Supporting Information

Acid- and metal-free synthesis of annulated pyrroles in deep eutectic solvent

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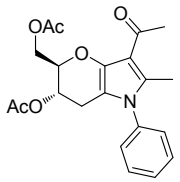
Content

Experimental Section

General Considerations: All solvents were purified by standard procedures. Thin-layer chromatography (TLC) was performed on Merck silica gel pre-coated on aluminum plates, spots were observed by spraying the plates with a solution of 10 % (v/v) aqueous H_2SO_4 with subsequent heating. Column chromatography was performed on 100-200 mesh silica gel. All the ^{1}H NMR spectra were recorded on a 400 MHz Bruker Spectrospin DPX FT-NMR spectrometer. Chemical shifts are expressed in parts per million (ppm) with TMS as internal standard. Coupling constant (*J*) are given in Hz.

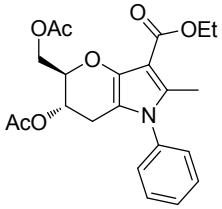
4.1. [(5R, 6S) 3-Acetyl-5-[(acetyloxy) methyl]-2-methyl-1-(phenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-6-yl acetate (5a).



Yield: 94%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50-7.41 (m, 5H), 5.20 (q, *J* = 7.2, 13.4 Hz, 1H), 4.55 (dd, J= 6.8, 12.0 Hz, 1H), 4.50-4.42 (m, 2H), 2.82 (dd, J= 6.0, 15.8 Hz, 1H), 2.49 (s, 3H), 2.48 (s, 3H), 2.46 (s, 3H), 2.09 (s, 3H).

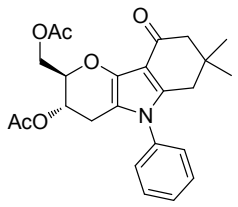
4.2. [(5R, 6S) Ethyl-5-[(acetyloxy) methyl]-2-methyl-1-(phenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-3-carboxylate (5b).



Yield: 92%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49-7.40 (m, 5H), 5.27 (q, J = 7.0, 13.2 Hz, 1H), 4.42 (dd, J= 6.8, 12.0 Hz, 1H), 4.38-4.32 (m, 2H), 2.88 (dd, J= 6.0, 15.8 Hz, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 2.32 (s, 3H), 2.10 (s, 3H), 1.38 (t, 3H).

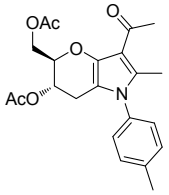
4.3. [(2R,3S)-3-Acetoxy-7,7-dimethyl-9-oxo-5-(phenyl)-2,3,4,5,6,7,8,9-octahydropyrano[3,2-b]indol-2-yl acetate (7a).



Yield: 84%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50-7.29 (m, 5H), 5.21 (q, J = 7.0, 13.2 Hz, 1H), 4.47 (dd, J= 6.8, 12.0 Hz, 1H), 4.39-4.33 (m, 2H), 2.84 (dd, J= 6.0, 15.8 Hz, 1H), 2.66 (dd, J= 6.0, 15.8 Hz, 1H), 2.31 (s, 3H), 2.09 (s, 3H), 2.04 (s, 3H), 1.36 (t, 3H), 1.28 d, 2H).

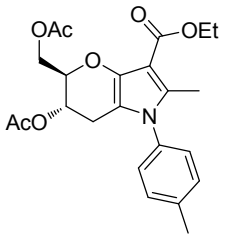
4.4. [(5R, 6S) 3-Acetyl-5-[(acetyloxy) methyl]-2-methyl-1-(4-methylphenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-6-yl acetate (5c).



Yield: 92%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 7.0, Hz, 2H), 7.26 (d, J = 7.0, Hz, 2H), 5.30 (q, J = 7.0, 13.2 Hz, 1H), 4.40 (dd, J= 6.8, 12.0 Hz, 1H), 4.38-4.32 (m, 2H), 2.84 (dd, J= 6.0, 15.8 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H).

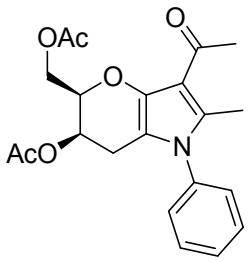
4.5. [(5R, 6S) Ethyl-5-[(acetyloxy) methyl]-2-methyl-1-(4-methylphenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-3-carboxylate (5d).



Yield: 90%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 7.0, Hz, 2H), 7.26 (d, J = 7.0, Hz, 2H), 5.30 (q, J = 7.0, 13.2 Hz, 1H), 4.40 (dd, J= 6.8, 12.0 Hz, 1H), 4.38-4.32 (m, 2H), 2.84 (dd, J= 6.0, 15.8 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 1.38 (t, 3H), 1.08 ((dd, J= 6.8, 15.1 Hz, 1H).

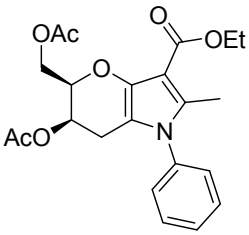
4.6. [(5R, 6R) 3-Acetyl-5-[(acetyloxy) methyl]-2-methyl-1-(phenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-6-yl acetate (5e).



Yield: 94%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50-7.44 (m, 5H), 5.28 (q, J = 7.4, 13.8 Hz, 1H), 4.56 (dd, J= 6.8, 12.0 Hz, 1H), 4.50-4.42 (m, 2H), 2.82 (dd, J= 6.0, 15.8 Hz, 1H), 2.49 (s, 3H), 2.48 (s, 3H), 2.46 (s, 3H), 2.09 (s, 3H).

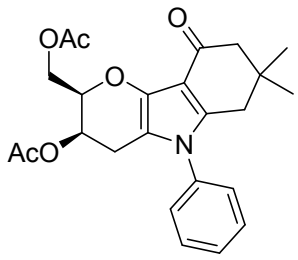
4.7. [(5R, 6R) Ethyl-5-[(acetyloxy) methyl]-2-methyl-1-(phenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-3-carboxylate (5f).



Yield: 92%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48-7.40 (m, 5H), 5.22 (q, J = 7.0, 13.2 Hz, 1H), 4.42 (dd, J= 6.8, 12.0 Hz, 1H), 4.37-4.32 (m, 2H), 2.84 (dd, J= 6.0, 15.8 Hz, 1H), 2.40 (s, 3H), 2.35 (s, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 1.34 (t, 3H).

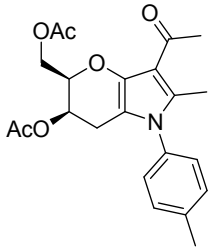
4.8. [(2R,3R)-3-Acetoxy-7,7-dimethyl-9-oxo-5-(phenyl)-2,3,4,5,6,7,8,9-octahydropyrano[3,2-b]indol-2-yl acetate (7b).



Yield: 84%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50-7.29 (m, 5H), 5.21 (q, J = 7.0, 13.2 Hz, 1H), 4.47 (dd, J= 6.8, 12.0 Hz, 1H), 4.39-4.33 (m, 2H), 2.84 (dd, J= 6.0, 15.8 Hz, 1H), 2.66 (dd, J= 6.0, 15.8 Hz, 1H), 2.31 (s, 3H), 2.09 (s, 3H), 1.36 (t, 3H), 1.28 d, 2H).

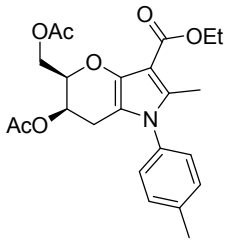
4.9. [(5R, 6R) 3-Acetyl-5-[(acetyloxy) methyl]-2-methyl-1-(4-methylphenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-6-yl acetate (5g).



Yield: 90%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 7.0, Hz, 2H), 7.20 (d, J = 7.0, Hz, 2H), 5.22 (q, J = 7.0, 13.2 Hz, 1H), 4.40 (dd, J= 6.8, 12.0 Hz, 1H), 4.36-4.32 (m, 2H), 2.74 (dd, J= 6.0, 15.8 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H).

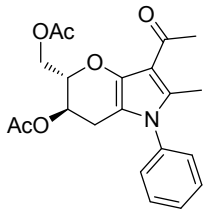
4.10. [(5R, 6R) Ethyl-5-[(acetyloxy) methyl]-2-methyl-1-(4-methylphenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-3-carboxylate (5h).



Yield: 92%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 7.0, Hz, 2H), 7.26 (d, J = 7.0, Hz, 2H), 5.26 (q, J = 7.0, 13.2 Hz, 1H), 4.35-4.32 (m, 2H), 4.28 (dd, J= 6.8, 12.0 Hz, 1H), 2.84 (dd, J= 6.0, 15.8 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 1.36 (t, 3H), 1.28 ((dd, J= 6.8, 15.1 Hz, 1H).

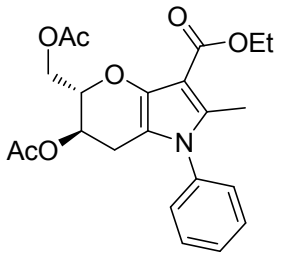
5.11. [(5S, 6R) 3-Acetyl-5-[(acetyloxy) methyl]-2-methyl-1-(phenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-6-yl acetate (5i).



Yield: 84%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48-7.41 (m, 5H), 5.20 (q, J = 7.0, 13.0 Hz, 1H), 4.55 (dd, J= 6.8, 12.2 Hz, 1H), 4.50-4.42 (m, 2H), 2.82 (dd, J= 6.0, 15.6 Hz, 1H), 2.49 (s, 3H), 2.48 (s, 3H), 2.46 (s, 3H), 2.09 (s, 3H).

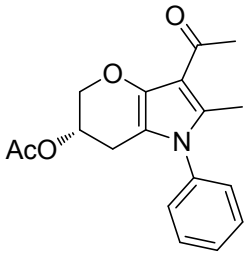
5.12. [(5S, 6R) Ethyl-5-[(acetyloxy) methyl]-2-methyl-1-(phenyl)-1, 5, 6, 7-tetrahydropyrano [3, 2-b]pyrrol-3-carboxylate (5j).



Yield: 85%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49-7.40 (m, 5H), 5.27 (q, J = 7.0, 13.2 Hz, 1H), 4.42 (dd, J= 6.8, 12.0 Hz, 1H), 4.38-4.32 (m, 2H), 2.88 (dd, J= 6.0, 15.8 Hz, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 2.32 (s, 3H), 2.10 (s, 3H), 1.38 (t, 3H).

5.13. (6S) 3-acetyl-2-methyl-1-phenyl-1, 5, 6, 7-tetrahydropyrano [3, 2-b] pyrrol-6-yl acetate (5k).

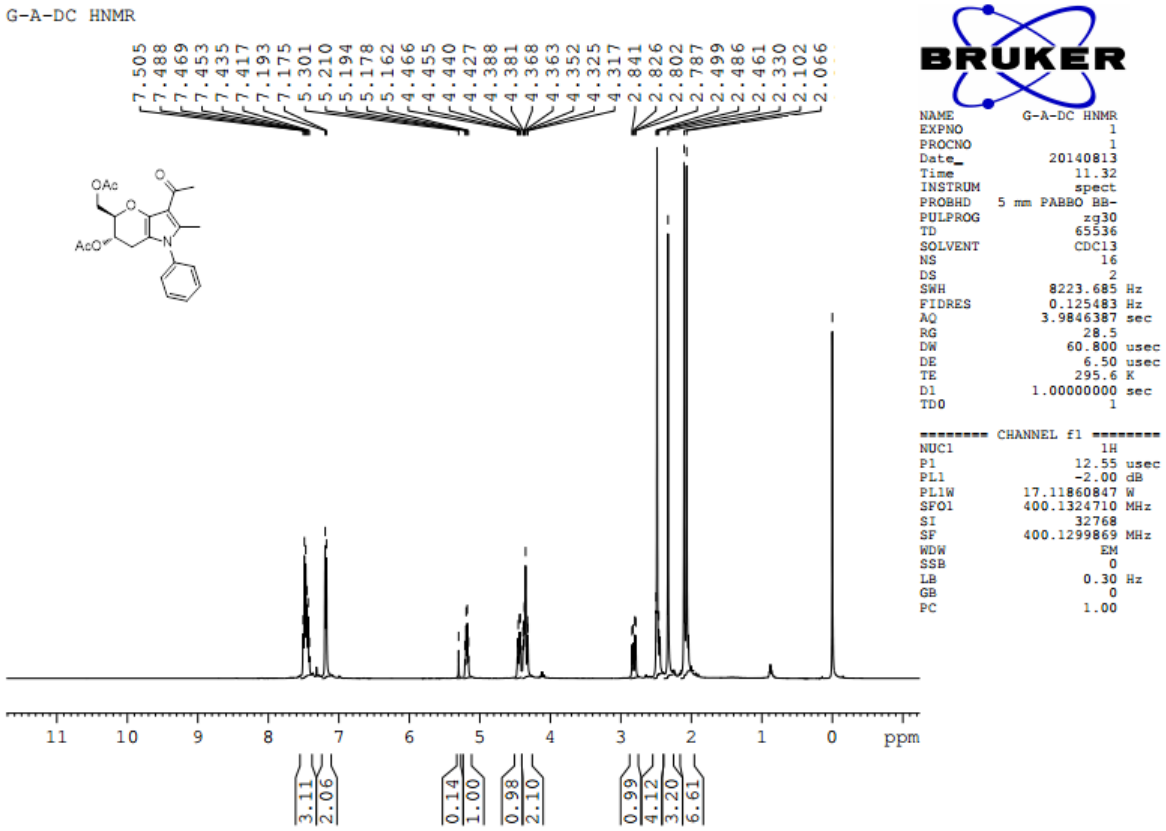


Yield: 94%

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49-7.41 (m, 3H), 7.18-7.16 (d, J = 7.8 Hz, 2H), 5.23 (s, 1H), 4.42-4.28 (m, 2H), 2.86 (dd, J= 6.0, 15.8 Hz, 1H), 2.42 (d, 1H), 2.32 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H).

^{1}H NMR copies:

^{1}H NMR of 5a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7.469
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7.193
7.175
5.301
5.210
5.194
5.178
5.162
4.466
4.455
4.440
4.427
4.388
4.381
4.368
4.363
4.352
4.325
4.317
2.841
2.826
2.802
2.787
2.499
2.486
2.461
2.330
2.102
2.066
OAc
AcO
BRUKER
NAME G-A-DC HNMR
EXPNO 1
PROCNO 1
Date_ 20140813
Time 11.32
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
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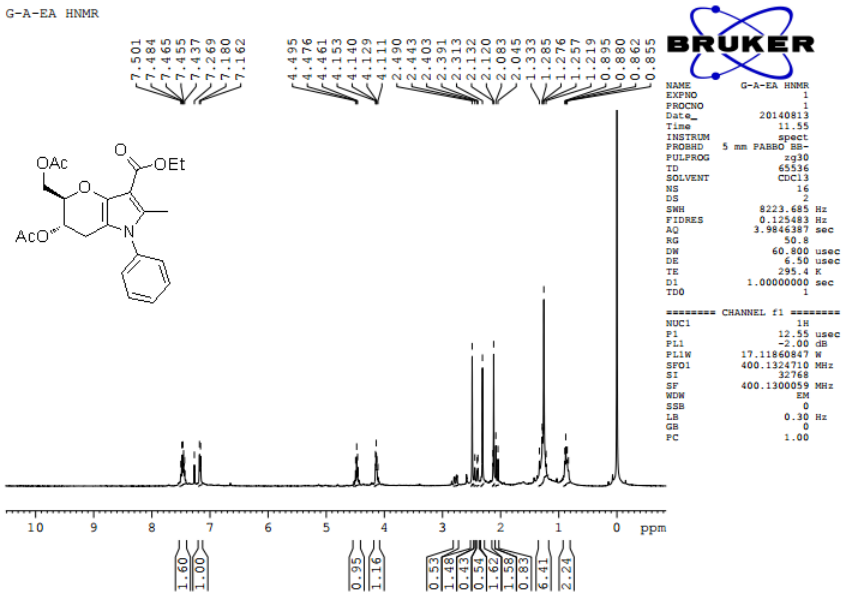
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 28.5
DW 60.800 usec
DE 6.50 usec
TE 295.6 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.55 usec
PL1 -2.00 dB
PL1W 17.11860847 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1299869 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 0 ppm
3.11 2.06 0.14 1.00 0.98 2.10 0.99 4.12 3.20 6.61

^{1}H NMR of 5b


G-A-EA HNMR
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7.465
7.455
7.437
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7.180
7.162
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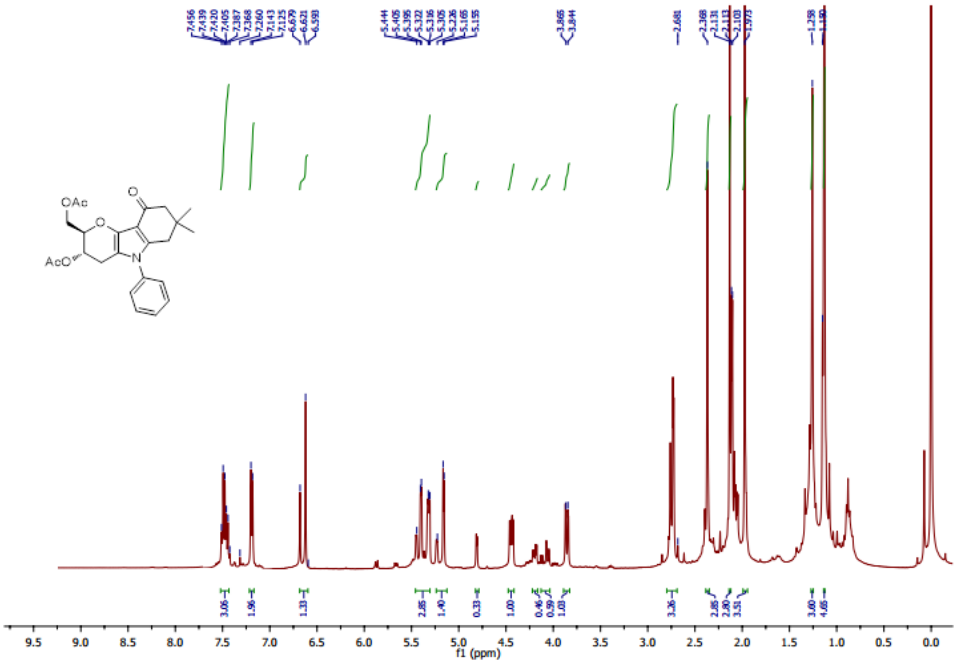
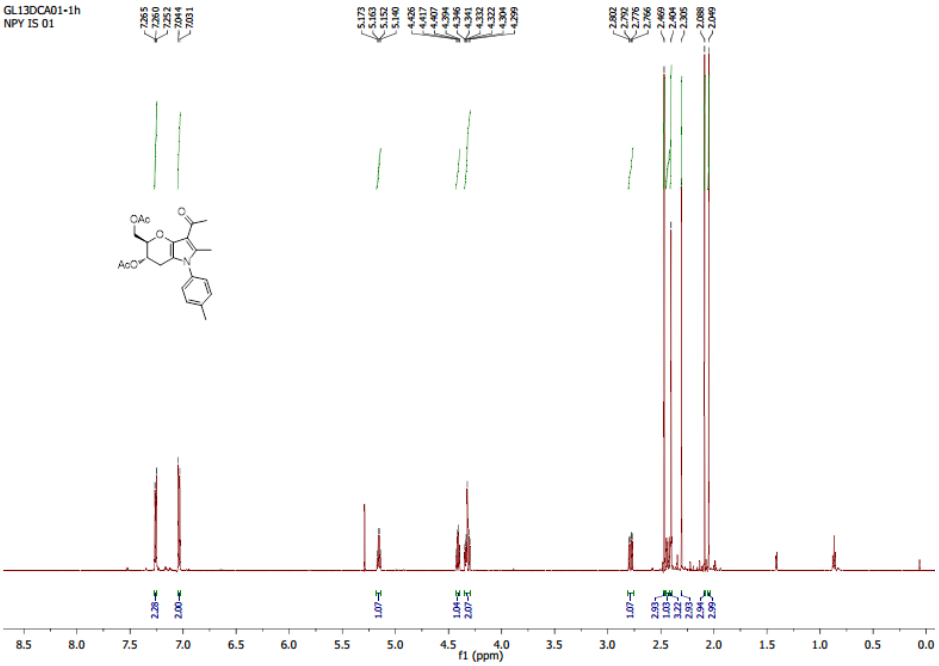
4.476
4.461
4.153
4.140
4.129
4.111
2.490
2.443
2.403
2.391
2.313
2.132
2.120
2.083
2.045
1.333
1.285
1.276
1.257
1.219
0.895
0.880
0.862
0.855
OAc
OEt
AcO
BRUKER
NAME G-A-EA HNMR
EXPNO 1
PROCNO 1
Date_ 20140813
Time 11.55
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 50.8
DW 60.800 usec
DE 6.50 usec
TE 295.4 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.55 usec
PL1 -2.00 dB
PL1W 17.11860847 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300059 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10 9 8 7 6 5 4 3 2 1 0 ppm
1.60 1.00 0.95 1.16 0.53 1.48 0.43 0.54 1.62 1.58 0.83 6.41 2.24

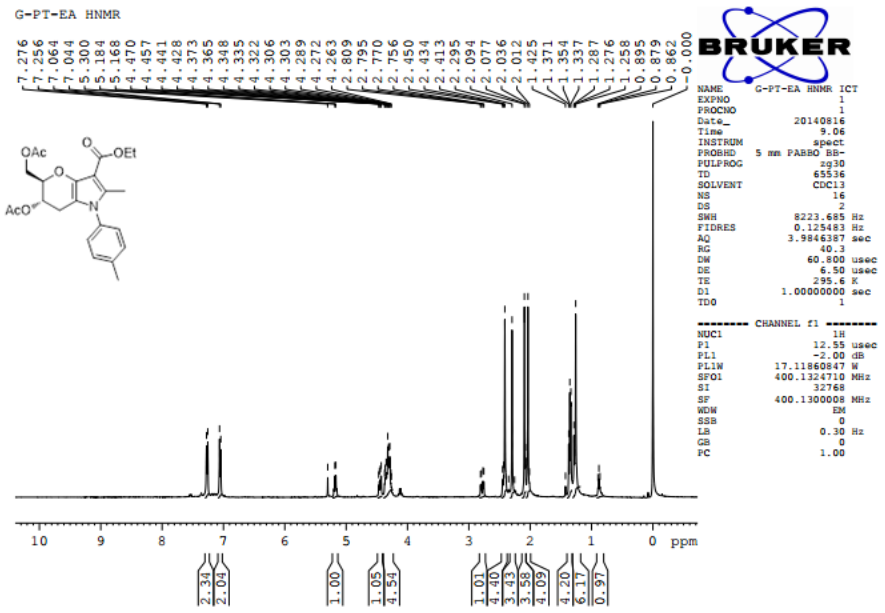
^{1}H NMR of 7a



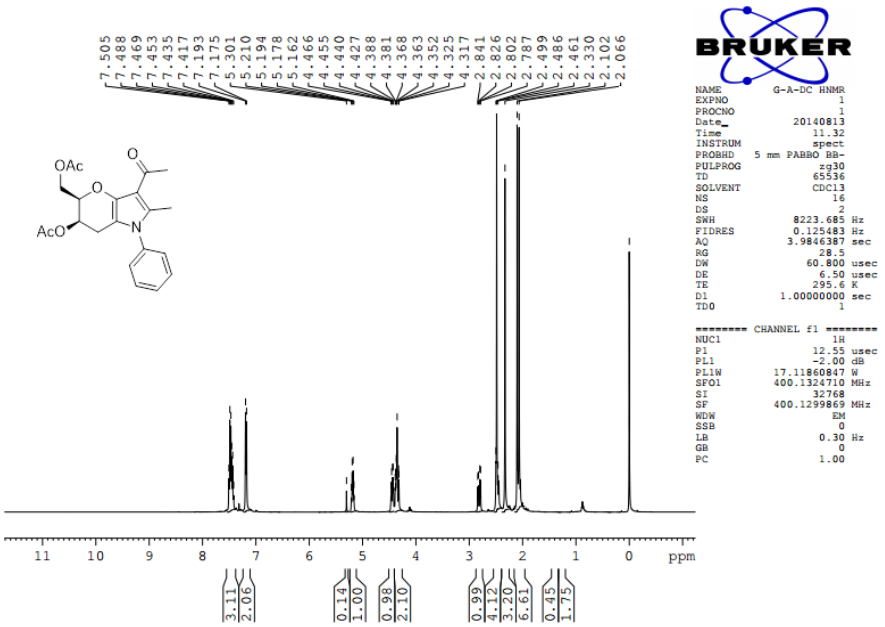
^{1}H NMR of 5c



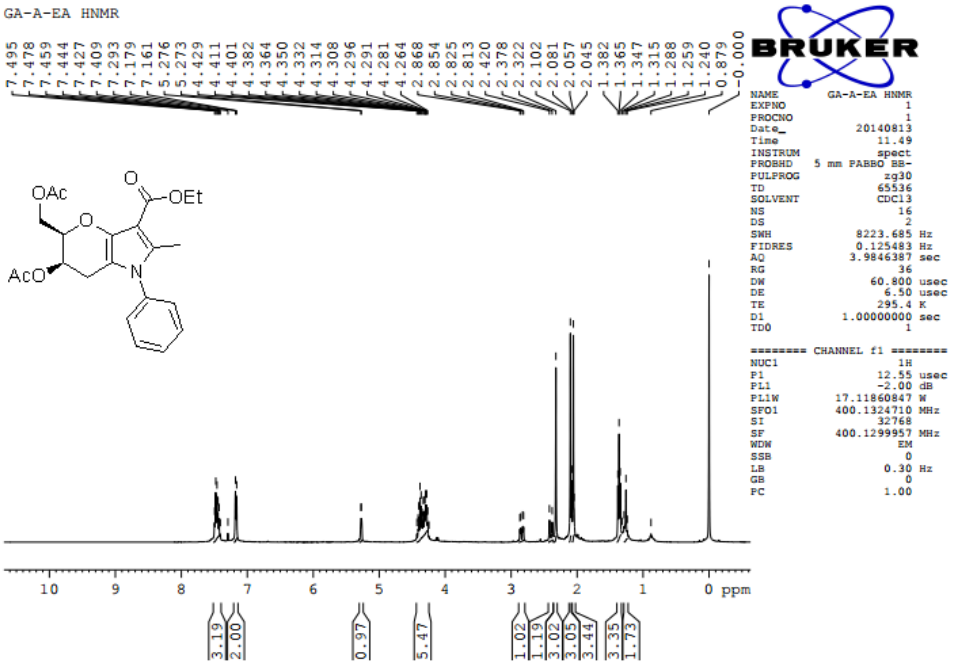
^{1}H NMR of 5d



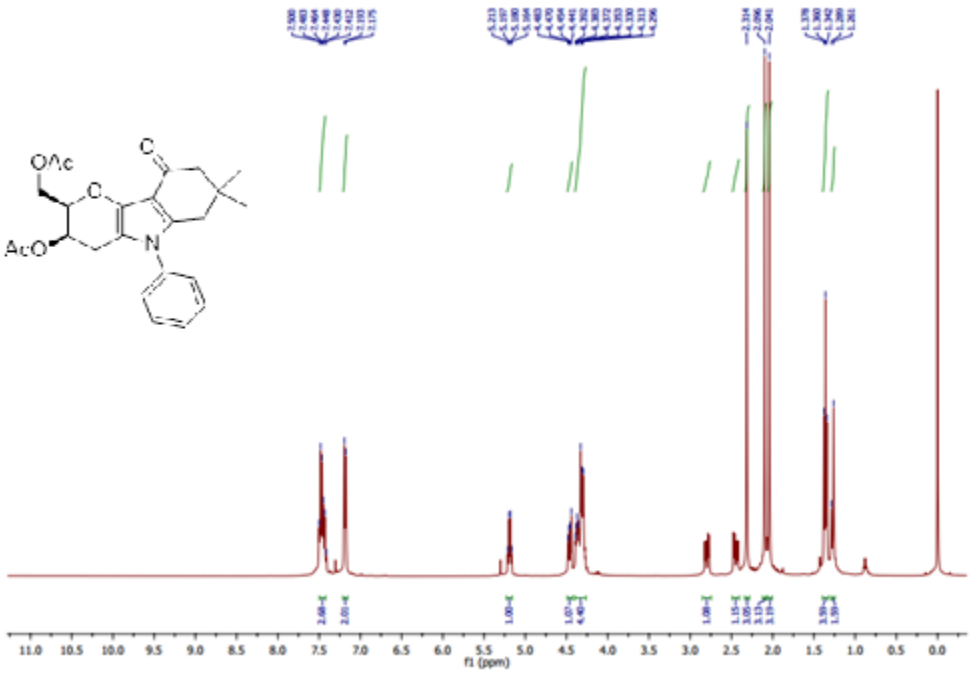
^{1}H NMR of 5e



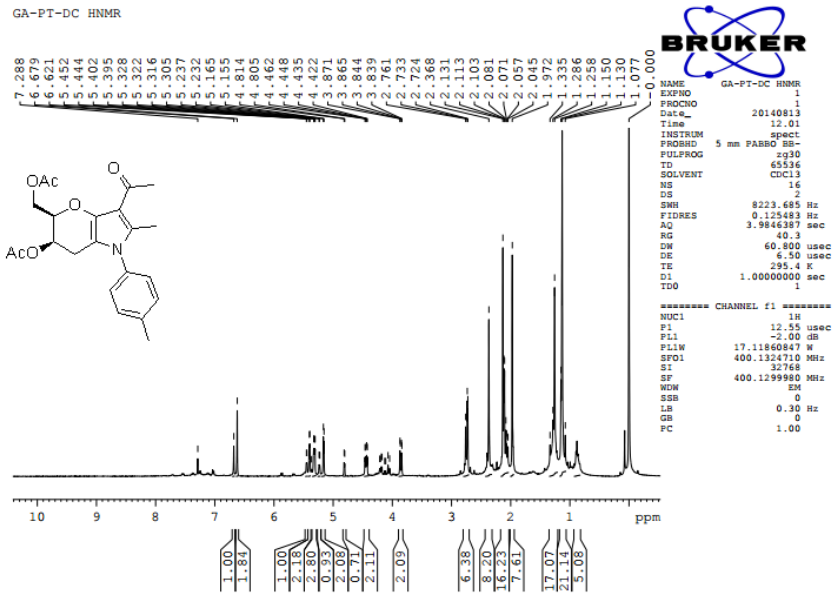
^{1}H NMR of 5f



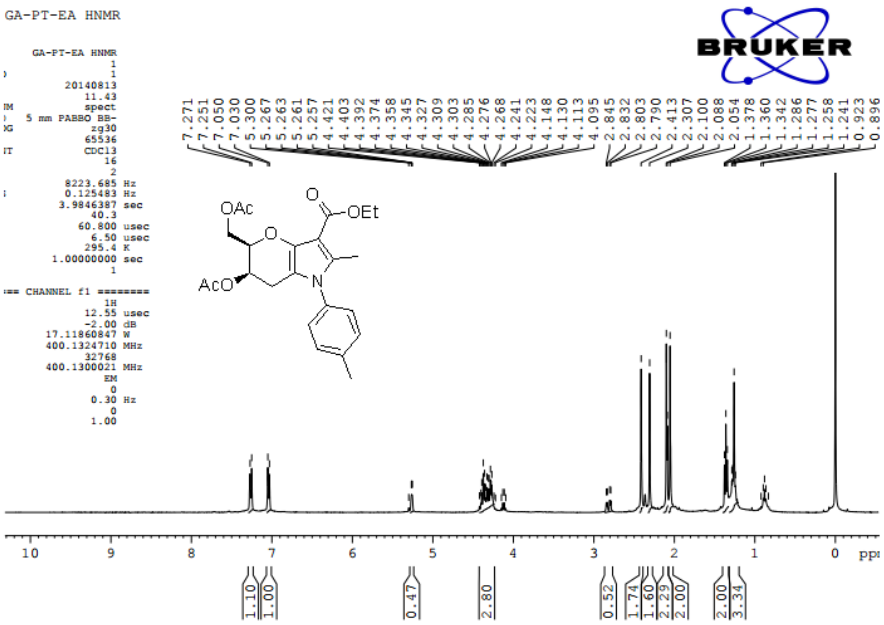
^{1}H NMR of 7b



^{1}H NMR of 5g



^{1}H NMR of 5h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AcO
OEt
O
N
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7.050
7.030
5.300
5.267
5.263
5.261
5.257
4.421
4.403
4.392
4.374
4.358
4.345
4.327
4.309
4.303
4.285
4.276
4.268
4.241
4.223
4.148
4.130
4.113
4.095
2.845
2.832
2.803
2.790
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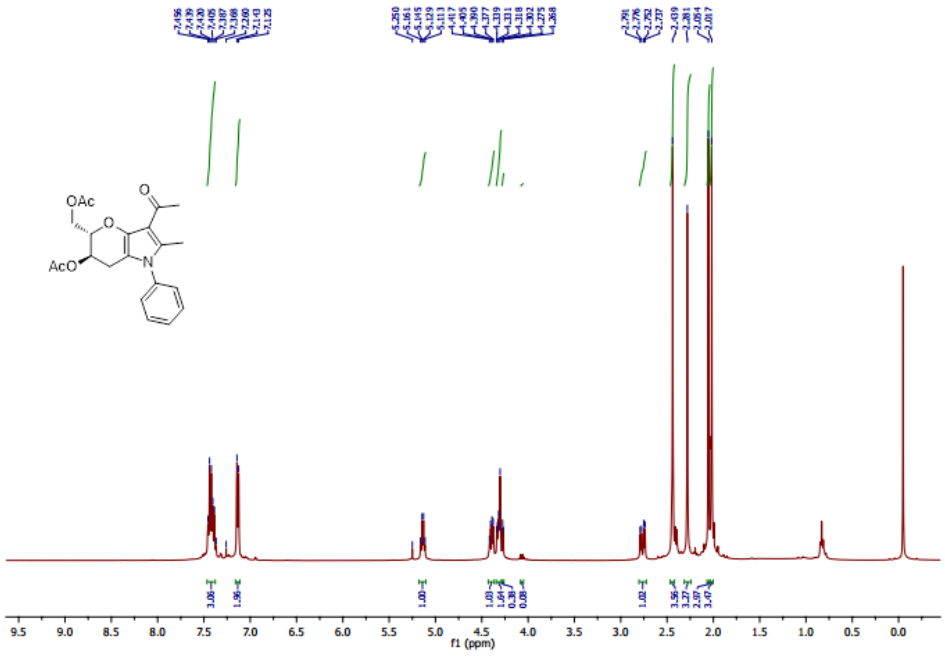
1.286
1.277
1.258
1.241
0.923
0.896
10
9
8
7
6
5
4
3
2
1
0
ppm
1.10
1.00
0.47
2.80
0.52
1.74
1.60
2.29
2.00
2.00
3.34

^{1}H NMR of 5i


OAc
AcO
O
N
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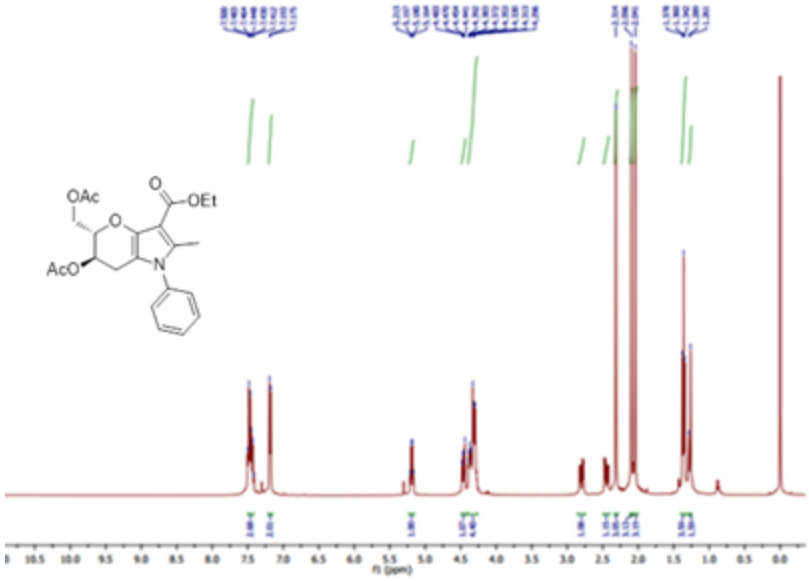
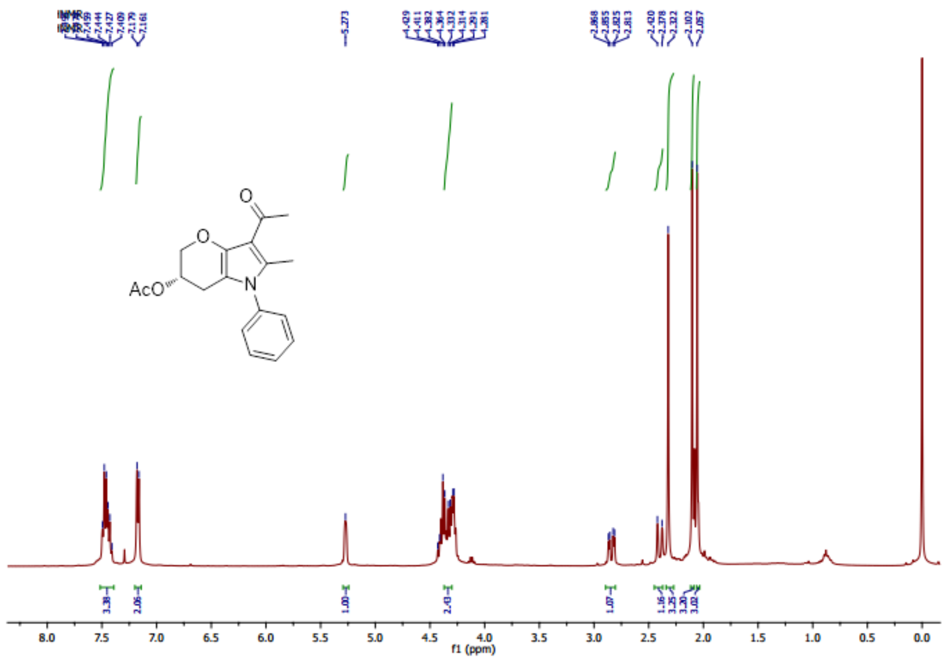
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

^{1}H NMR of 5j



^{1}H NMR of 5k


AcO
O
N
f1 (ppm)