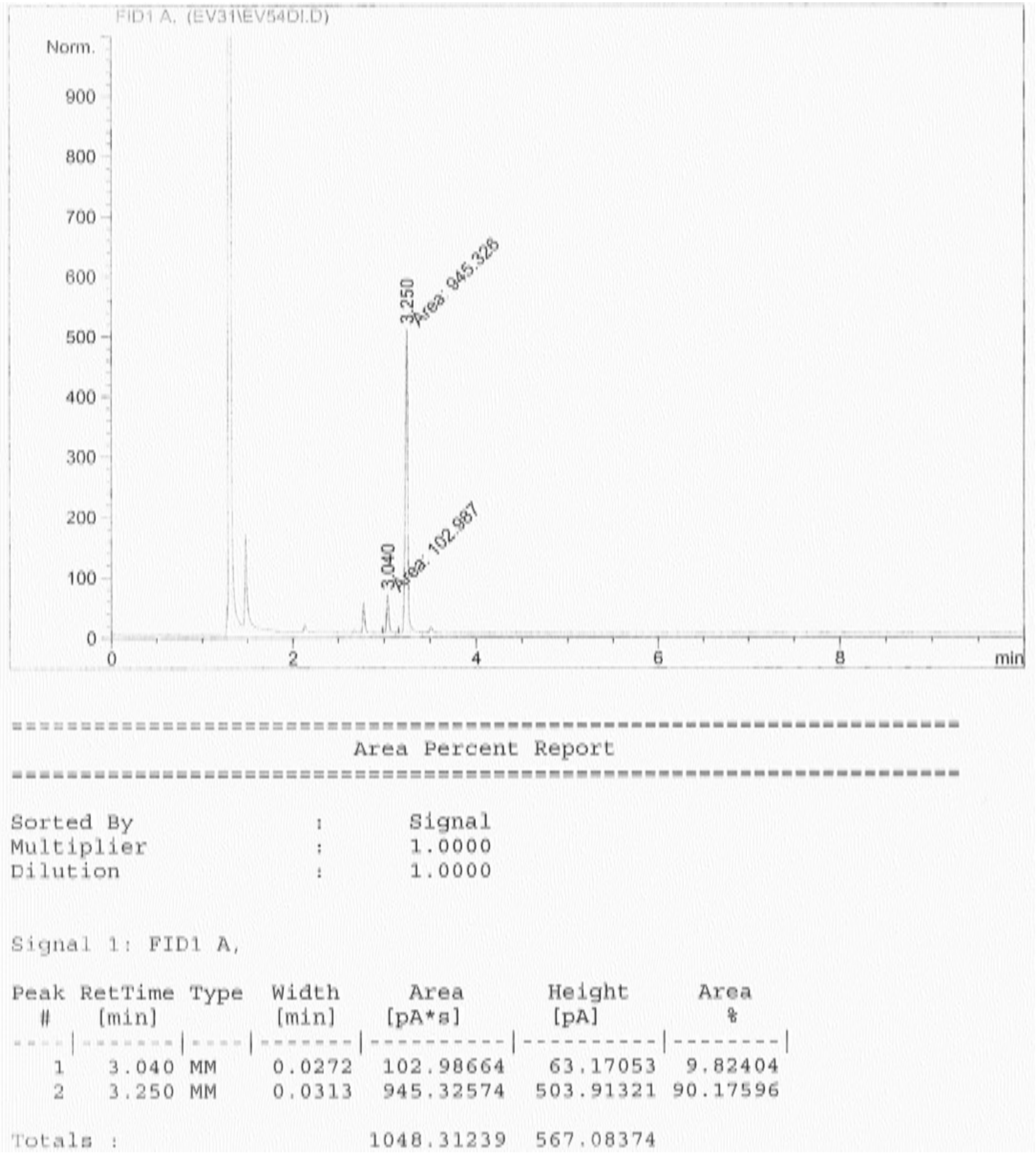
Figure S27: GC spectrum for Scheme 6, with trichloroethylene as solvent



11

12β (S_N2)

12α (S_N1)



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1   3.040 MM    0.0272  102.98664   63.17053  9.82404
   2   3.250 MM    0.0313  945.32574  503.91321 90.17596

Totals :                   1048.31239  567.08374
```

VII. Literature Cited

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
2. Krumper, J. R.; Salamant, W. A.; Woerpel, K. A. *J. Org. Chem.* **2009**, *74*, 8039.
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