

Supporting Information

Cyclofenil Derivatives as Estrogen Receptor Ligands: Syntheses, Biological Evaluation, and SAR Study.

Jai Woong Seo,^a Dae Yoon Chi,^a Dong Wook Kim, Kathryn Carlson, and John A. Katzenellenbogen*

Department of Chemistry, University of Illinois, Urbana, IL 61801, USA

^aDepartment of Chemistry, Inha University, 253 Yonghyundong Namgu, Incheon 402-751, Korea,

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1. Elemental analysis data for evaluated compounds

Compd.	Formula	Calculated		Found	
		C	H	C	H
2	C ₁₇ H ₁₆ O ₂ ·0.1 H ₂ O	80.35	6.43	80.51	6.48
3	C ₁₈ H ₁₈ O ₂	81.17	6.81	81.25	6.88
4	C ₁₉ H ₂₀ O ₂	81.40	7.19	81.43	7.23
5	C ₂₀ H ₂₂ O ₂	81.60	7.53	81.54	7.61
18	C ₁₉ H ₂₀ O ₃ ·0.2 H ₂ O	76.54	6.83	76.49	6.89
20	C ₁₉ H ₁₉ O ₂ F·0.1 H ₂ O	76.03	6.45	75.88	6.56
21a	C ₂₂ H ₂₄ O ₄ ·0.2 H ₂ O	74.22	6.91	74.26	6.86
21b	C ₂₂ H ₂₄ O ₄	74.98	6.86	79.87	7.02
24a	C ₂₀ H ₂₂ O ₃	77.39	7.14	77.21	7.15
24b	C ₂₁ H ₂₄ O ₃	77.75	7.46	77.73	7.47
26a	C ₂₀ H ₂₁ O ₂ F	76.90	6.78	76.73	6.82
26b	C ₂₁ H ₂₃ O ₂ F·0.1 H ₂ O	76.85	7.12,	76.61	7.19
27	C ₂₂ H ₂₆ O ₃	78.07	7.74	77.82	7.82.
28	C ₂₁ H ₂₄ O ₃ ·0.1 H ₂ O	74.67	7.87	74.63	7.61
29a	C ₂₀ H ₂₂ O ₂ ·0.1 H ₂ O	81.10	7.55	81.16	7.77
29b	C ₂₁ H ₂₄ O ₂	81.78	7.84	81.38	7.85
30a	C ₂₁ H ₂₂ O ₄	74.54	6.55	74.28	6.90
30b	C ₂₄ H ₂₆ O ₆	70.23	6.38	69.97	6.26
32	C ₂₂ H ₂₄ O ₄	74.98	6.86	74.68	6.84
35a	C ₂₀ H ₂₂ O ₃	77.39	7.14	77.57	7.42
35b	C ₂₁ H ₂₄ O ₃	77.75	7.46	77.43	7.69
35c	C ₂₂ H ₂₆ O ₃	78.07	7.74	78.15	7.96

2. ¹H and ¹³C NMR spectra

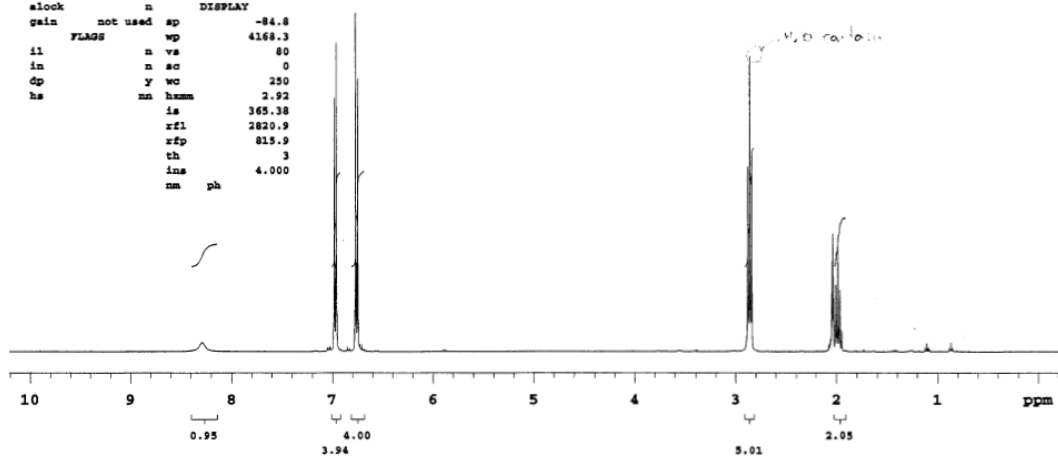
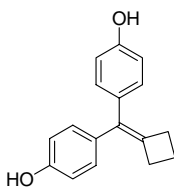
Bis(4-hydroxyphenyl)methylenecyclobutane (2). ¹H NMR (400 MHz, acetone-d₆)

Bis(4-hydroxyphenyl)methylenecyclobutane (2)

expt1 std1h

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ct 32 wnt
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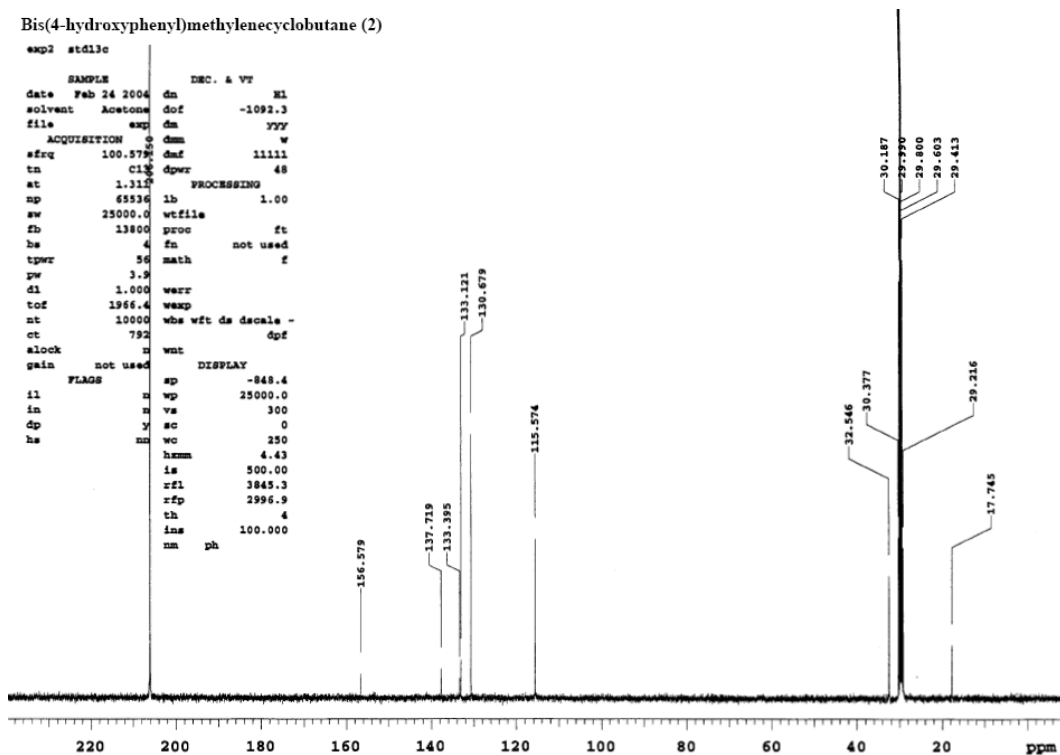
¹³C NMR (100 MHz, acetone-d₆)

Bis(4-hydroxyphenyl)methylenecyclobutane (2)

expt2 std13c

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sv 25000.0 wfile
fb 13800 proc ft
bs 4 fn not used
tpwr 56 math f
pw 3.9
d1 1.000 warr
tof 1966.4 wexp
nt 10000 wbs wft ds decale -
ct 792 wnt dpf
alock n DISPLAY
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nm ph
    
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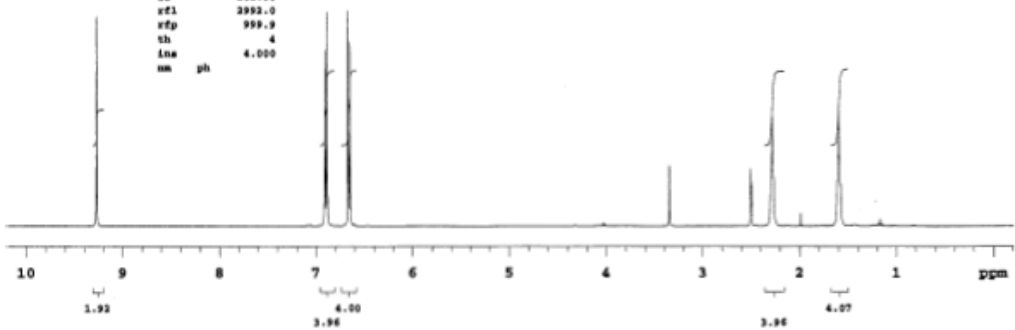
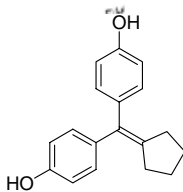
Bis(4-hydroxyphenyl)methylenecyclopentane (3). ^1H NMR (400 MHz, $\text{DMSO-}d_6$)

Bis(4-hydroxyphenyl)methylenecyclopentane (3)

exp1 std1h

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sw      8000.0 wtf1le
fb      4400 proc      ft
hs      3 fn      not used
tpwr    63 math      f
pw      9.6
d1      0 verr
tof    -425.7 wexp
nt      32 wbs      ft
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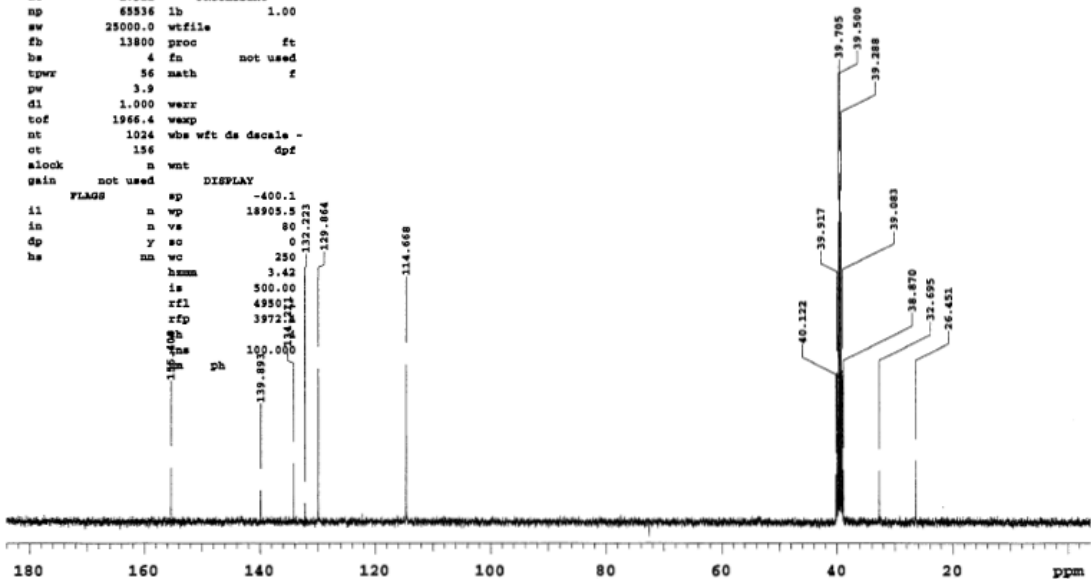
^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)

Bis(4-hydroxyphenyl)methylenecyclopentane (3)

exp2 std13c

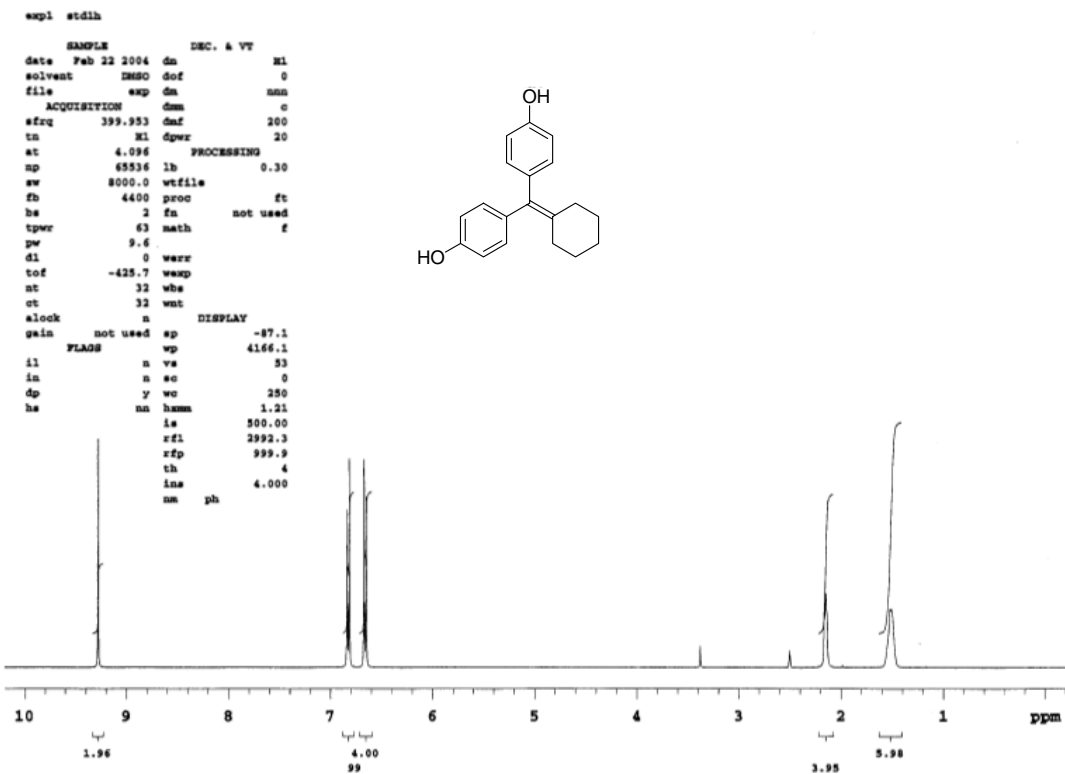
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fb      13800 proc      ft
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pw      3.9
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tof    1946.4 wexp
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        nm      ph
    
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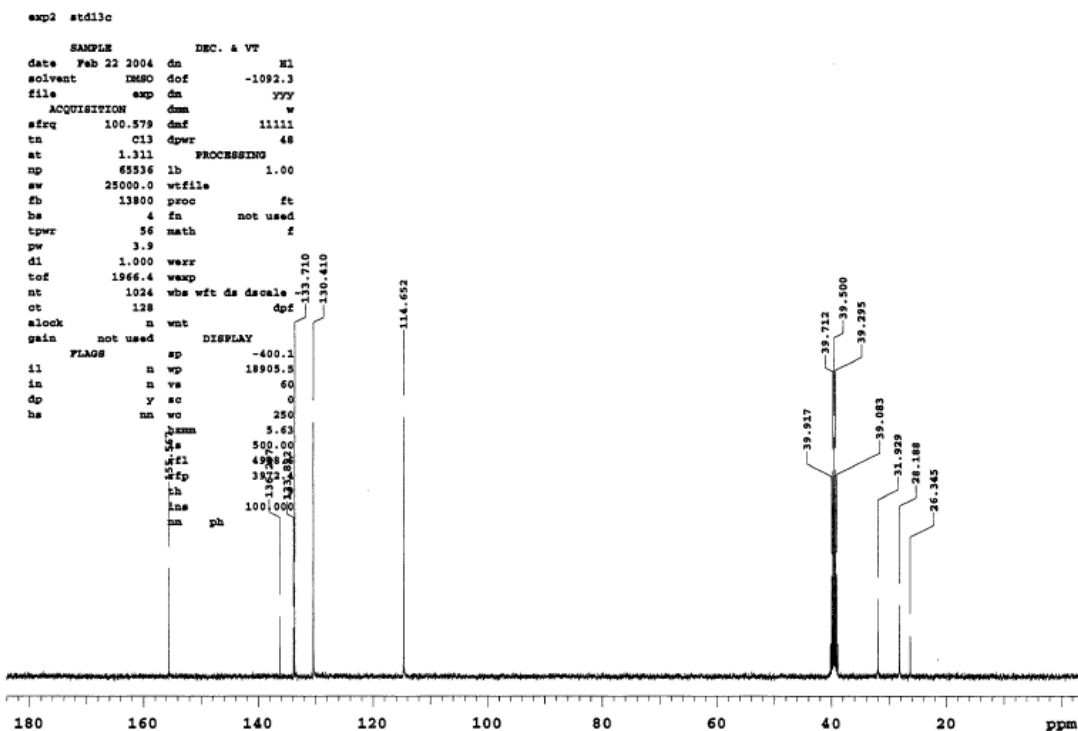
Bis(4-hydroxyphenyl)methylenecyclohexane (4). ¹H NMR (400 MHz, DMSO-d₆)

Bis(4-hydroxyphenyl)methylenecyclohexane (4)



¹³C NMR (100 MHz, DMSO-d₆)

Bis(4-hydroxyphenyl)methylenecyclohexane (4)



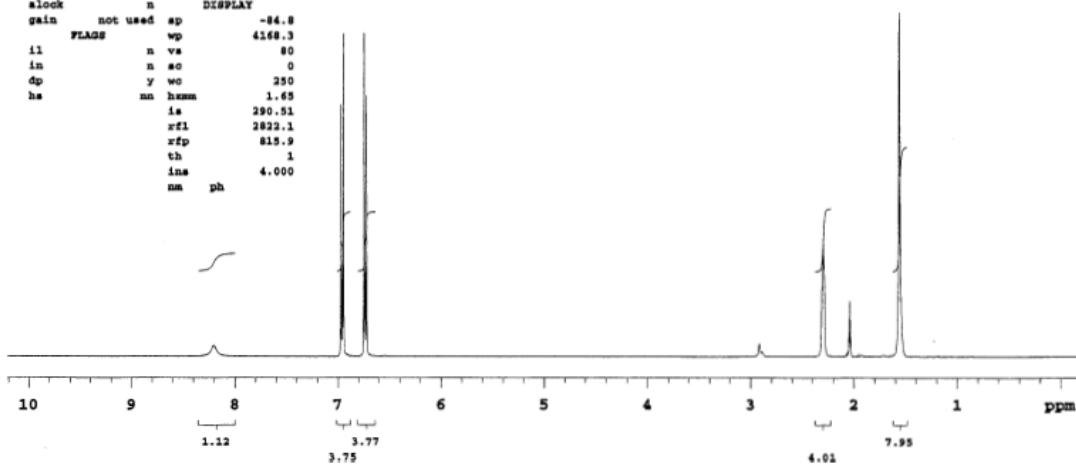
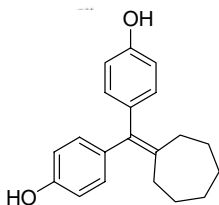
Bis(4-hydroxyphenyl)methylenecycloheptane (5). ¹H NMR (400 MHz, acetone-d₆)

Bis(4-hydroxyphenyl)methylenecycloheptane (5)

exp1 std1b

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fb 4400 proc          ft
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pw 9.6
dl 0 warr
tof -425.7 wexp
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nm ph
    
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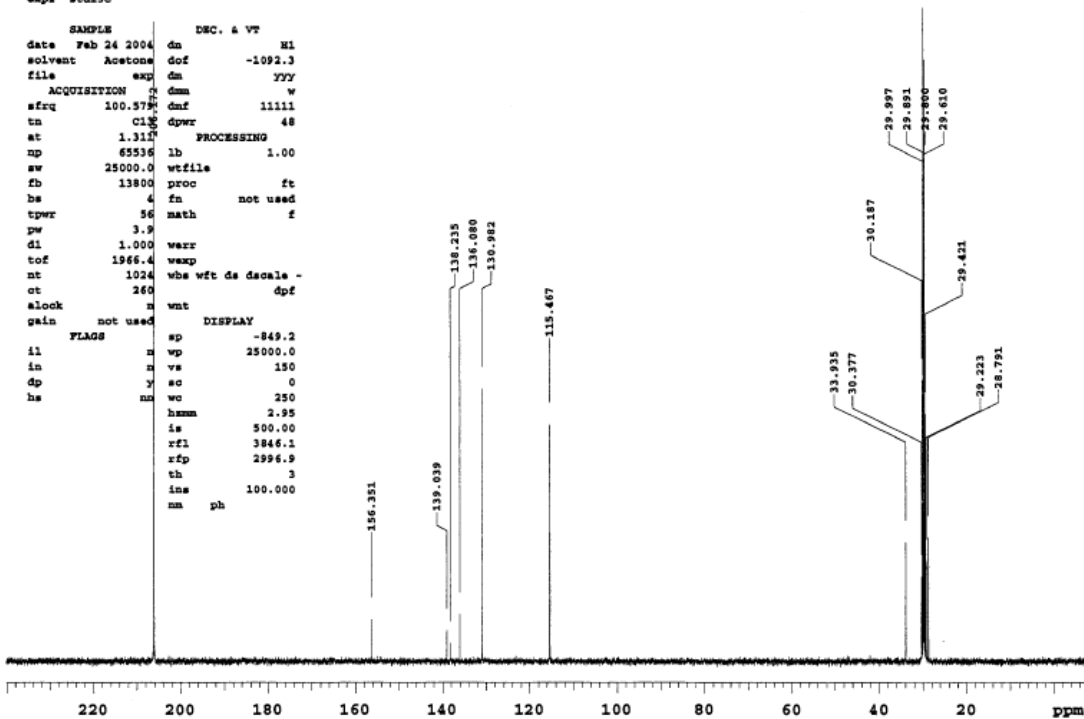
¹³C NMR (100 MHz, acetone-d₆)

Bis(4-hydroxyphenyl)methylenecycloheptane (5)

exp2 std1c

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tof 1966.4 wexp
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ot 260 dpf
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nm ph
    
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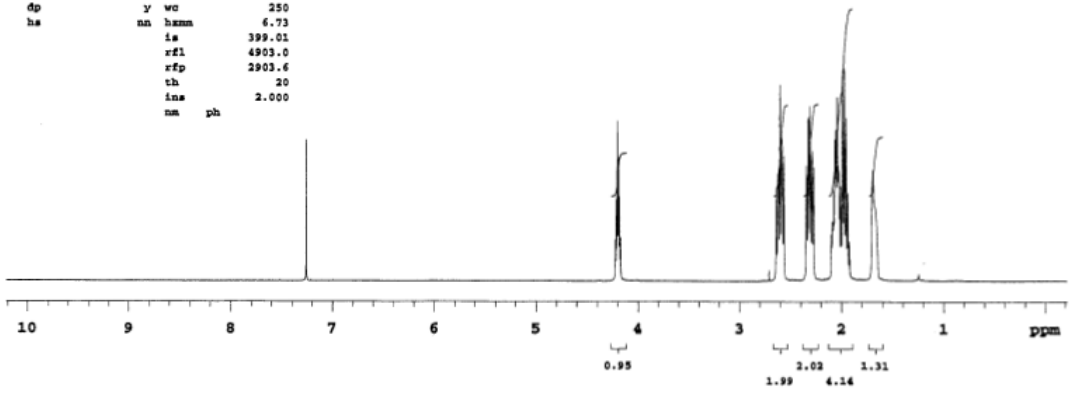
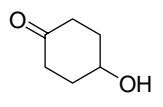


4-Hydroxyhexanone (7). ¹H NMR (400 MHz, CDCl₃)

4-Hydroxyhexanone (7)

```

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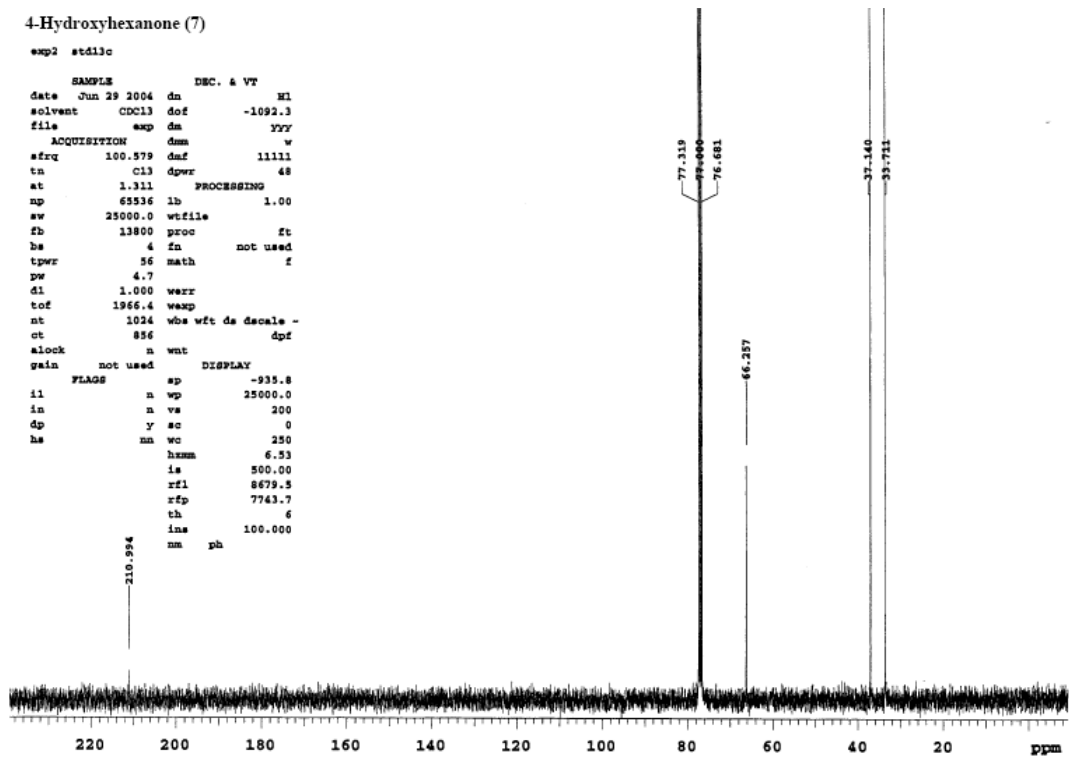


¹³C NMR (100 MHz, CDCl₃).

4-Hydroxyhexanone (7)

```

exp2 std13c
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sw      25000.0 wfile
fb      13800 proc          ft
hs      4 fn              not used
tpwr    56 math
pw      4.7
dl      1.000 werr
tof     1965.4 wexp
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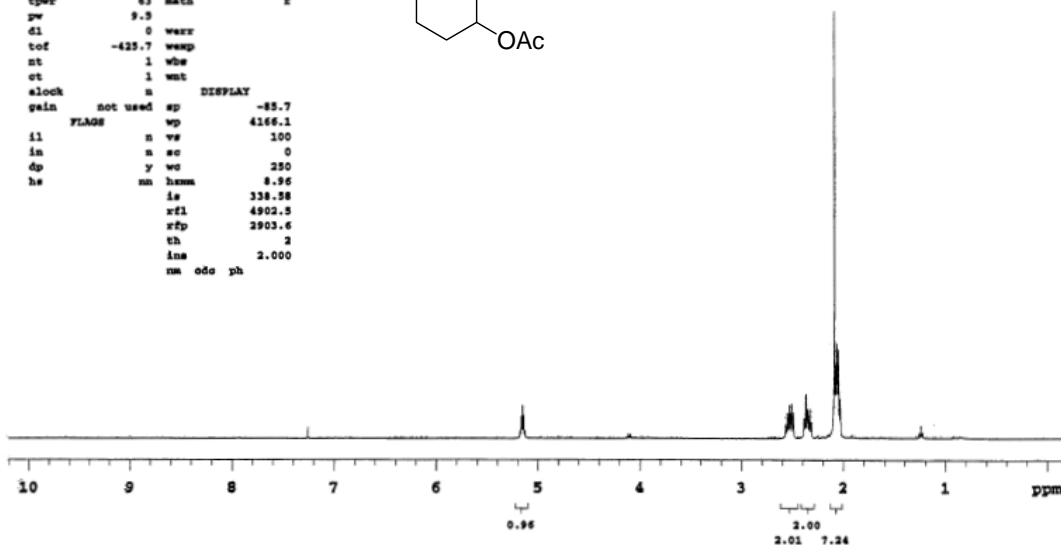
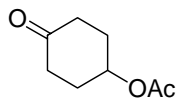


4-Acetoxycyclohexanone (8). ¹H NMR (400 MHz, CDCl₃) Registry No. 41043-88-3

4-Acetoxycyclohexanone (8)

```

expt atdh
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sw 8000.0 wfile
fb 4400 proc          ft
hs 16 fn          not used
tpwr 43 math          f
pw 9.5
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ct 1 wnt
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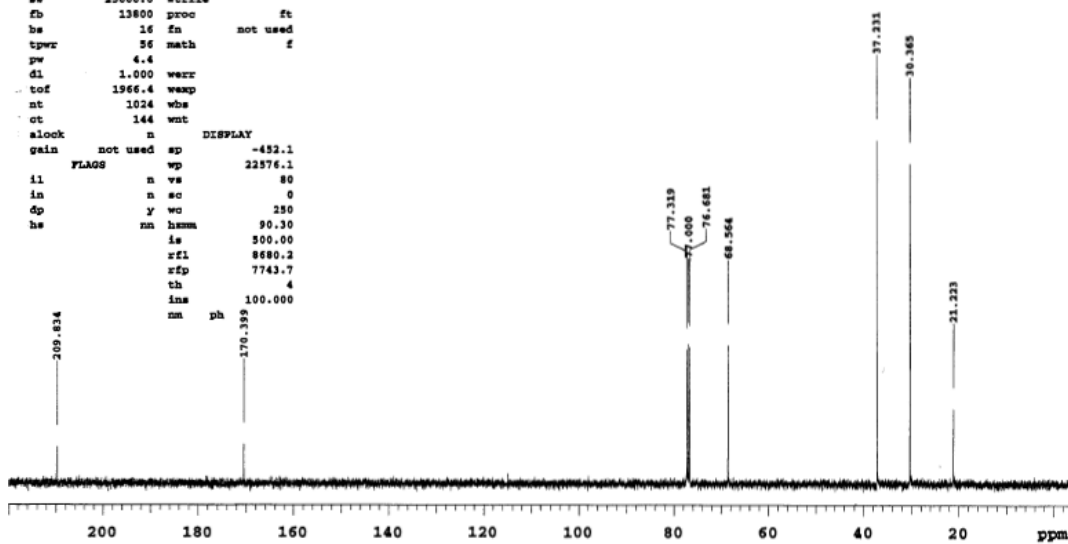


¹³C NMR (100 MHz, CDCl₃).

4-Acetoxycyclohexanone (8)

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fb 13600 proc          ft
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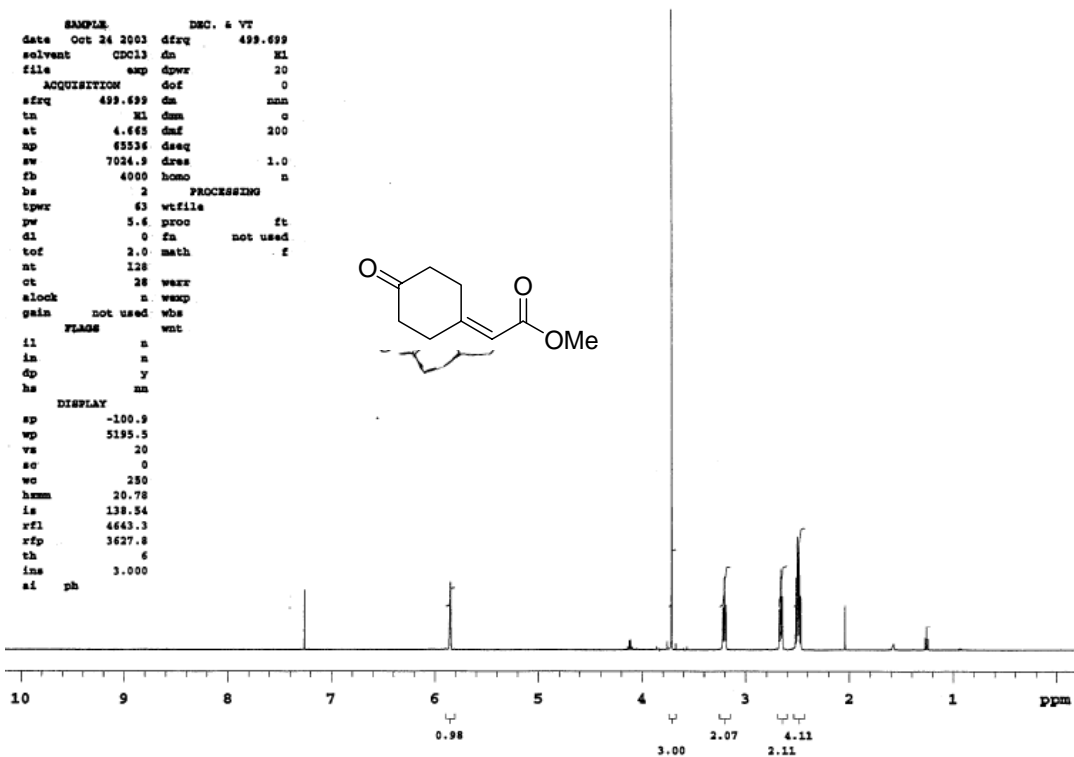
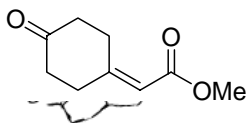


Methyl (4-Oxocyclohexylidene)acetate. ¹H NMR (500 MHz, CDCl₃) Registry No91158-10-0

Methyl (4-Oxocyclohexylidene)acetate

```

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tn KI dm o
at 4.665 dmF 200
np 65536 dseq
sw 7024.9 dres 1.0
fb 4000 homo n
bs 2 PROCESSING
tpwr 63 wfile
pw 5.6 proc ft
dl 0 fa not used
tof 2.0 math f
nt 128
ct 28 warr
slock n wexp
gain not used wbs
FLAG wnt
il n
in n
dp y
hs mn
DISPLAY
sp -100.9
wp 5195.5
vs 20
sc 0
wc 250
hmm 20.78
is 138.54
rf1 4643.3
rfp 3627.8
th 6
ins 3.000
si ph
    
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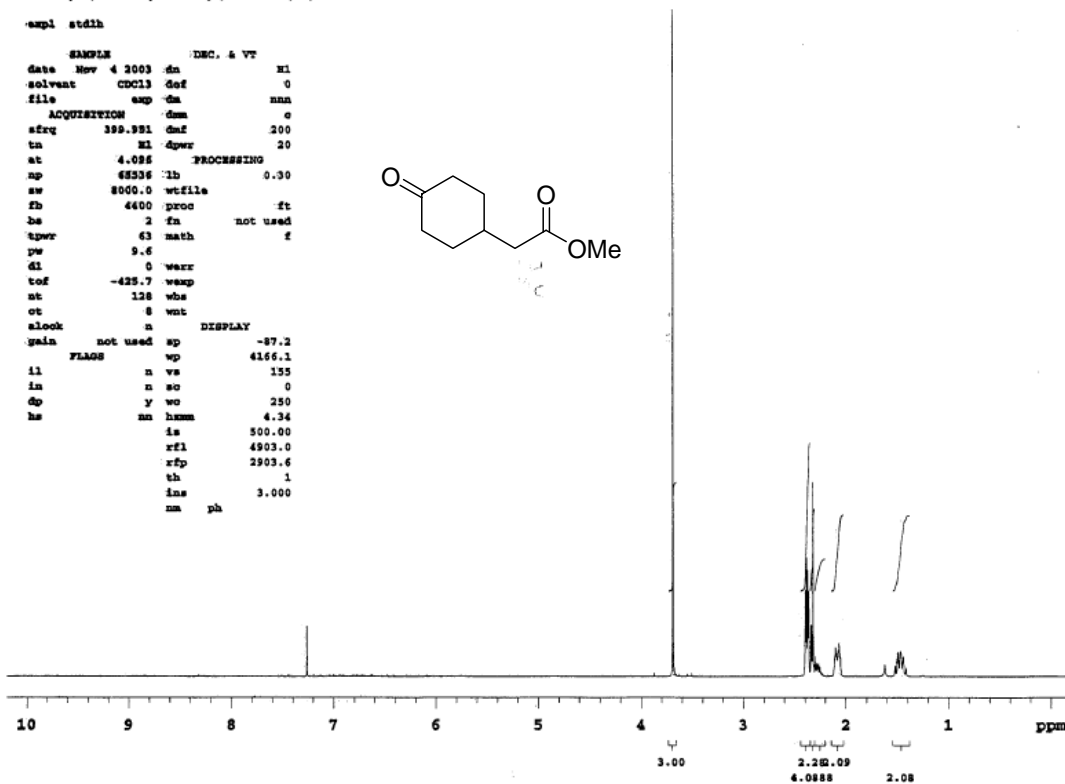
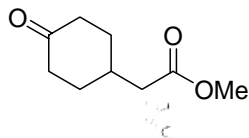


Methyl (4-Oxocyclohexyl)acetate (10). ¹H NMR (400 MHz, CDCl₃) Registry No. 66405-41-2

Methyl (4-Oxocyclohexyl)acetate (10)

```

exp1 std1h
SAMPLE
date Nov 4 2003 dn DEC. & VT H1
solvent CDCl3 dof 0
file exp da nnn
ACQUISITION
sfreq 399.991 dmz 200
tm H1 dpwr 20
at 4.086 PROCESSING
ap 65336 lb 0.30
sw 8000.0 wtfile
fb 4400 proc ft
ba 2 fa not used
tpwr 63 math f
pw 9.6
dl 0 warr
tof -429.7 wamp
at 128 wbs
ot 8 wnt
alock n DISPLAY
gain not used sp -87.2
FLAG wp 4166.1
il n vs 155
in n so 0
dp y wo 250
hs nn hnm 4.34
is 500.00
rf1 4903.0
rfp 2903.6
th 1
ins 3.000
nm ph
    
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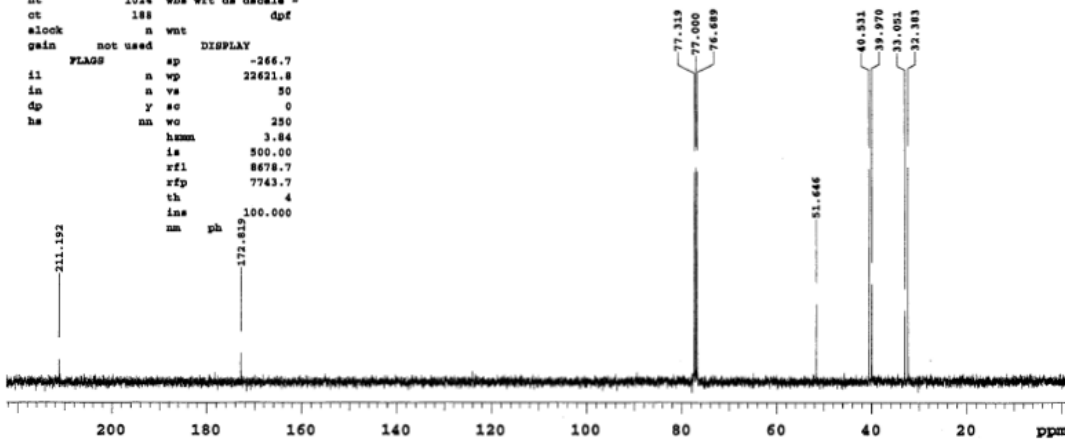


¹³C NMR (100 MHz, CDCl₃)

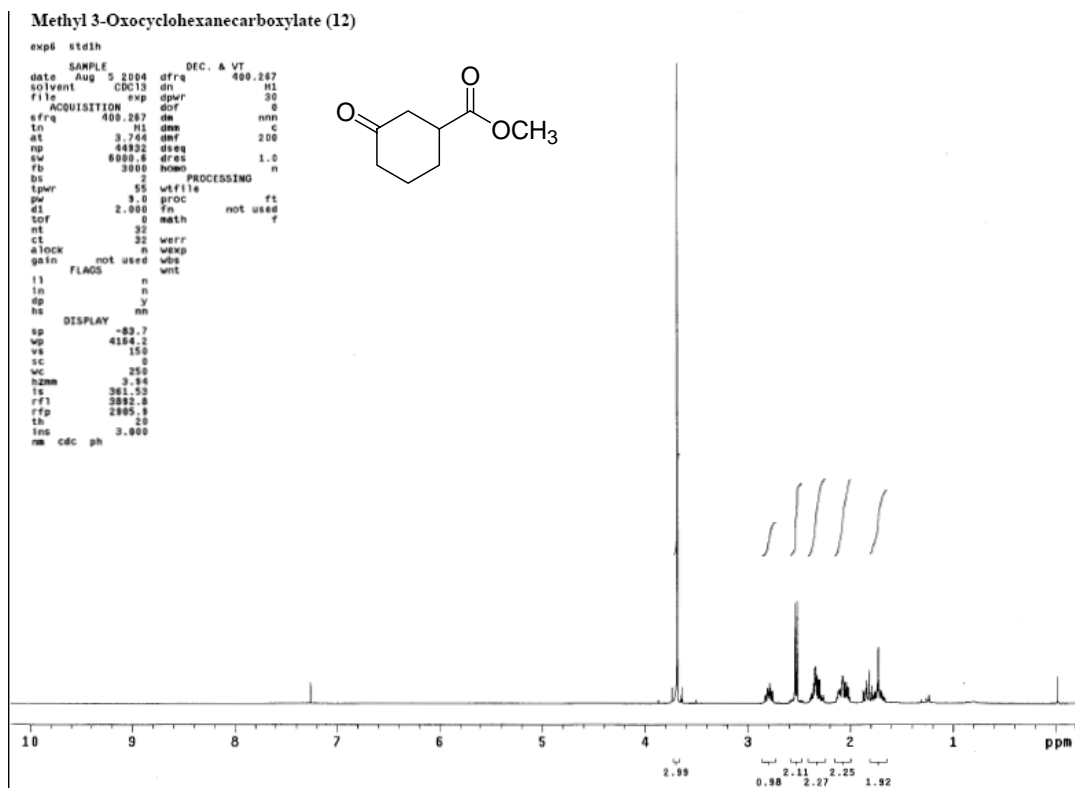
Methyl (4-Oxocyclohexyl)acetate (10)

```

exp2 std1b
SAMPLE
date Nov 4 2003 dn DEC. & VT H1
solvent CDCl3 dof -1092.3
file exp da YYY
ACQUISITION
sfreq 100.579 dmz 11111
tm C13 dpwr 48
at 1.311 PROCESSING
ap 65336 lb 1.00
sw 25000.0 wtfile
fb 13800 proc ft
ba 4 fa not used
tpwr 56 math f
pw 3.9
dl 1.000 warr
tof 1966.4 wamp
nt 1024 wbs wft ds dscale -
ot 188 dpf
alock n wnt DISPLAY
gain not used sp -266.7
FLAG wp 22621.8
il n vs 50
in n so 0
dp y wo 250
hs nn hnm 3.84
is 500.00
rf1 8678.7
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th 4
ins 100.000
nm ph
    
```

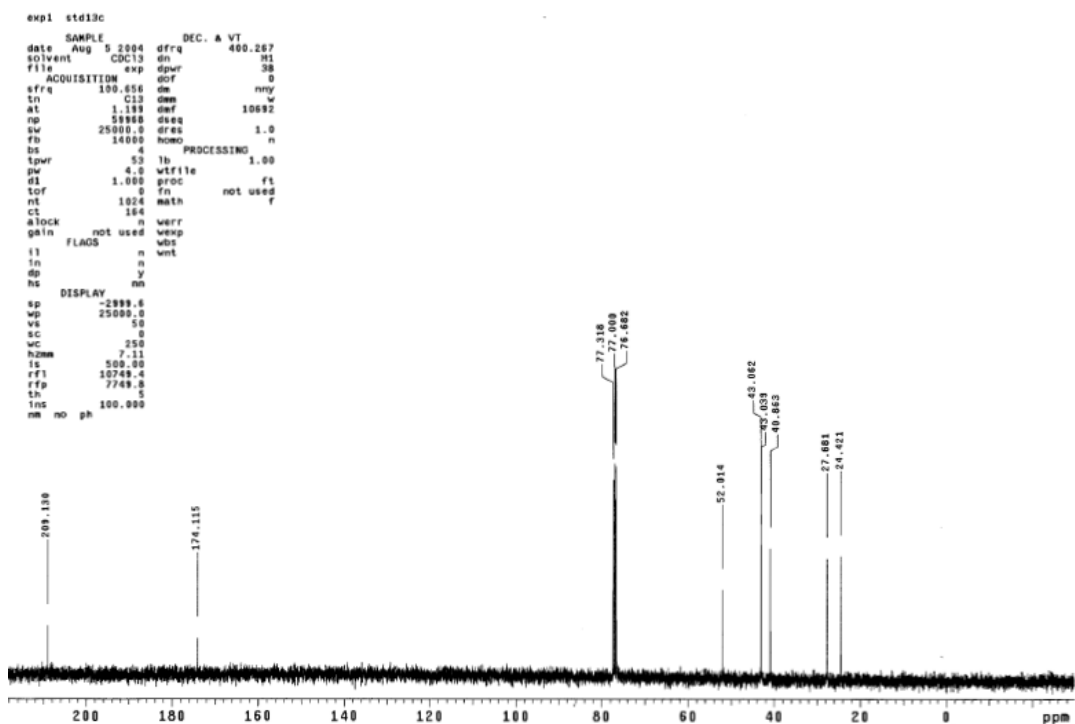


Methyl 3-Oxocyclohexanecarboxylate (12). ¹H NMR (400 MHz, CDCl₃) Registry No. 13148-83-9



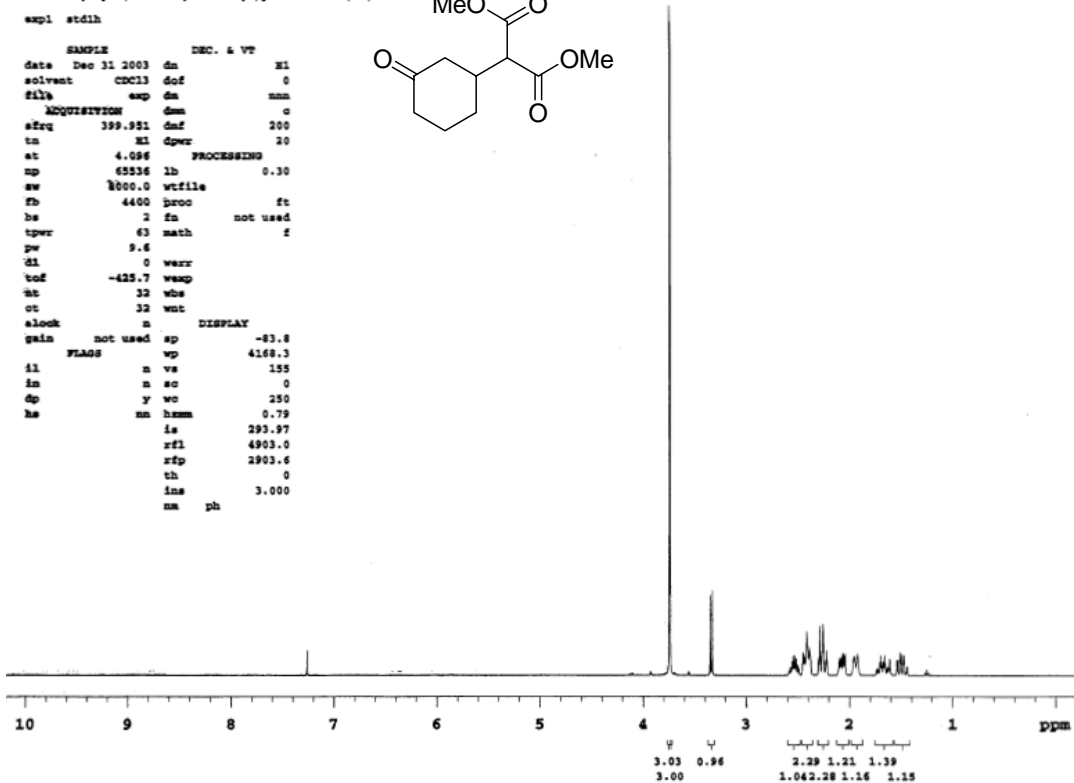
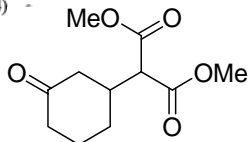
¹³C NMR (100 MHz, CDCl₃)

Methyl 3-Oxocyclohexanecarboxylate (12)



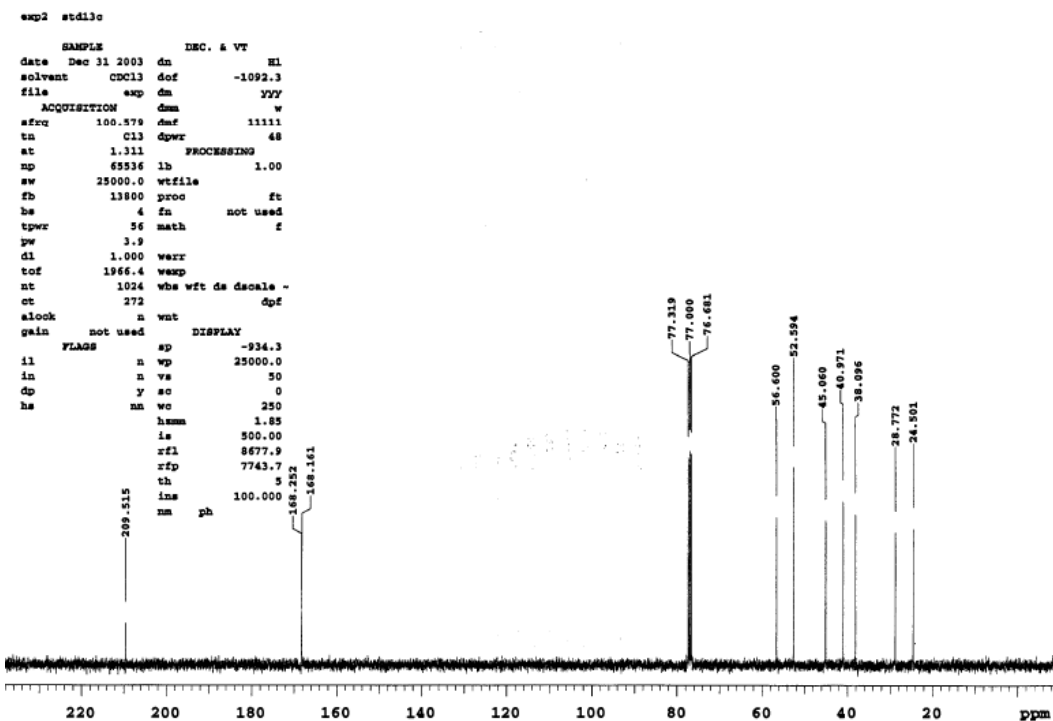
Dimethyl [2-(3-Oxocyclohexyl)]malonate (14). ¹H NMR (400 MHz, CDCl₃) Registry No. 33646-18-3

Dimethyl [2-(3-Oxocyclohexyl)]malonate (14)

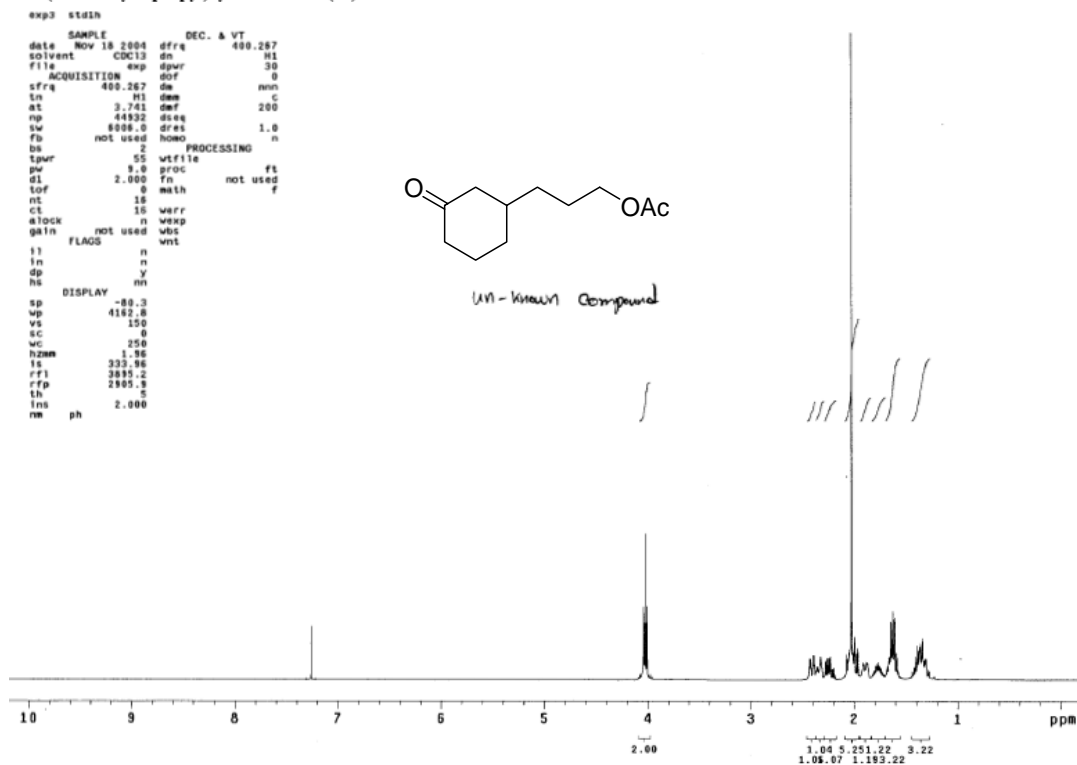


¹³C NMR (100 MHz, CDCl₃)

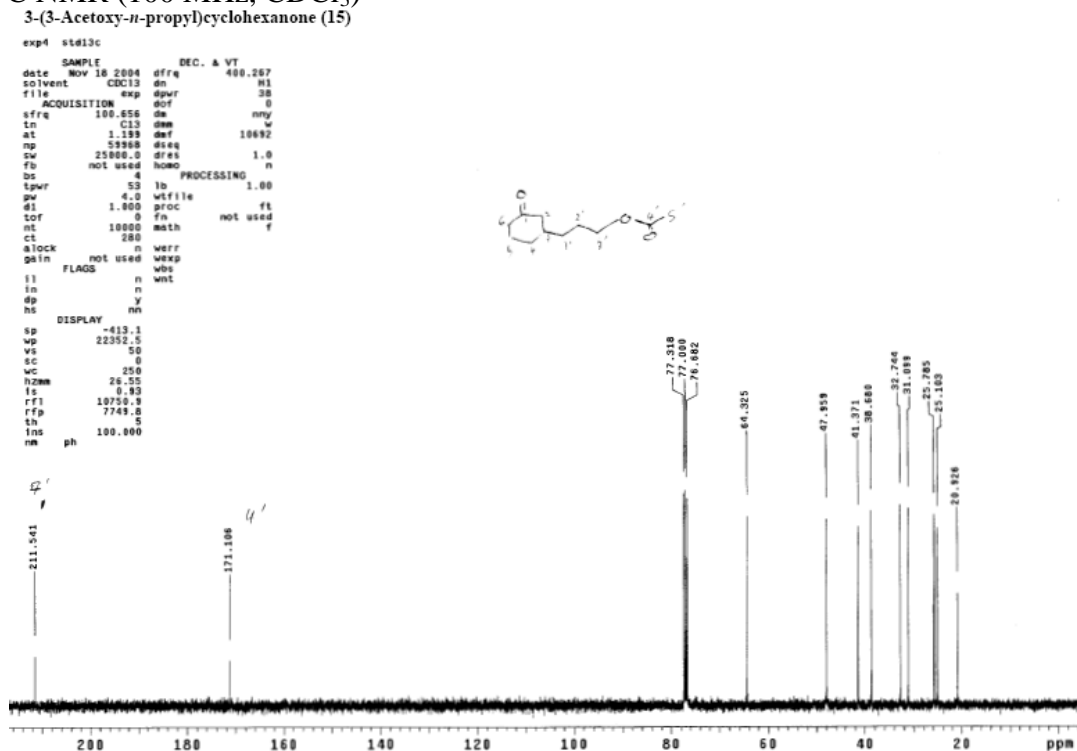
Dimethyl [2-(3-Oxocyclohexyl)]malonate (14)



3-(3-Acetoxy-*n*-propyl)cyclohexanone (15). ^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (100 MHz, CDCl_3)



4-Acetoxy-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (16).

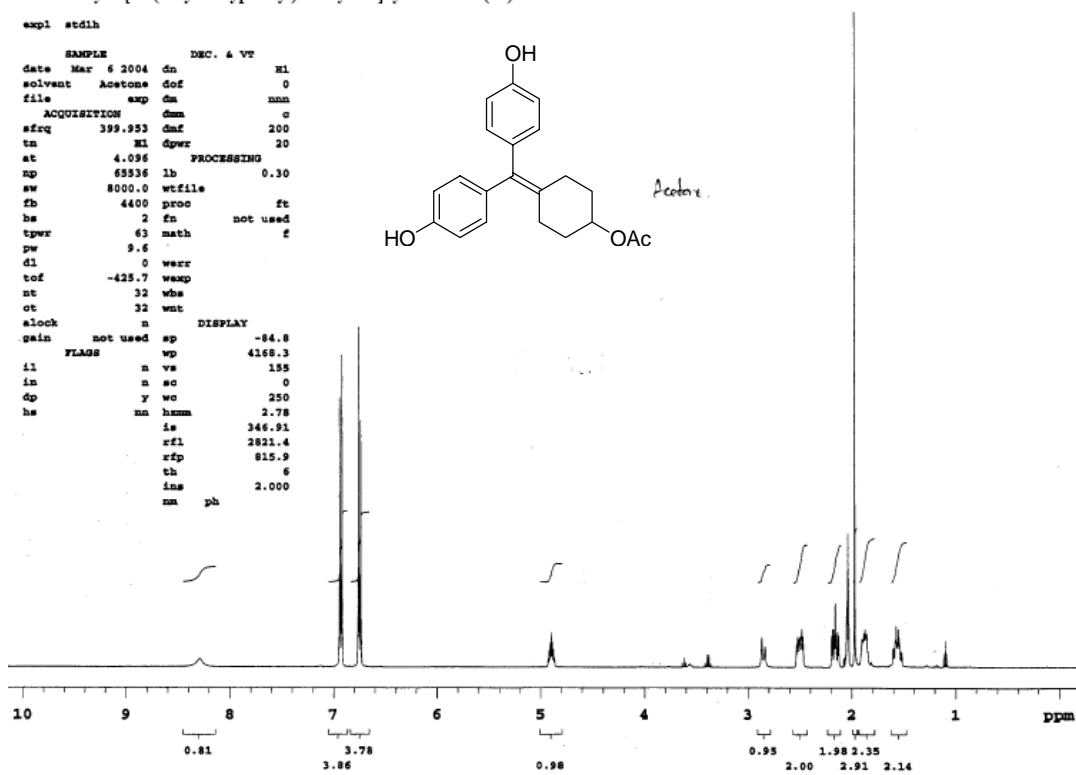
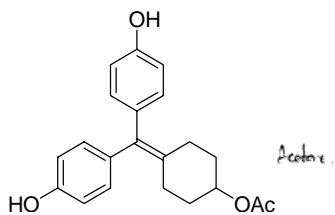
¹H NMR (400 MHz, acetone-d₆)

4-Acetoxy-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (16)

expl stdlh

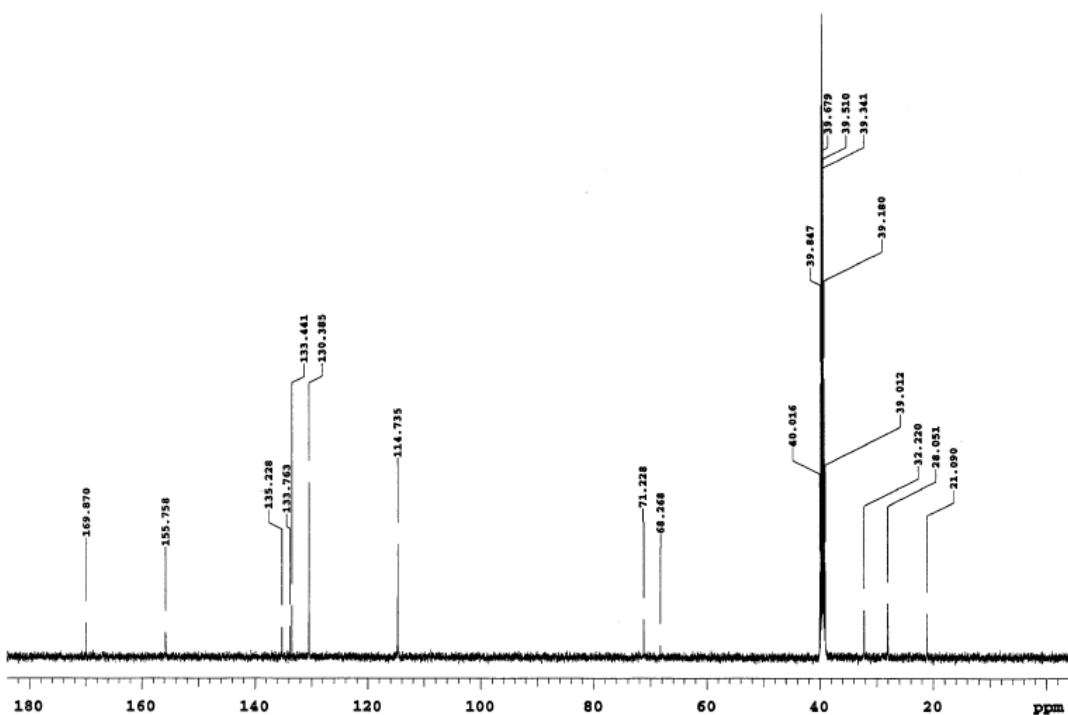
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SAMPLE          DEC. & VT
date Mar 6 2004 dn          H1
solvent Acetone dof         0
file           exp dn       nnn
ACQUISITION    dnm         c
sfrq 399.953 dmf          200
tn      H1 dprz          20
at      4.096          PROCESSING
ap      65536 lb         0.30
sw      8000.0 wf file
fb      4400 proc       ft
hs      2 fn           not used
tprz    63 math        f
pw      9.6
dl      0 werr
tof    -425.7 wamp
nt      32 wba
ot      32 wnt
alock   n             DISPLAY
gain   not used sp    -84.8
        FLAGS      wp    4168.3
il      n vs         155
in      n so         0
dp      y wo         250
hs      mn hnmn      2.78
        is         346.91
        rfl        2821.4
        rfp         815.9
        th         6
        ins         2.000
        nm         ph
    
```



¹³C NMR (125 MHz, DMSO-d₆)

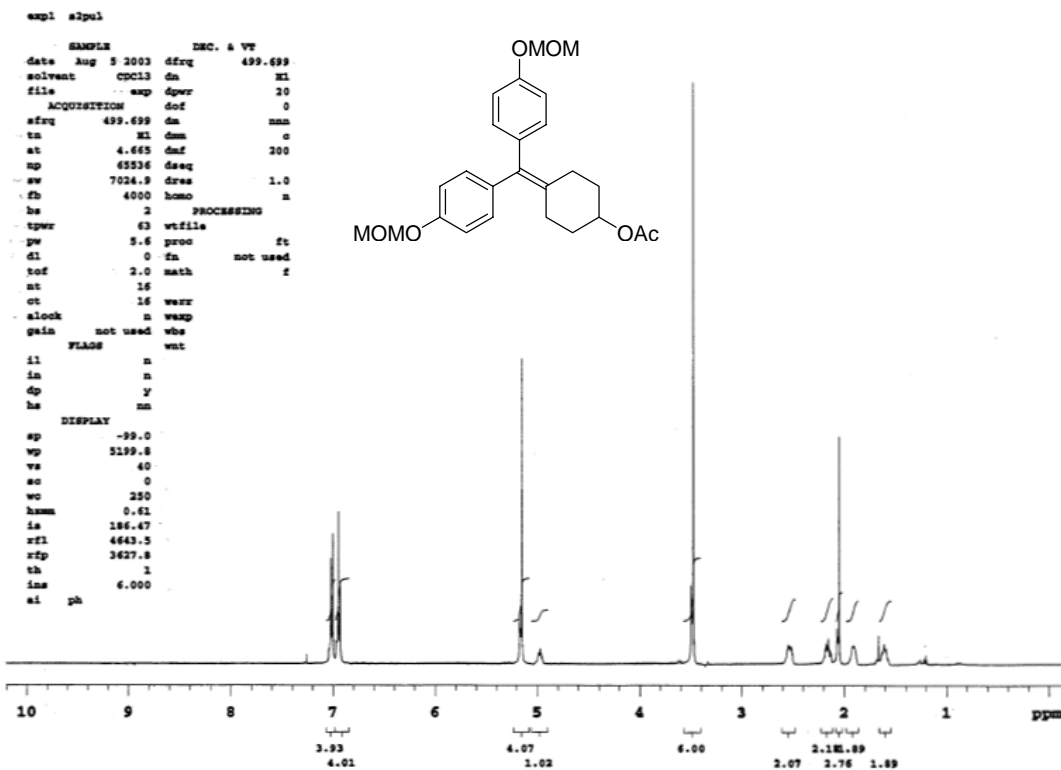
4-Acetoxy-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (16)



4-Acetoxy-1-[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (17a).

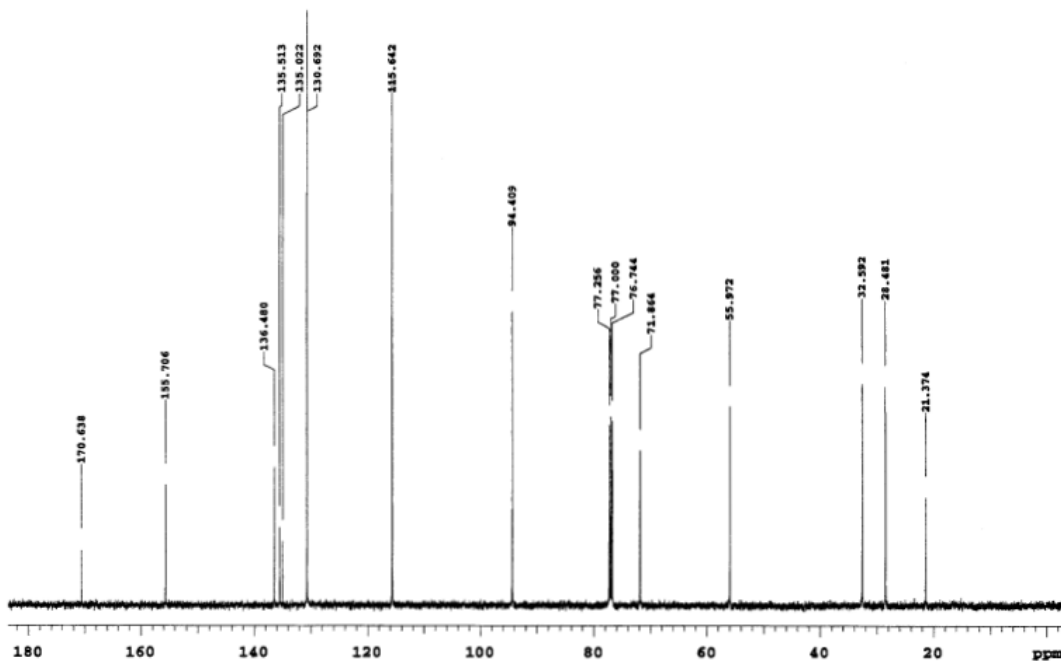
¹H NMR (500 MHz, CDCl₃)

4-Acetoxy-1-[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (17a)



¹³C NMR (125 MHz, CDCl₃)

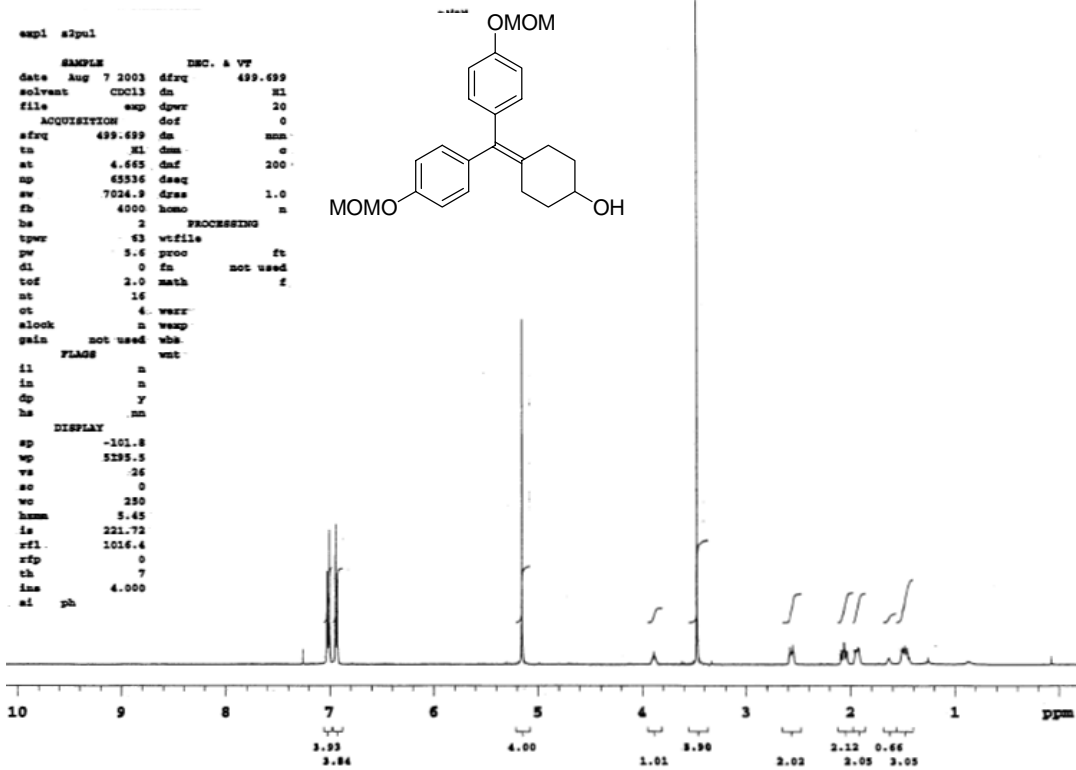
4-Acetoxy-1-[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (17a)



4-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexanol (17b).

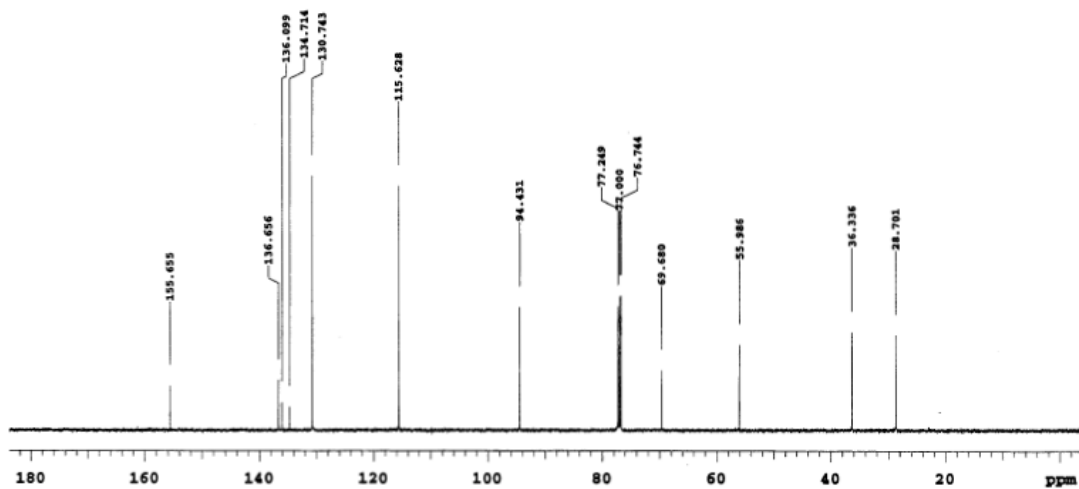
¹H NMR (500 MHz, CDCl₃)

4-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexanol (17b)



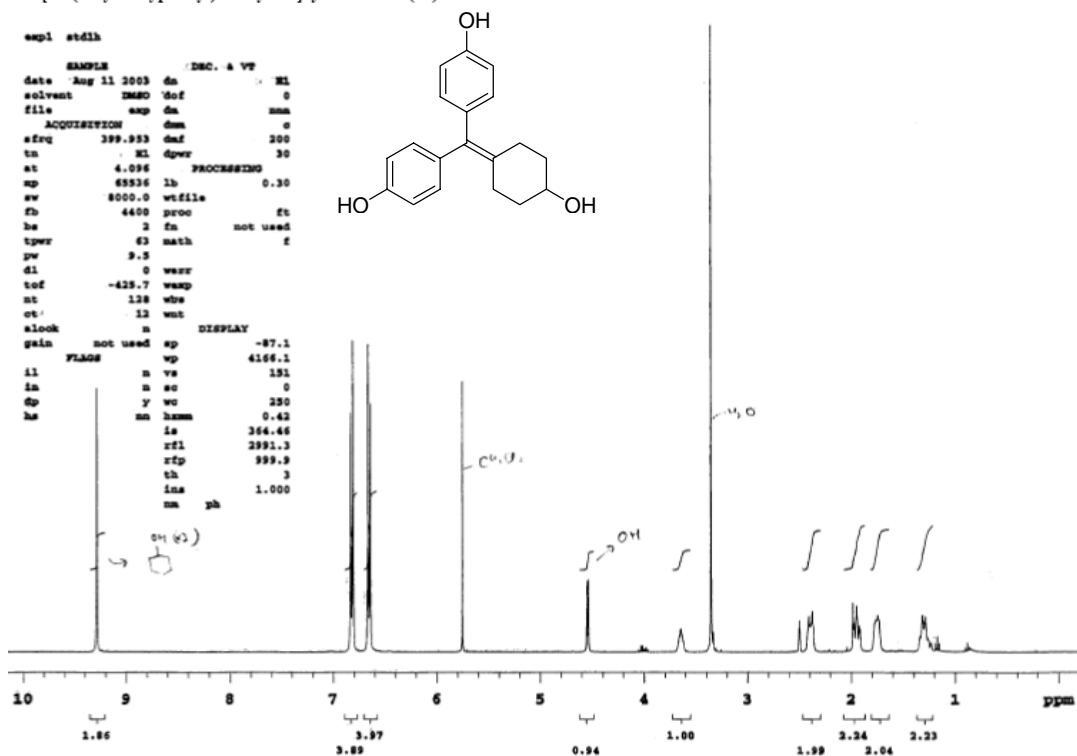
¹³C NMR (125 MHz, CDCl₃)

4-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexanol (17b)



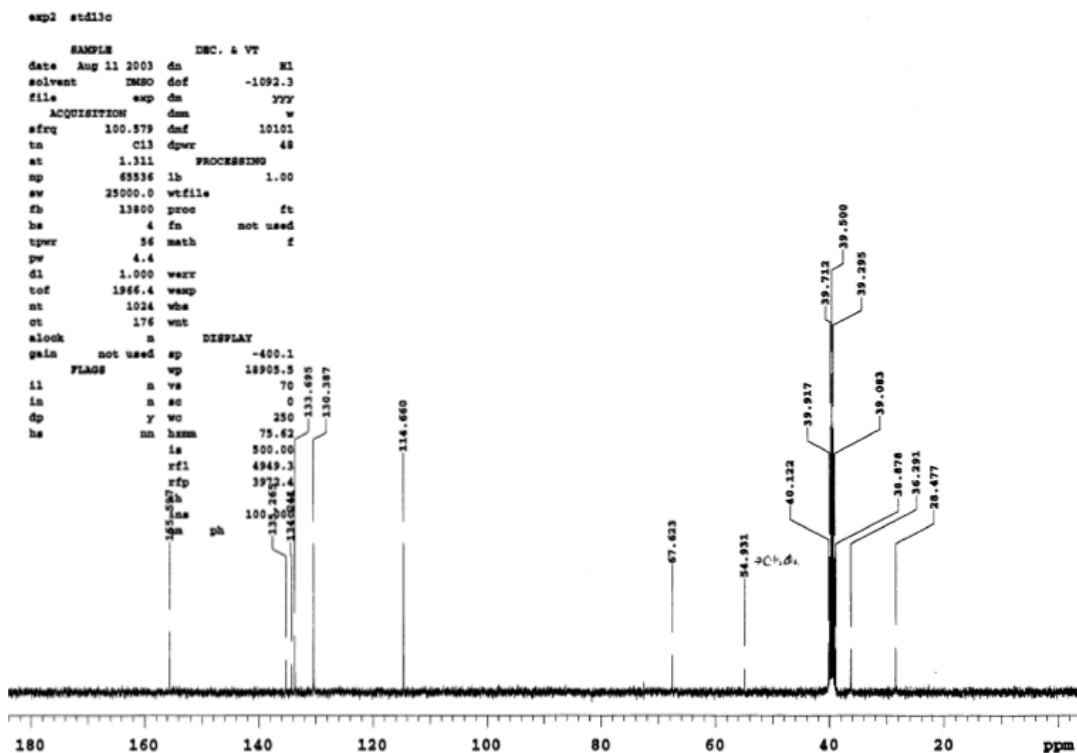
4-[Bis(4-hydroxyphenyl)methylene]cyclohexanol (18). ¹H NMR (400 MHz, DMSO-d₆)

4-[Bis(4-hydroxyphenyl)methylene]cyclohexanol (18)



¹³C NMR (100 MHz, DMSO-d₆)

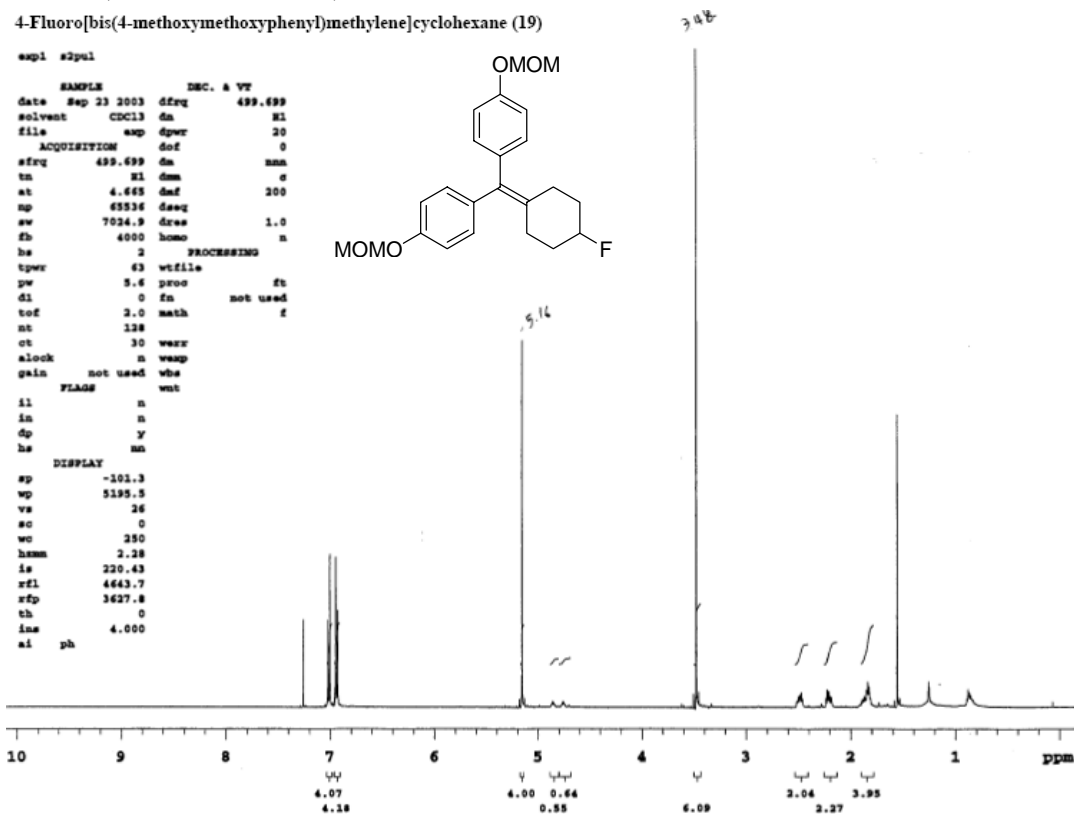
4-[Bis(4-hydroxyphenyl)methylene]cyclohexanol (18)



4-Fluoro[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (19).

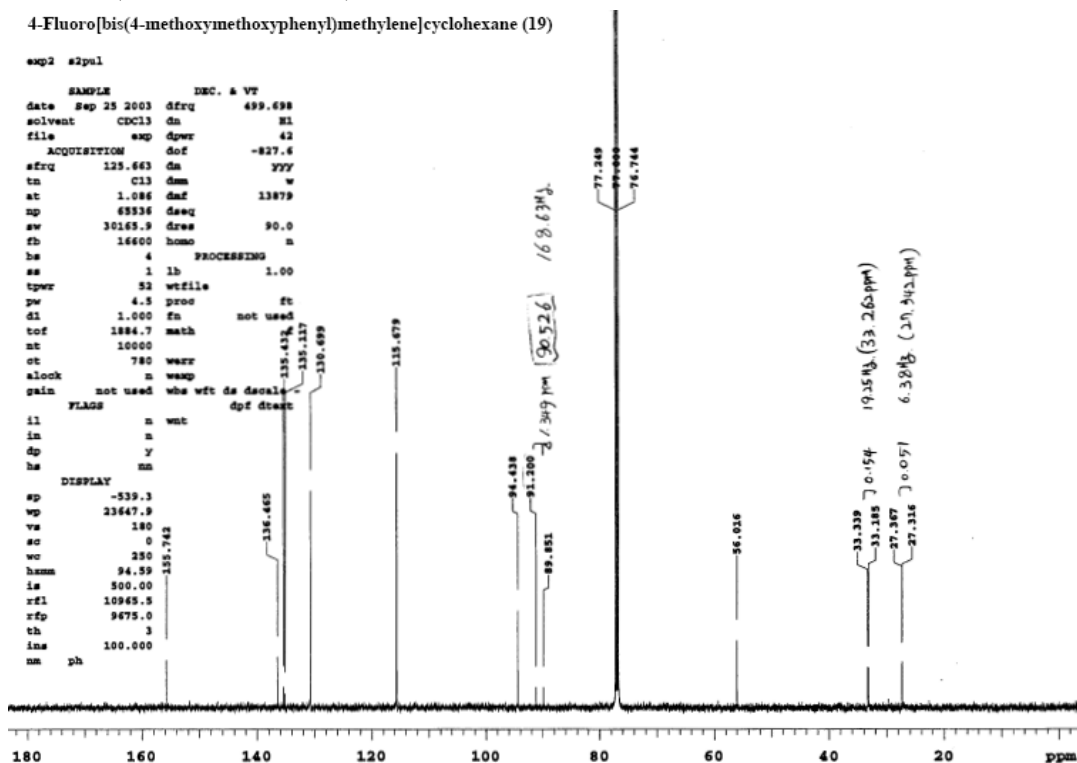
¹H NMR (500 MHz, CDCl₃)

4-Fluoro[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (19)



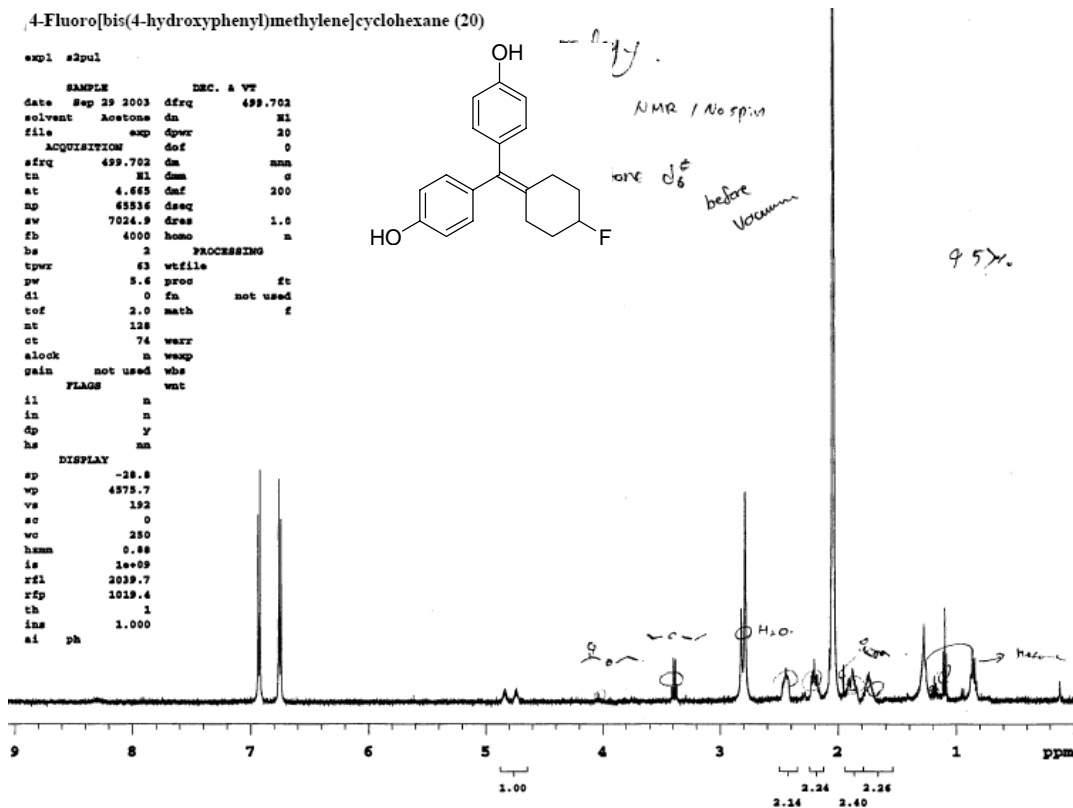
¹³C NMR (125 MHz, CDCl₃)

4-Fluoro[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (19)

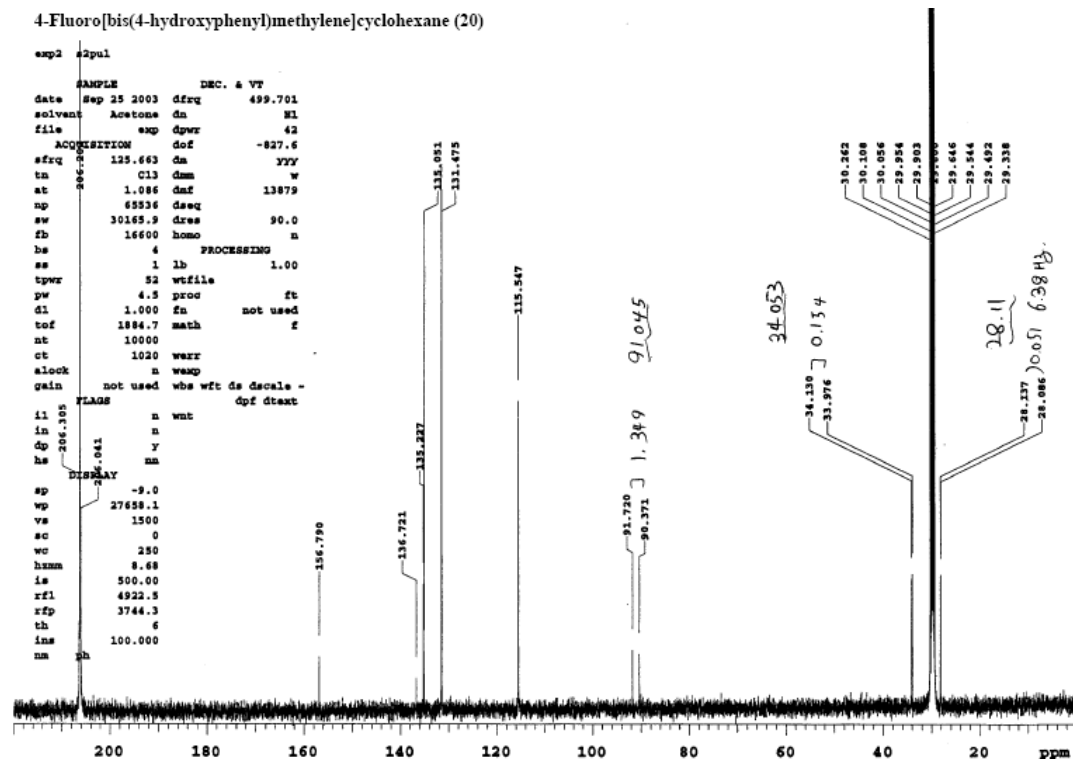


4-Fluoro[bis(4-hydroxyphenyl)methylene]cyclohexane (20).

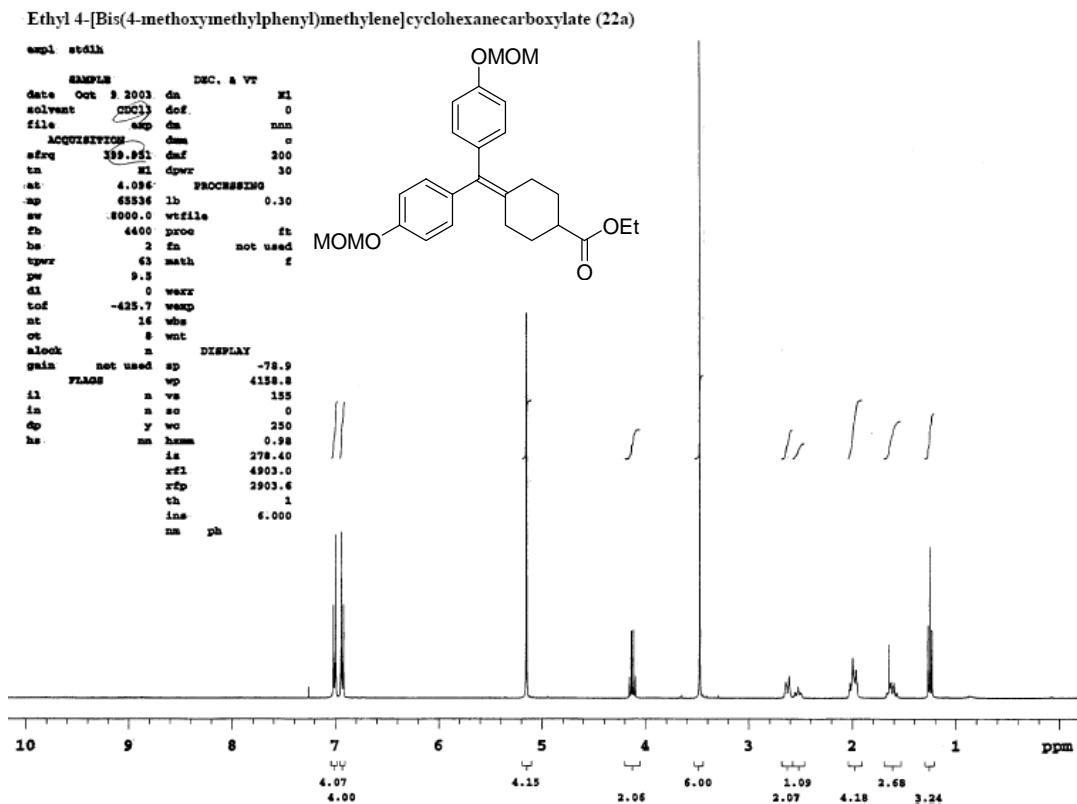
¹H NMR (500 MHz, acetone-d₆)



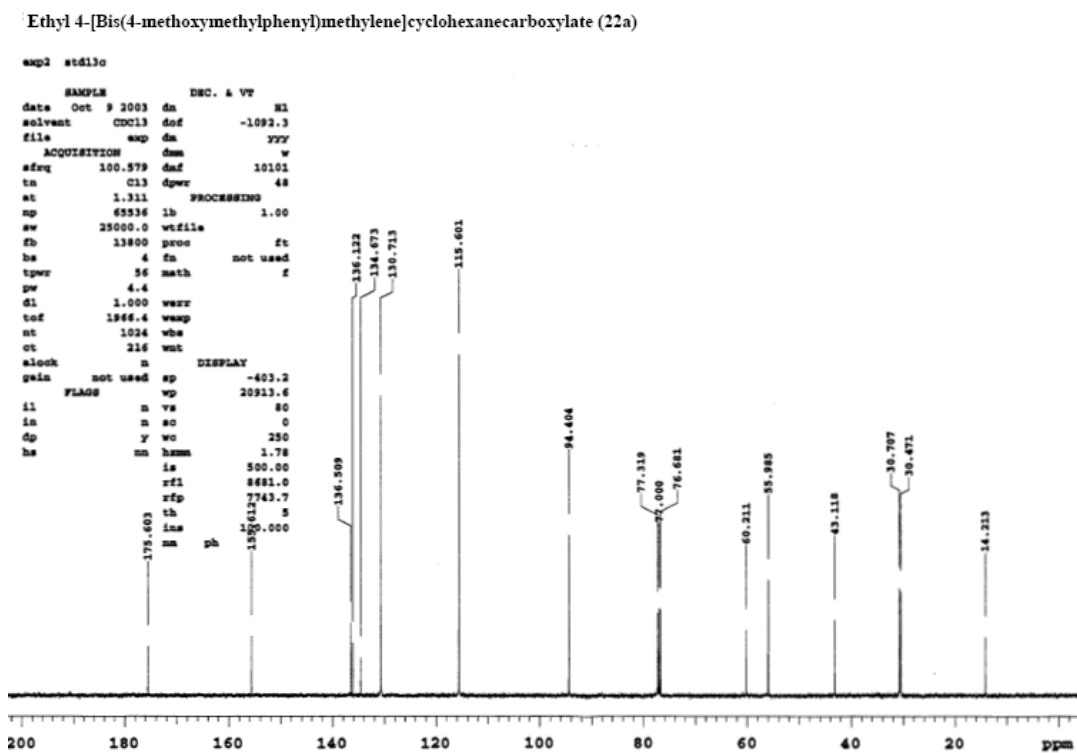
¹³C NMR (125 MHz, acetone-d₆)



Ethyl 4-[Bis(4-methoxymethylphenyl)methylene]cyclohexanecarboxylate (22a).
¹H NMR (400 MHz, CDCl₃)

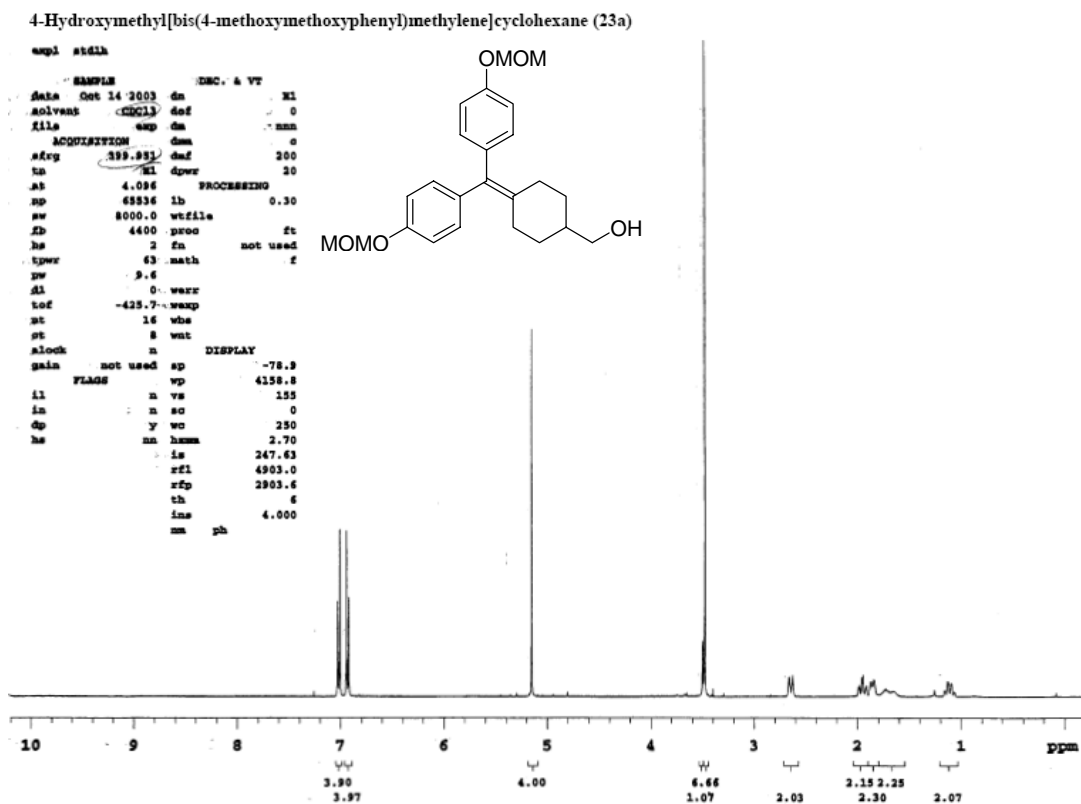


¹³C NMR (100 MHz, CDCl₃)

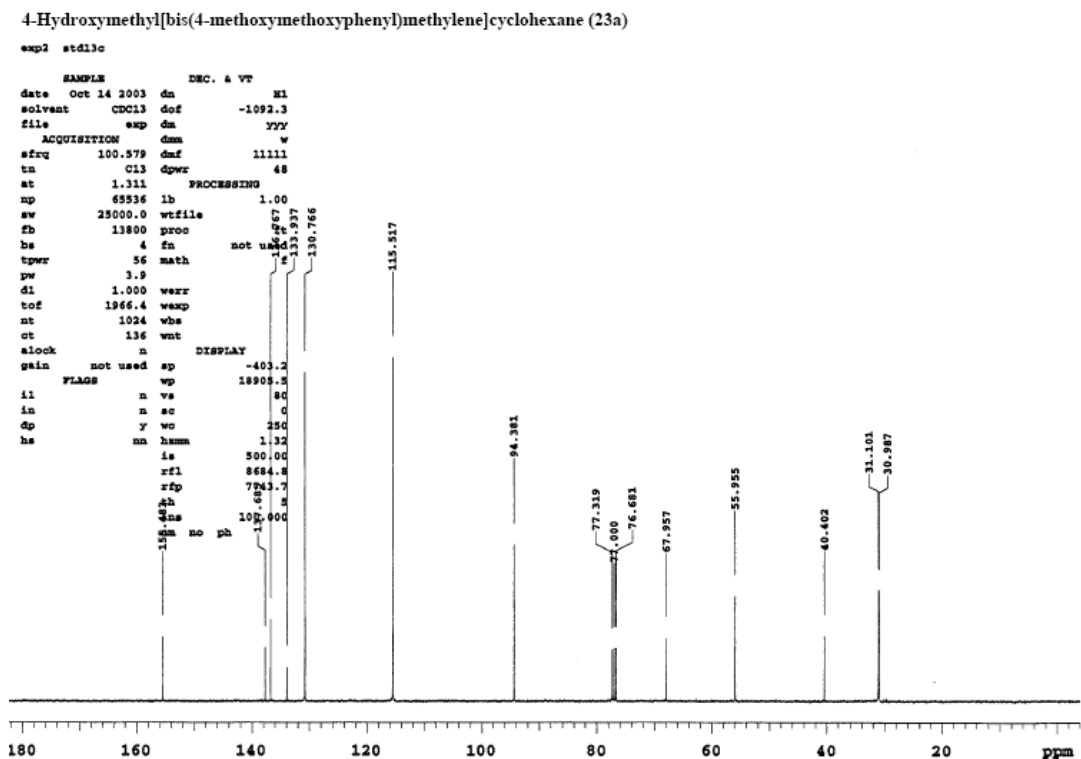


4-Hydroxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (23a).

¹H NMR (400 MHz, CDCl₃)



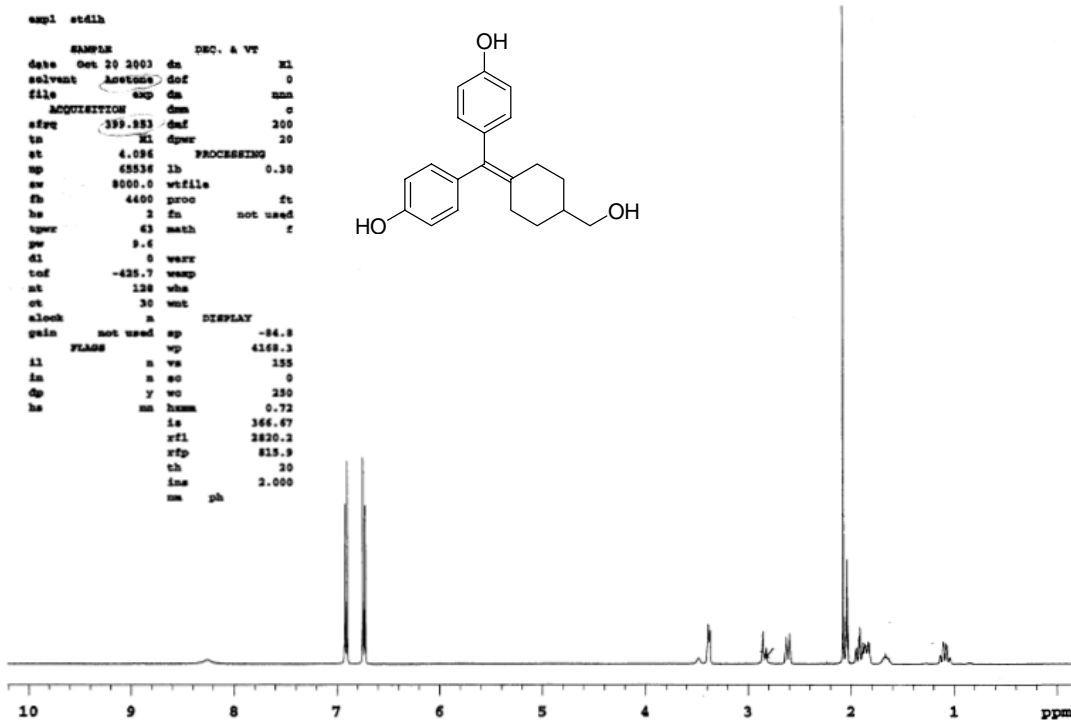
¹³C NMR (100 MHz, CDCl₃)



4-Hydroxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (24a).

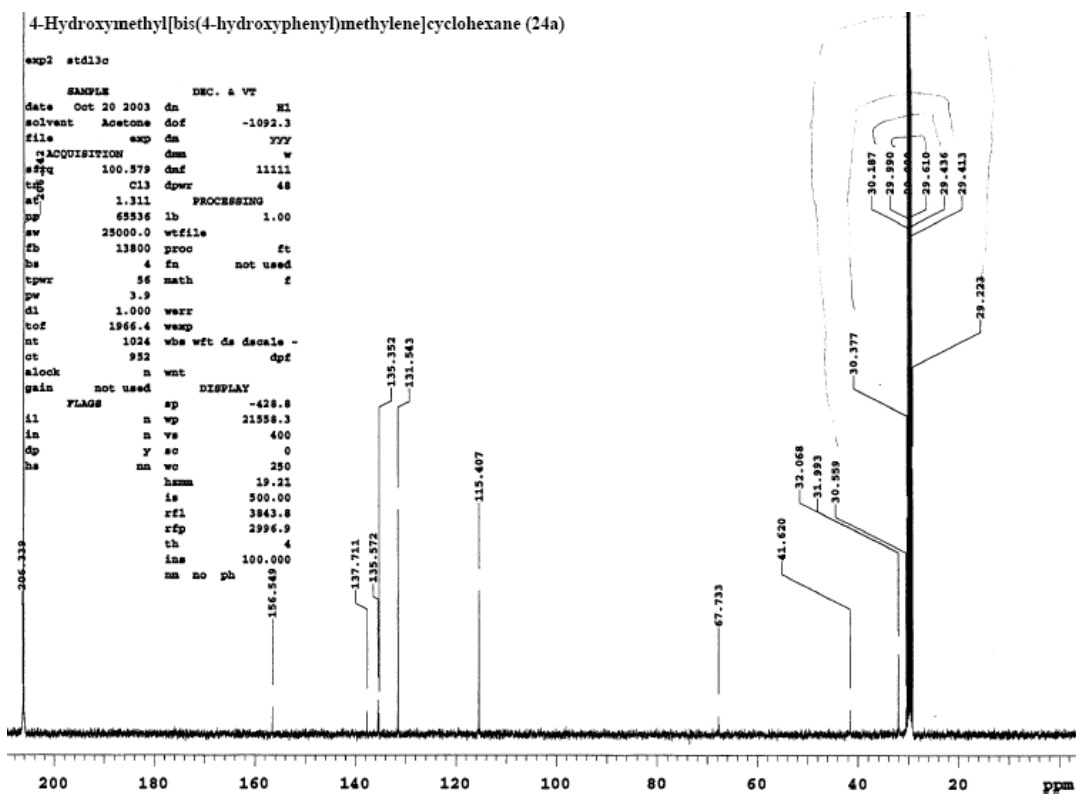
¹H NMR (400 MHz, acetone-*d*₆)

4-Hydroxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (24a)



¹³C NMR (100 MHz, acetone-*d*₆)

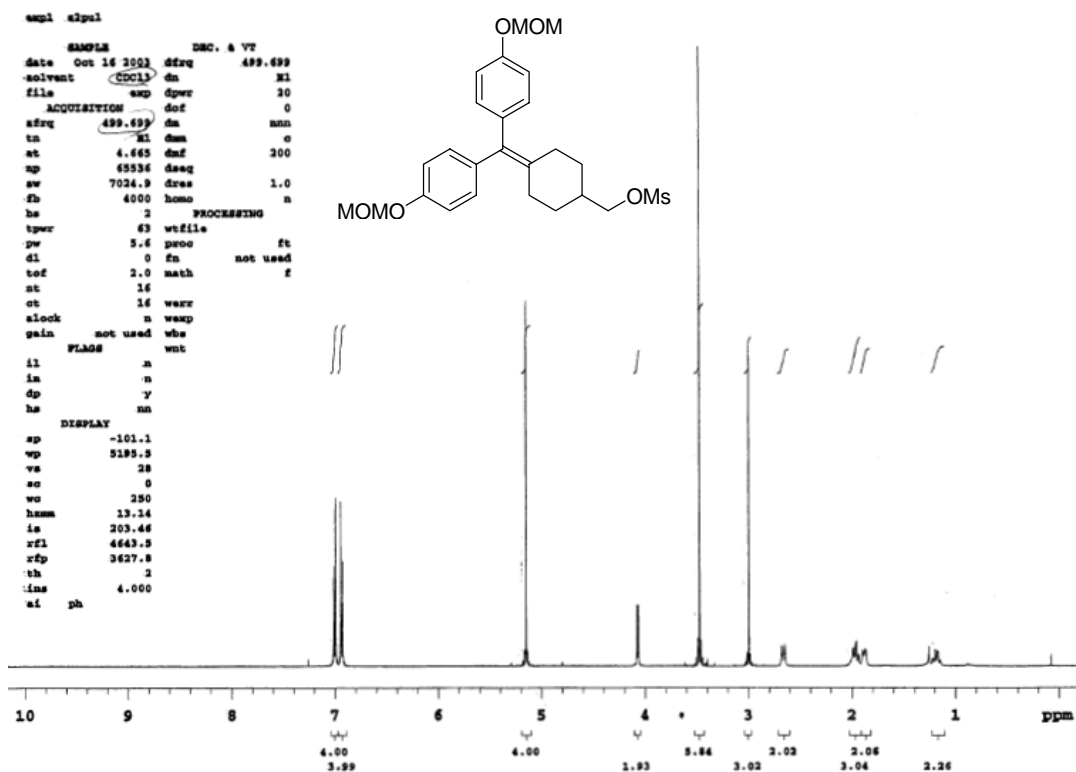
4-Hydroxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (24a)



4-Methanesulfonyloxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (25a).

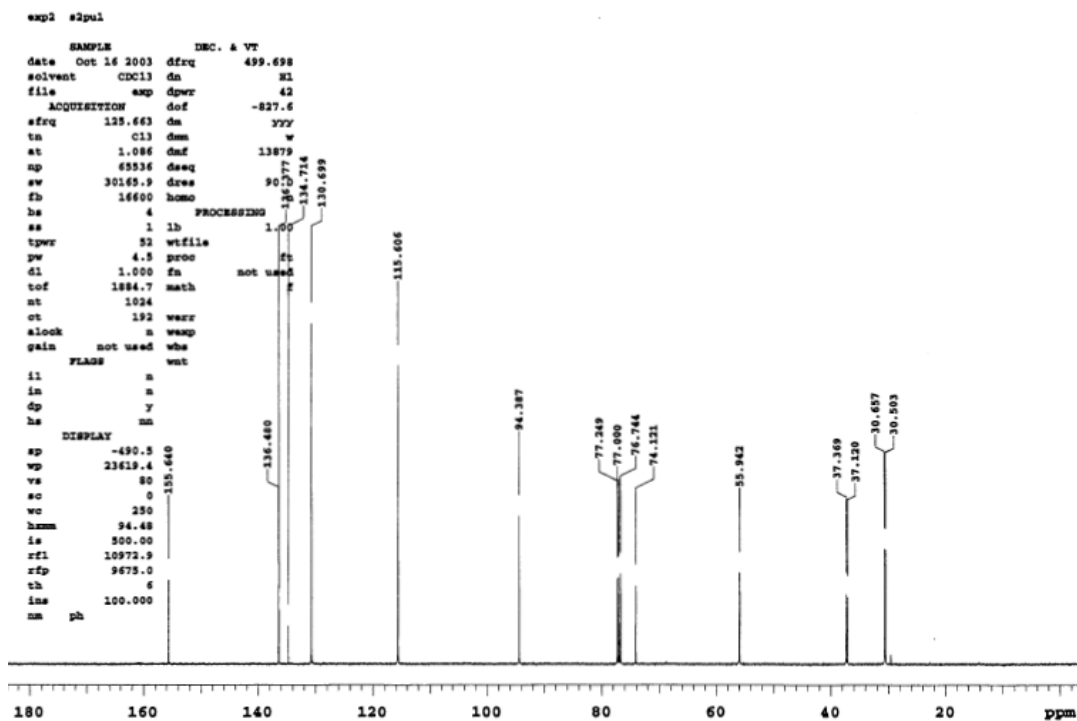
¹H NMR (500 MHz, CDCl₃)

4-Methanesulfonyloxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (25a)



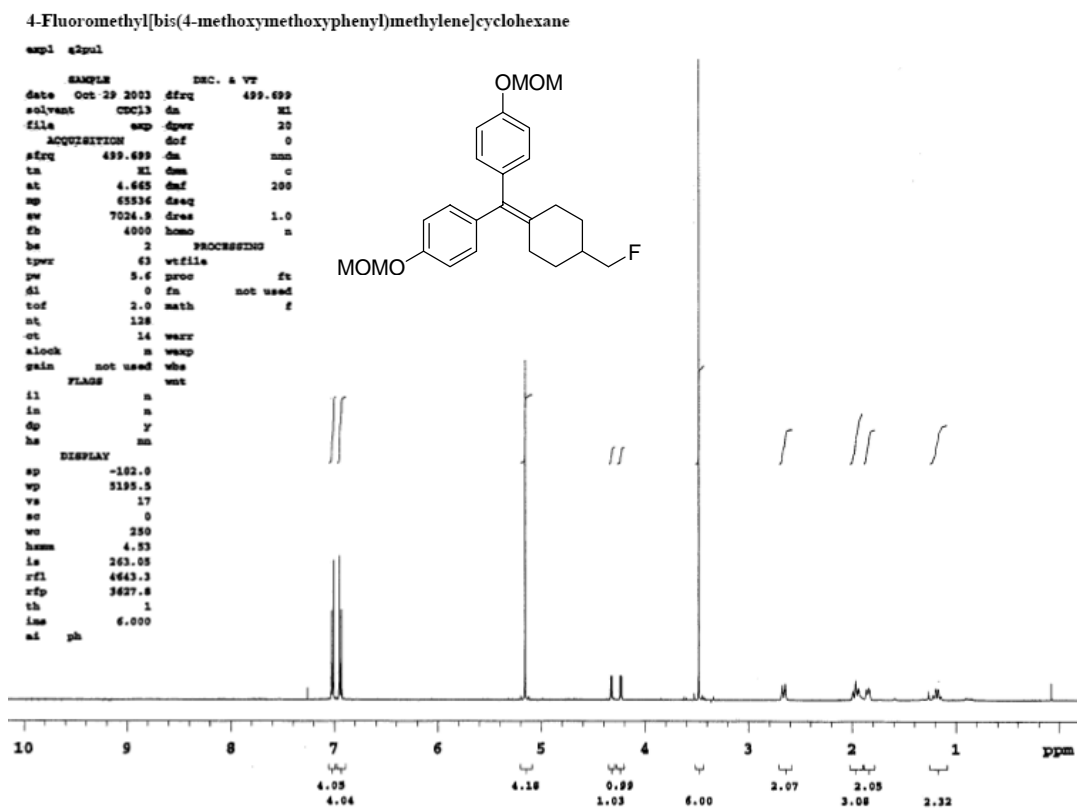
¹³C NMR (125 MHz, CDCl₃)

4-Methanesulfonyloxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (25a)

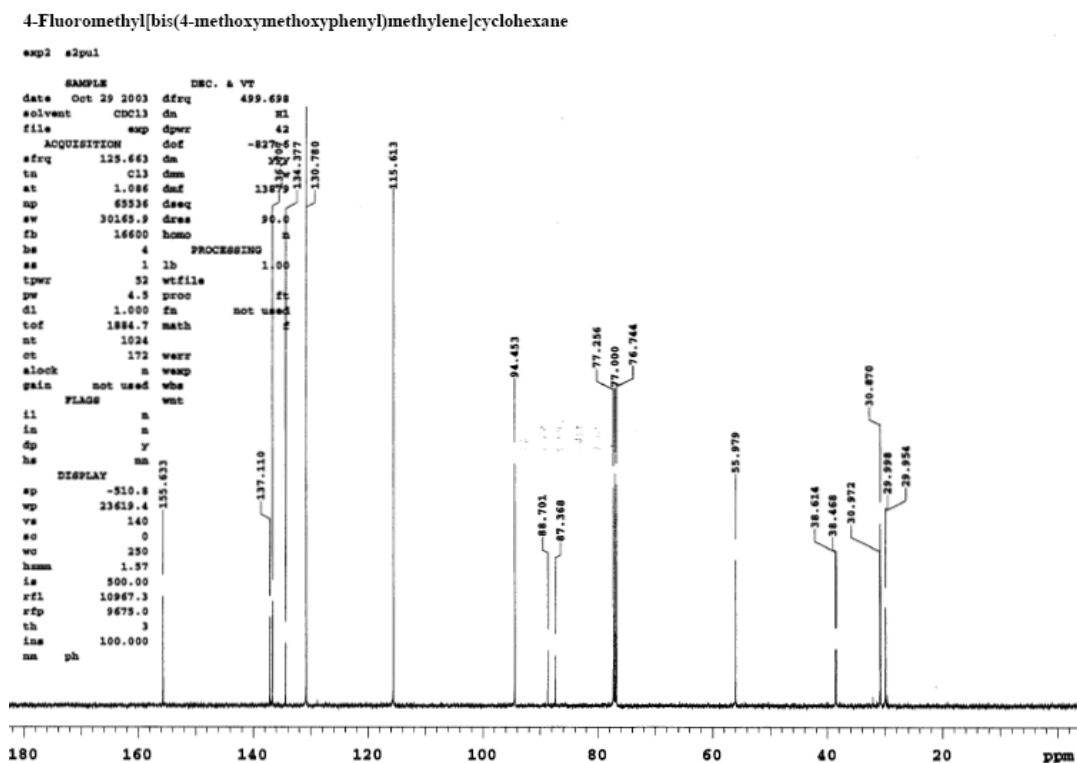


4-Fluoromethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

¹H NMR (500 MHz, CDCl₃)



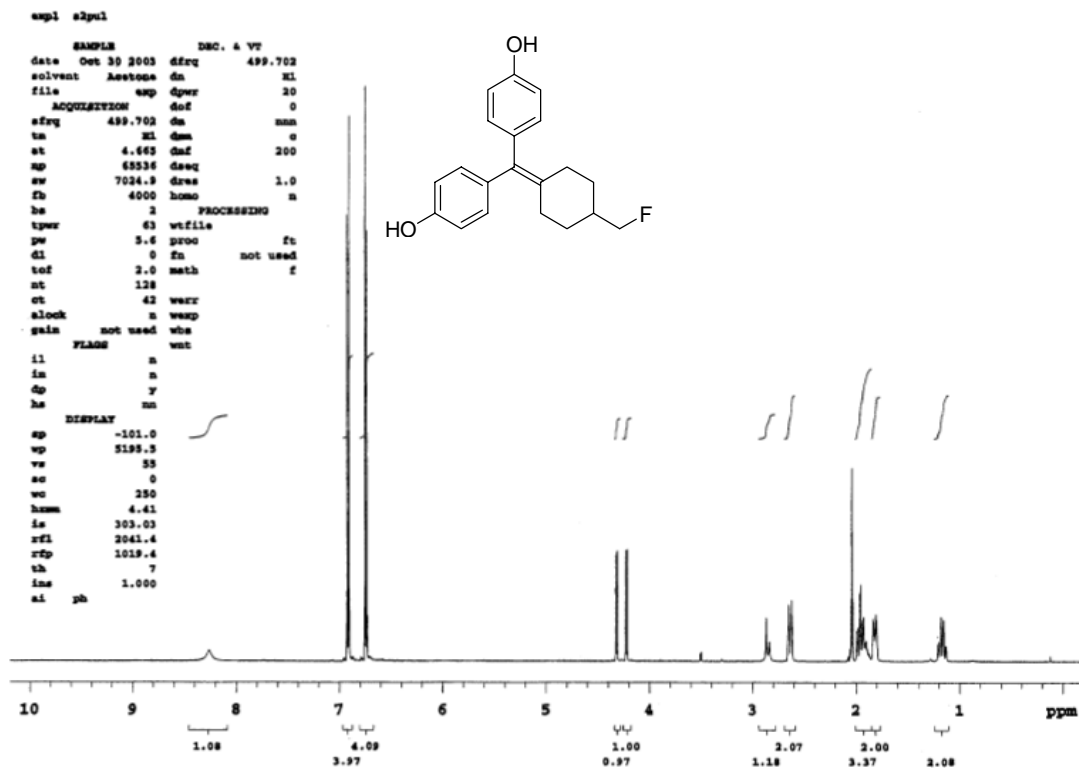
¹³C NMR (125 MHz, CDCl₃)



4-Fluoromethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (26a).

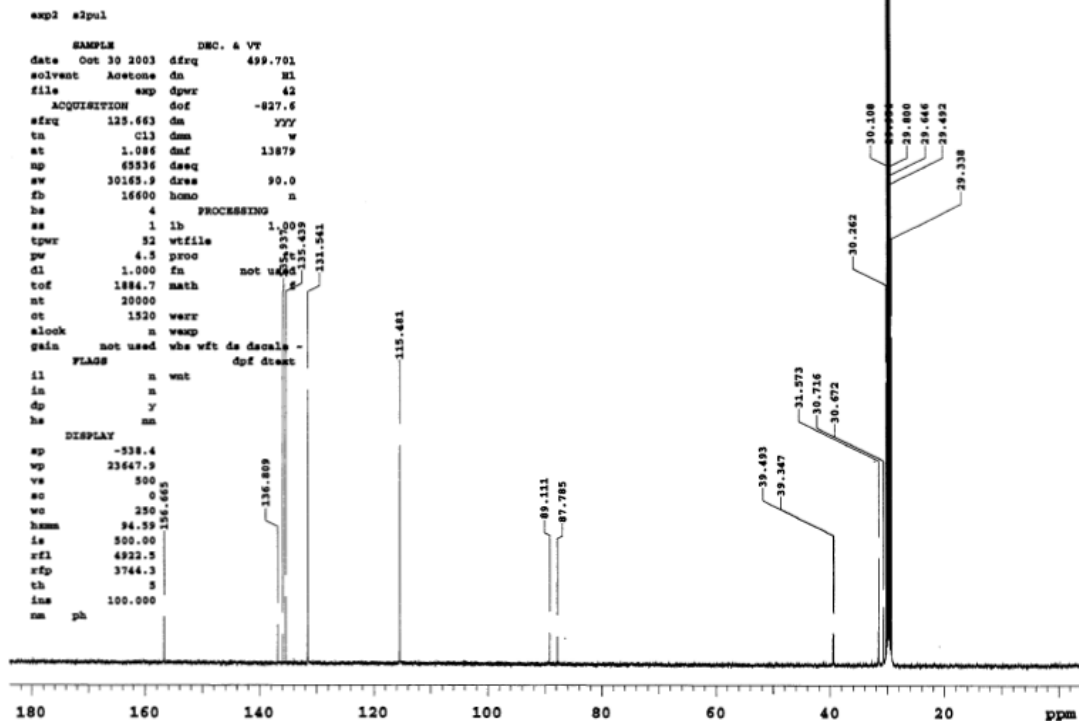
¹H NMR (500 MHz, acetone-d₆)

4-Fluoromethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (26a)



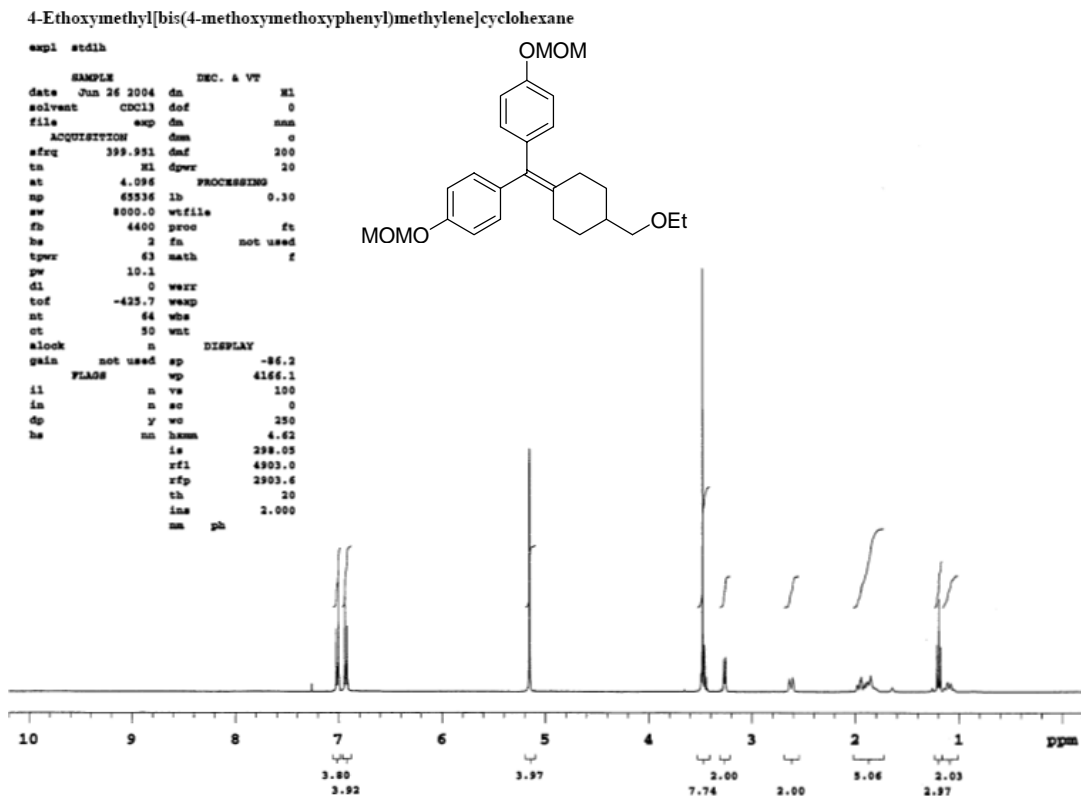
¹³C NMR (125 MHz, acetone-d₆)

4-Fluoromethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (26a)

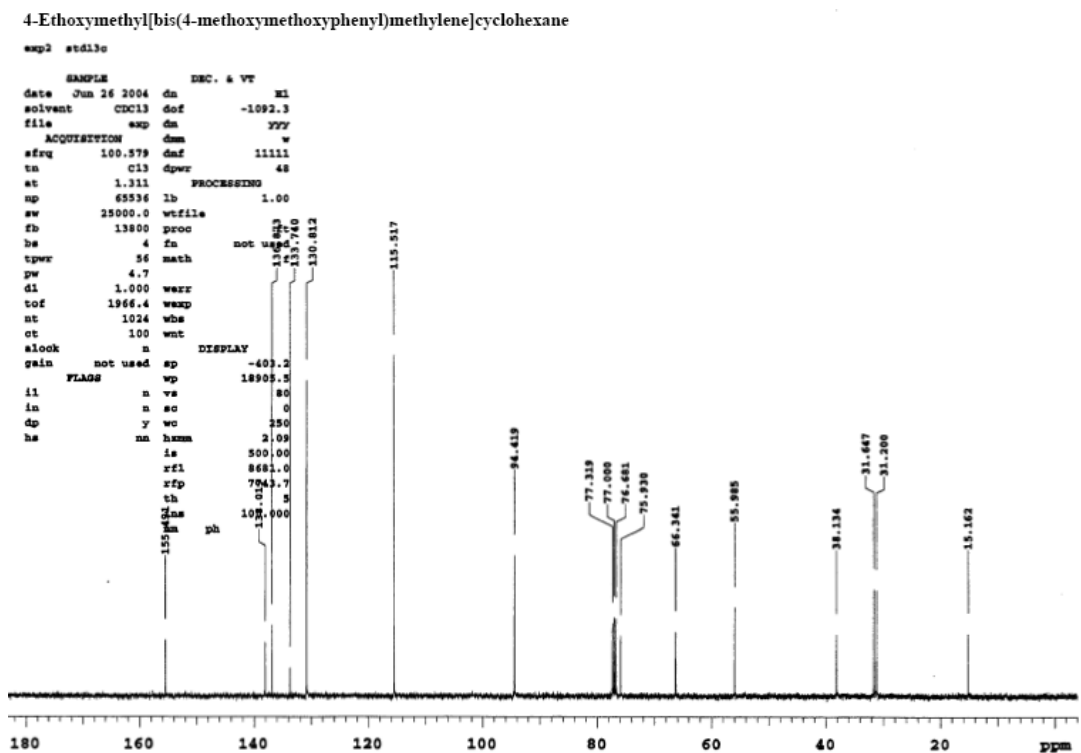


4-Ethoxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

¹H NMR (400 MHz, CDCl₃)

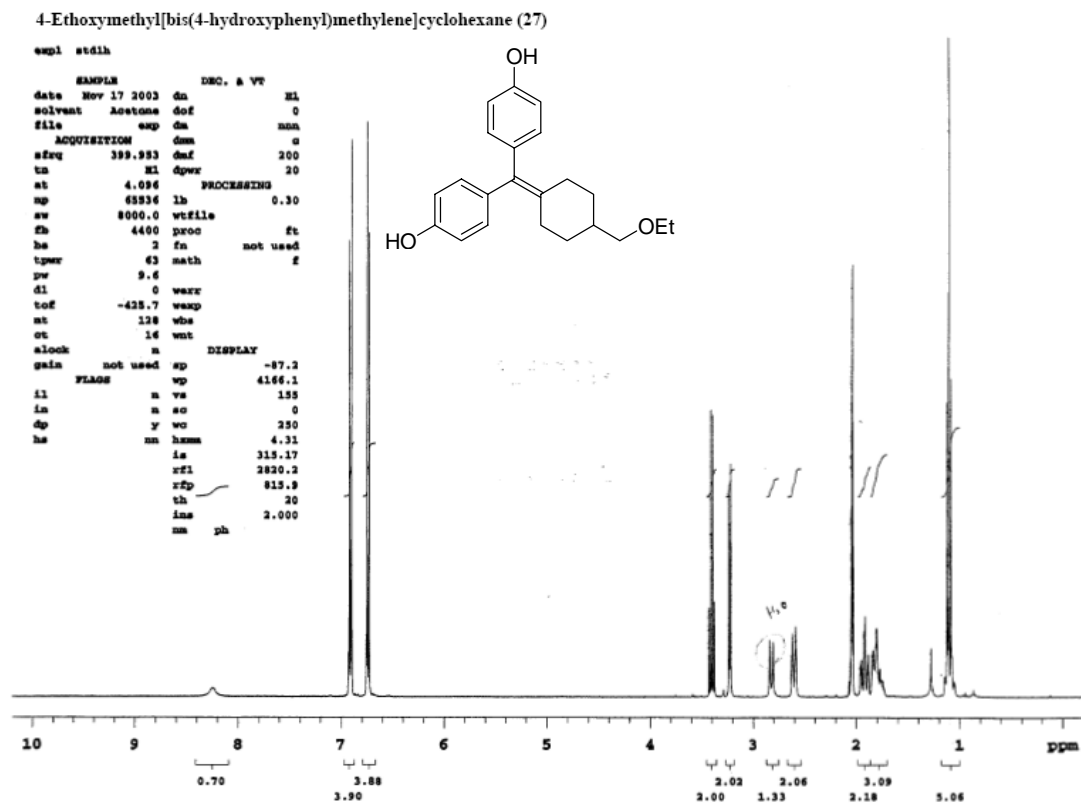


¹³C NMR (100 MHz, CDCl₃)

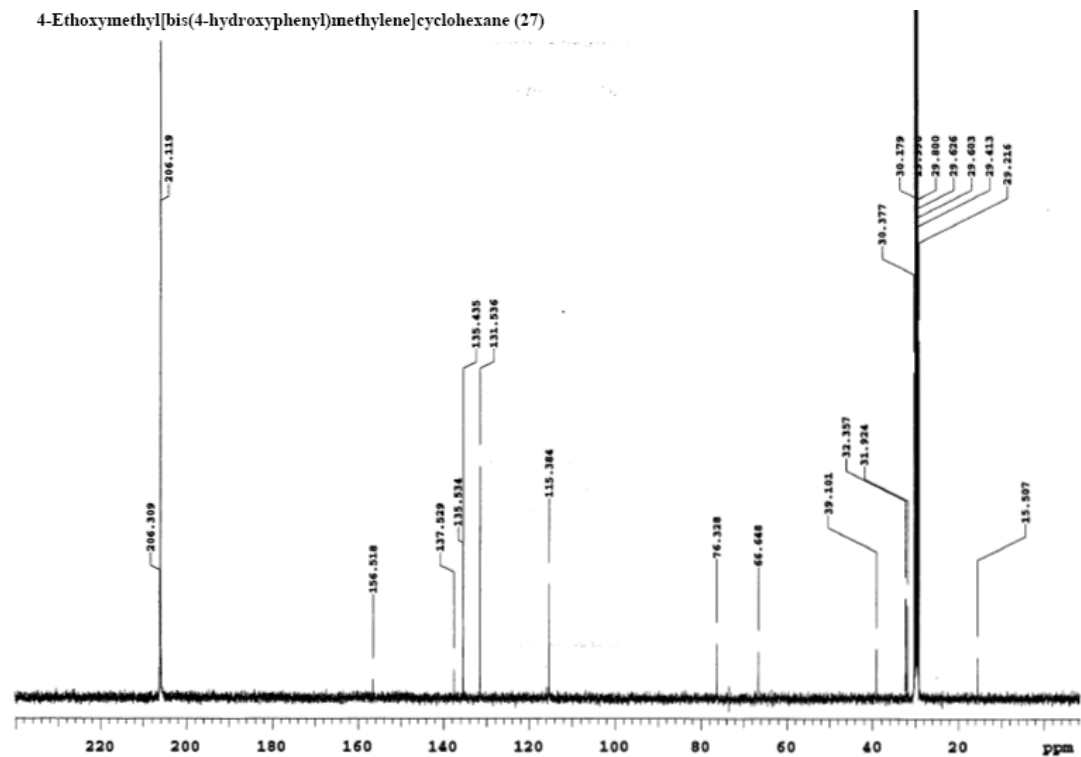


4-Ethoxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (27).

¹H NMR (400 MHz, acetone-*d*₆)



¹³C NMR (100 MHz, acetone-*d*₆)



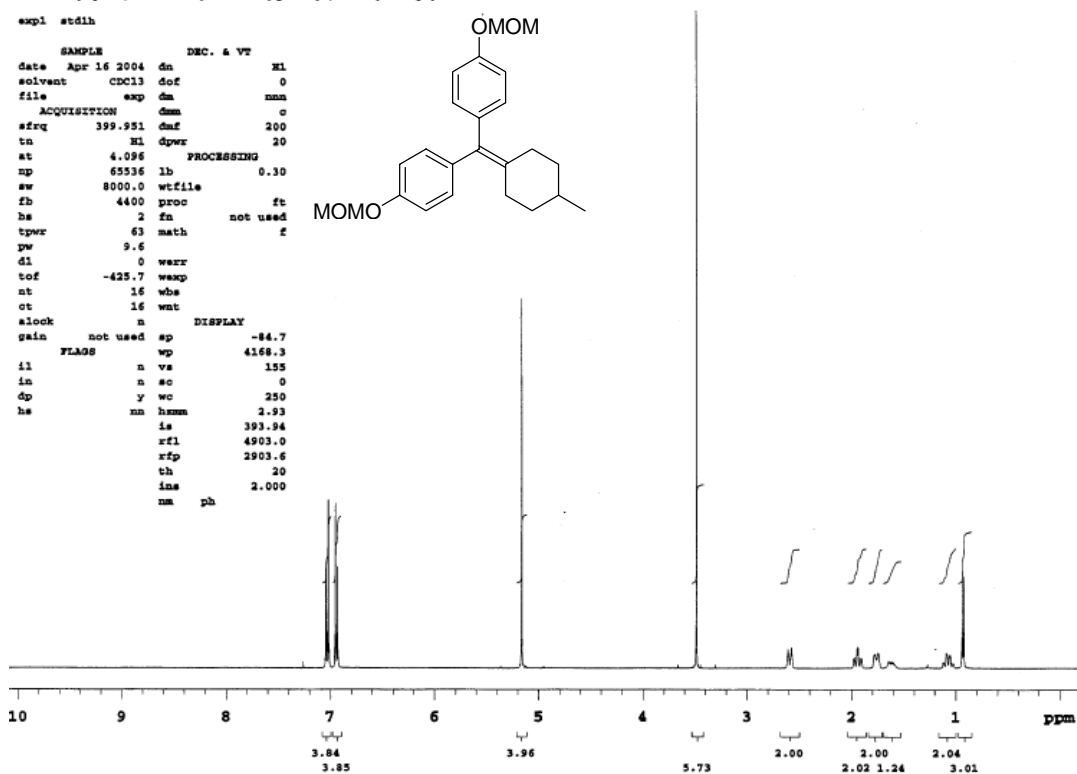
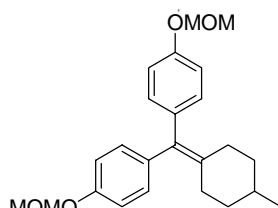
4-Methyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

¹H NMR (400 MHz, CDCl₃)

4-Methyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane

```

expl std1h
SAMPLE
date Apr 16 2004 dn DEC. & VT H1
solvent CDCl3 dof 0
file exp dn mmn
ACQUISITION dnm c
sfrq 399.951 dmf 200
tn H1 dpwr 20
at 4.096 PROCESSING
np 65536 lb 0.30
sw 8000.0 wtfile
fb 4400 proc ft
bs 2 fn not used
tpwr 63 math f
pw 9.6
dl 0 warr
tof -425.7 wexp
nt 16 wba
ot 16 wat
alock n
gain not used sp DISPLAY
        sp -84.7
        sp 4168.3
        sp 155
        sp 0
        sp 250
        sp 2.93
        sp 393.94
        sp 4903.0
        sp 2903.6
        sp 20
        sp 2.000
        sp ph
    
```

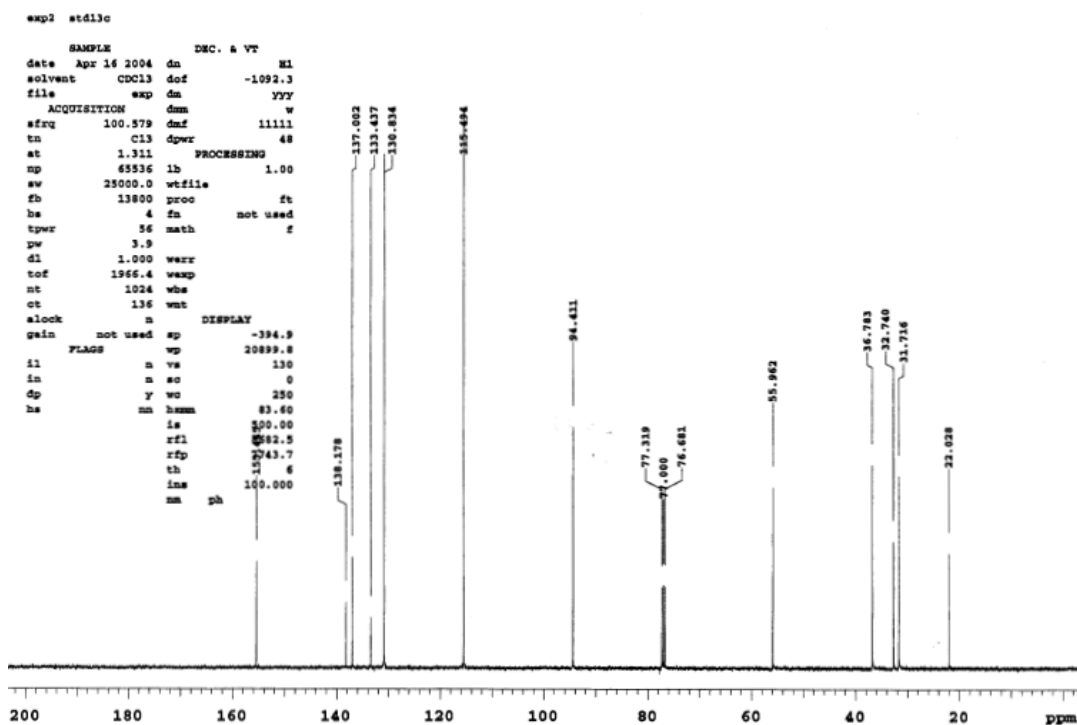


¹³C NMR (100 MHz, CDCl₃)

4-Methyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane

```

expl std13c
SAMPLE
date Apr 16 2004 dn DEC. & VT H1
solvent CDCl3 dof -1092.3
file exp dn VVY
ACQUISITION dnm w
sfrq 100.579 dmf 11111
tn C13 dpwr 48
at 1.311 PROCESSING
np 65536 lb 1.00
sw 25000.0 wtfile
fb 13800 proc ft
bs 4 fn not used
tpwr 56 math f
pw 3.9
dl 1.000 warr
tof 1966.4 wexp
nt 1024 wba
ot 136 wat
alock n
gain not used sp DISPLAY
        sp -394.9
        sp 20899.8
        sp 130
        sp 0
        sp 250
        sp 83.60
        sp 300.00
        sp 582.5
        sp 2743.7
        sp 11111
        sp 100.000
        sp ph
    
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4-Methyl[bis(4-hydroxyphenyl)methylene]cyclohexane (29a).

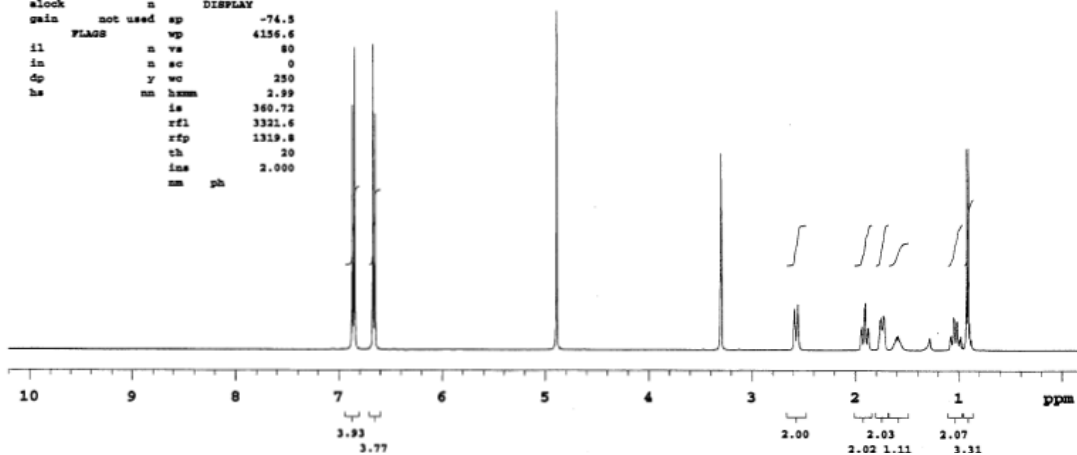
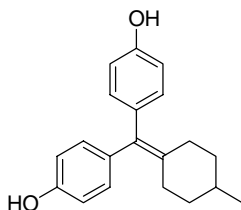
¹H NMR (400 MHz, methanol-d₄)

4-Methyl[bis(4-hydroxyphenyl)methylene]cyclohexane (29a)

exp1 std1h

```

SAMPLE          DEC. & VT
date Apr 19 2004 dn          H1
solvent CD3OD dof          0
file           exp dn          nmh
ACQUISITION    dnm          c
sfreq 399.952 dmf          200
tn      H1 dpwr          20
at      4.096 PROCESSING
np      65536 lb          0.30
sw      8000.0 wfile
fb      4400 proc          ft
bs      2 fn          not used
tpwr    63 math          f
pw      9.6
dl      0 werr
tof     -425.7 wexp
nt      15 wbs
ct      16 wnt
alock   n
gain   not used sp          -74.5
        FLAGS          wp          4156.6
il      n vs          80
in      n sc          0
dp      y wo          250
hs      nn hnm          2.99
        is          360.72
        rfl          3321.6
        rfp          1319.8
        th          20
        lns          2.000
        nm          ph
    
```



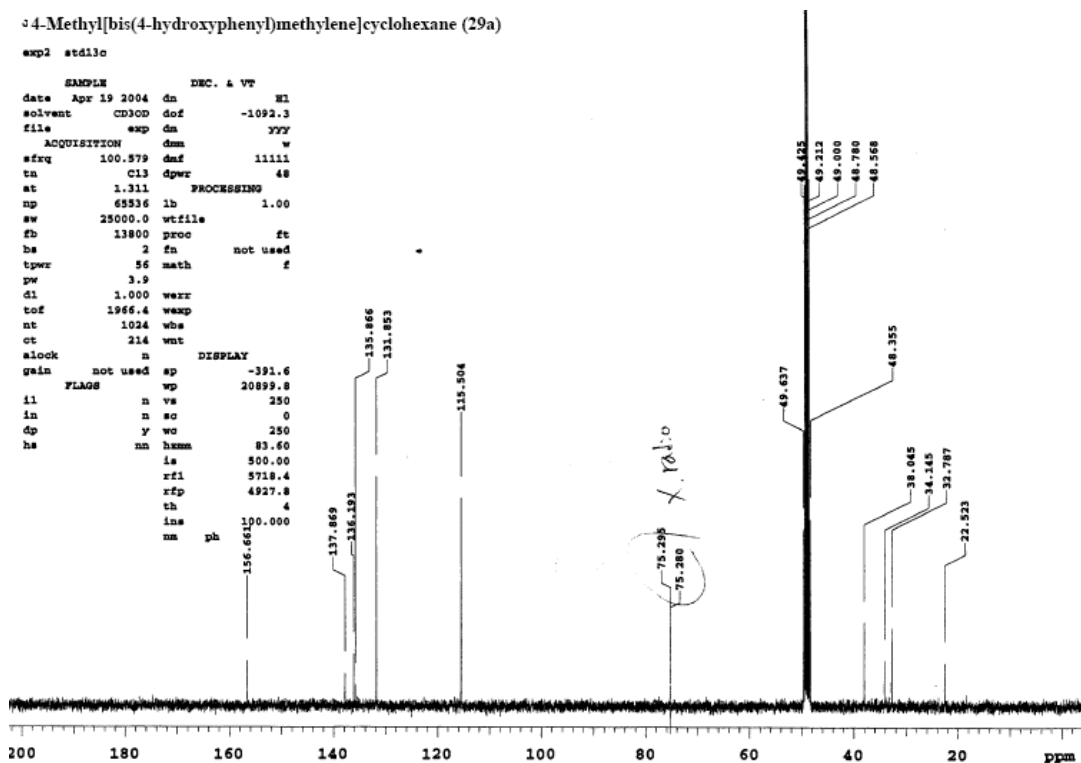
¹³C NMR (100 MHz, methanol-d₄)

4-Methyl[bis(4-hydroxyphenyl)methylene]cyclohexane (29a)

exp2 std13c

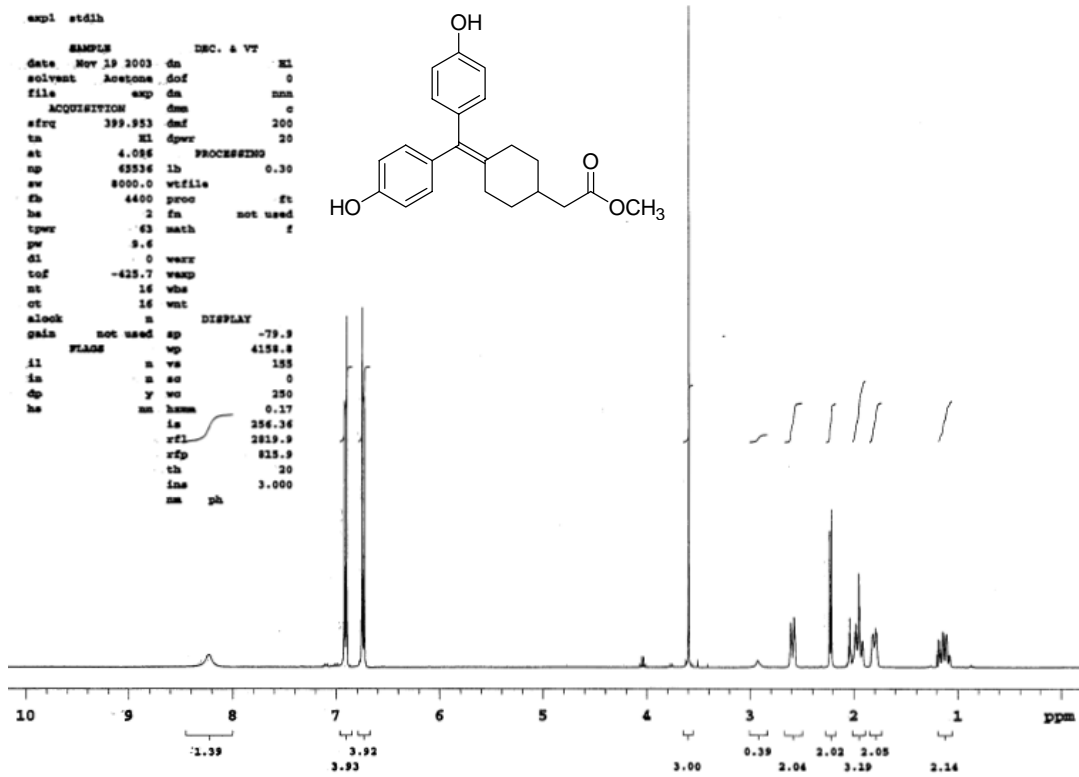
```

SAMPLE          DEC. & VT
date Apr 19 2004 dn          H1
solvent CD3OD dof          -1092.3
file           exp dn          YYY
ACQUISITION    dnm          w
sfreq 100.579 dmf          11111
tn      C13 dpwr          48
at      1.311 PROCESSING
np      65536 lb          1.00
sw      25000.0 wfile
fb      13800 proc          ft
bs      2 fn          not used
tpwr    56 math          f
pw      3.9
dl      1.000 werr
tof     1966.4 wexp
nt      1024 wbs
ct      214 wnt
alock   n
gain   not used sp          -391.6
        FLAGS          wp          20899.8
il      n vs          250
in      n sc          0
dp      y wo          250
hs      nn hnm          83.60
        is          500.00
        rfl          5718.4
        rfp          4927.8
        th          4
        lns          100.000
        nm          ph
    
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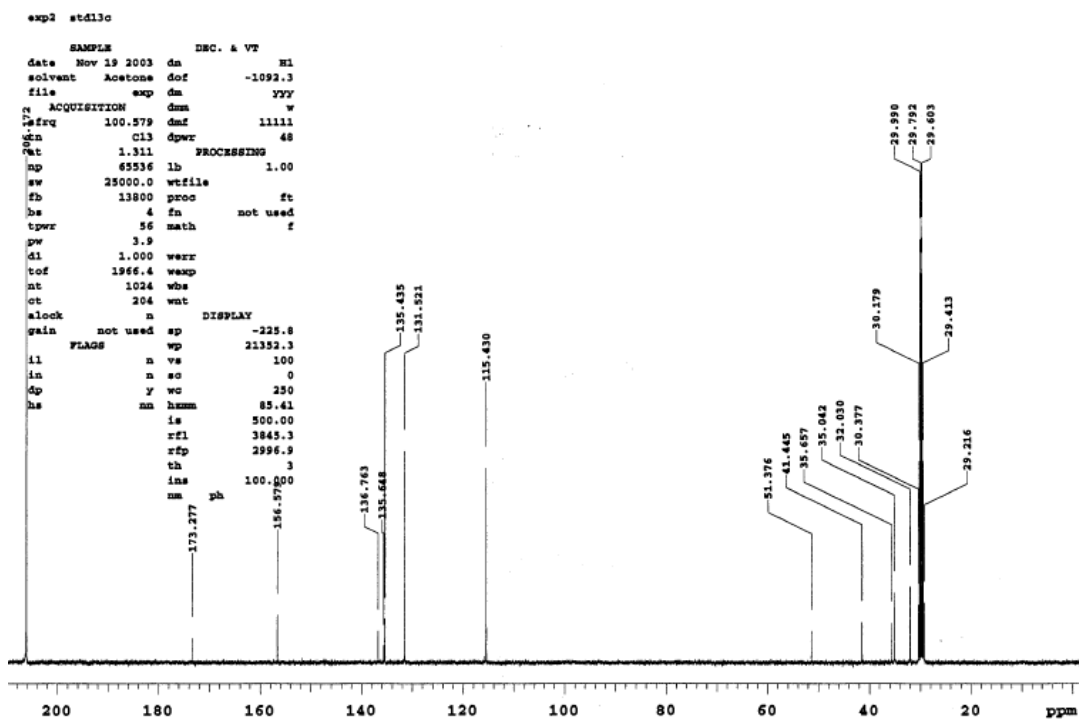
Methyl {4-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}acetate (21b).

¹H NMR (400 MHz, acetone-d₆)
Methyl {4-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}acetate (21b)



¹³C NMR (100 MHz, acetone-d₆)

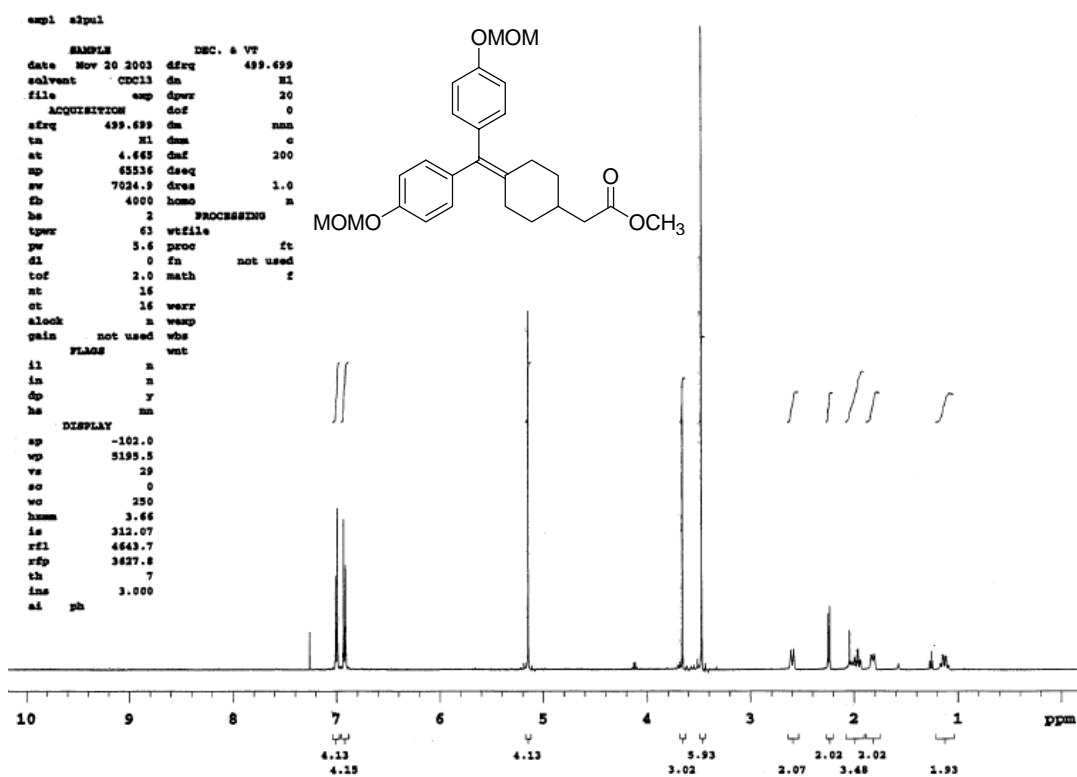
Methyl {4-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}acetate (21b)



Methyl {4-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexyl}acetate (22b).

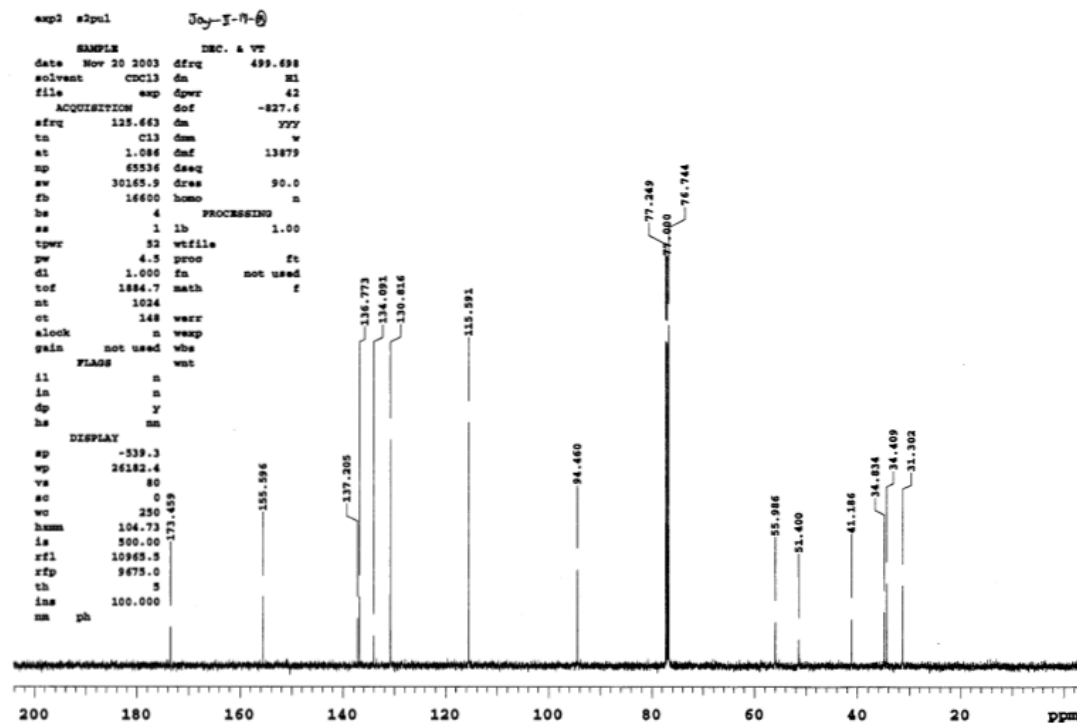
¹H NMR (500 MHz, CDCl₃)

Methyl {4-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexyl}acetate (22b)



¹³C NMR (125 MHz, CDCl₃)

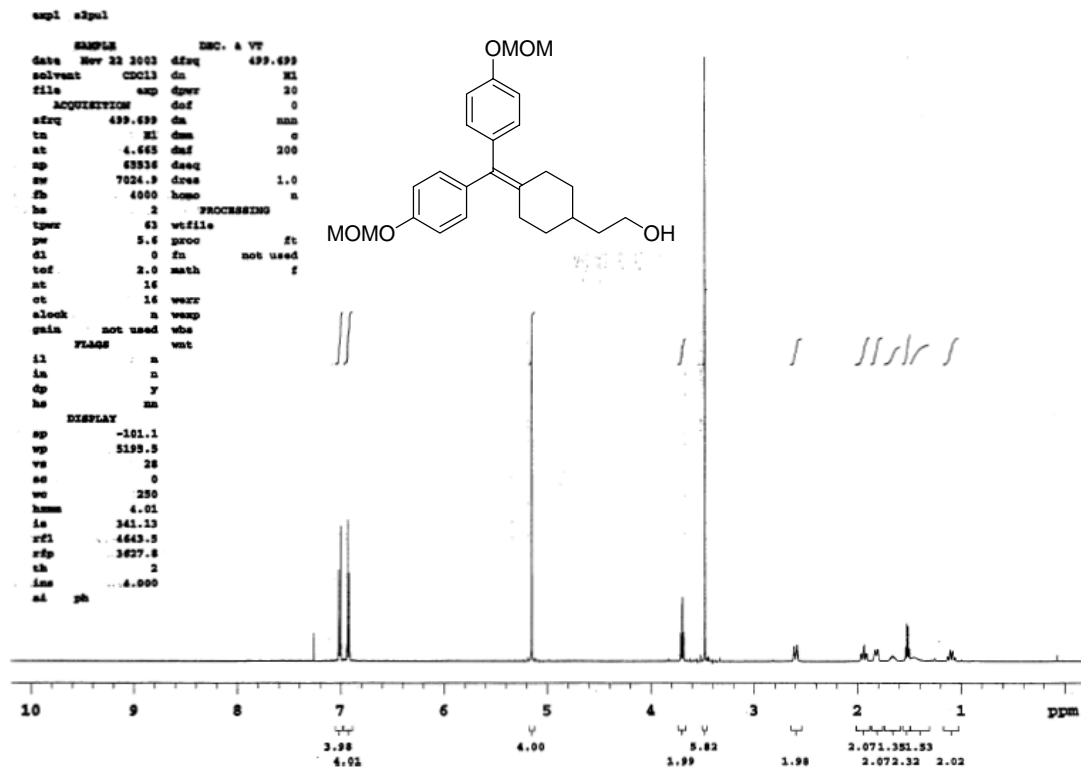
Methyl {4-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexyl}acetate (22b)



4-(2-Hydroxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (23b).

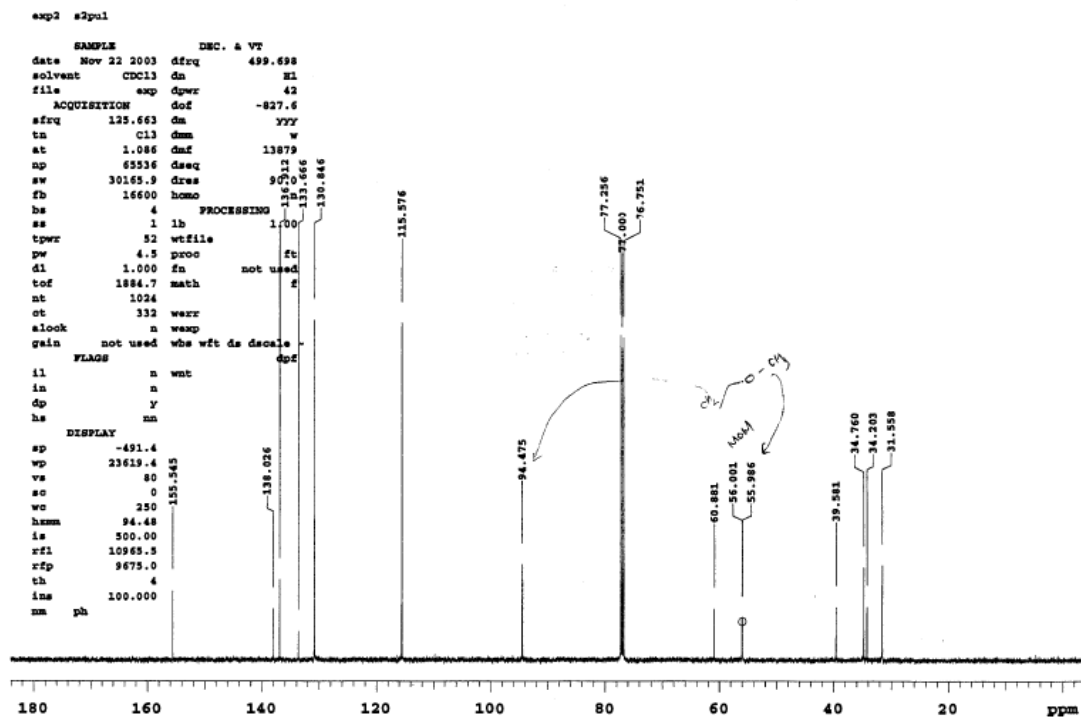
¹H NMR (500 MHz, CDCl₃)

4-(2-Hydroxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (23b)



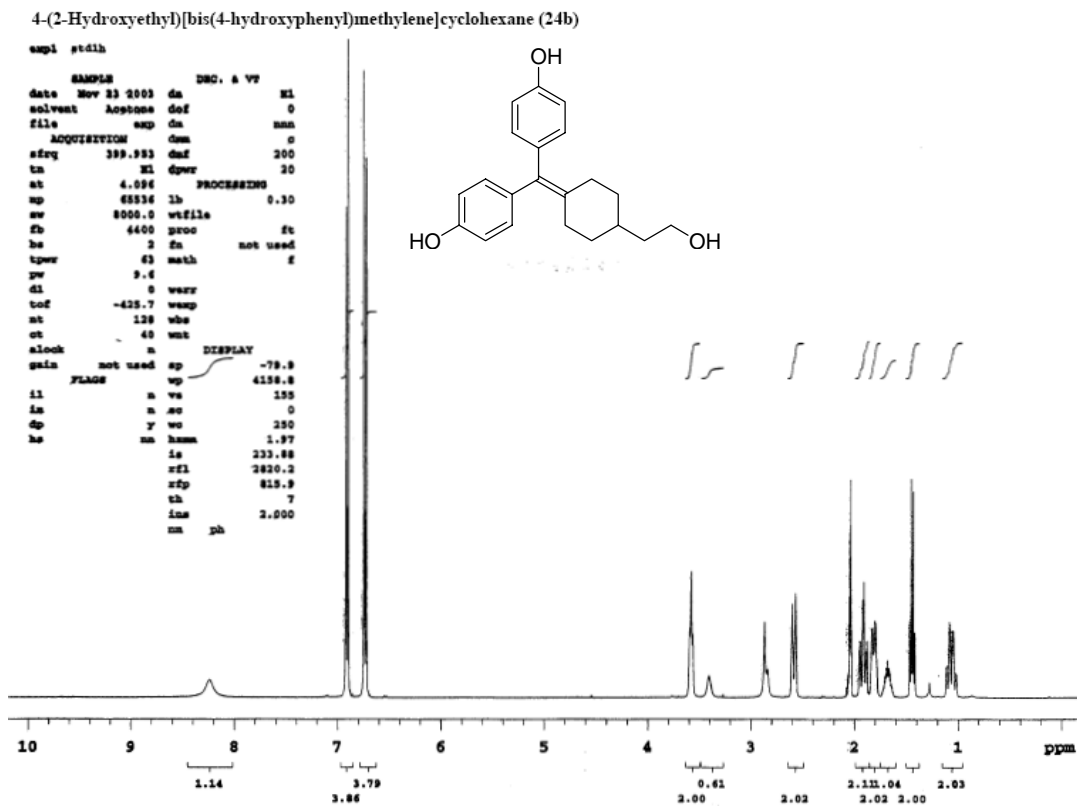
¹³C NMR (125 MHz, CDCl₃)

4-(2-Hydroxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (23b)

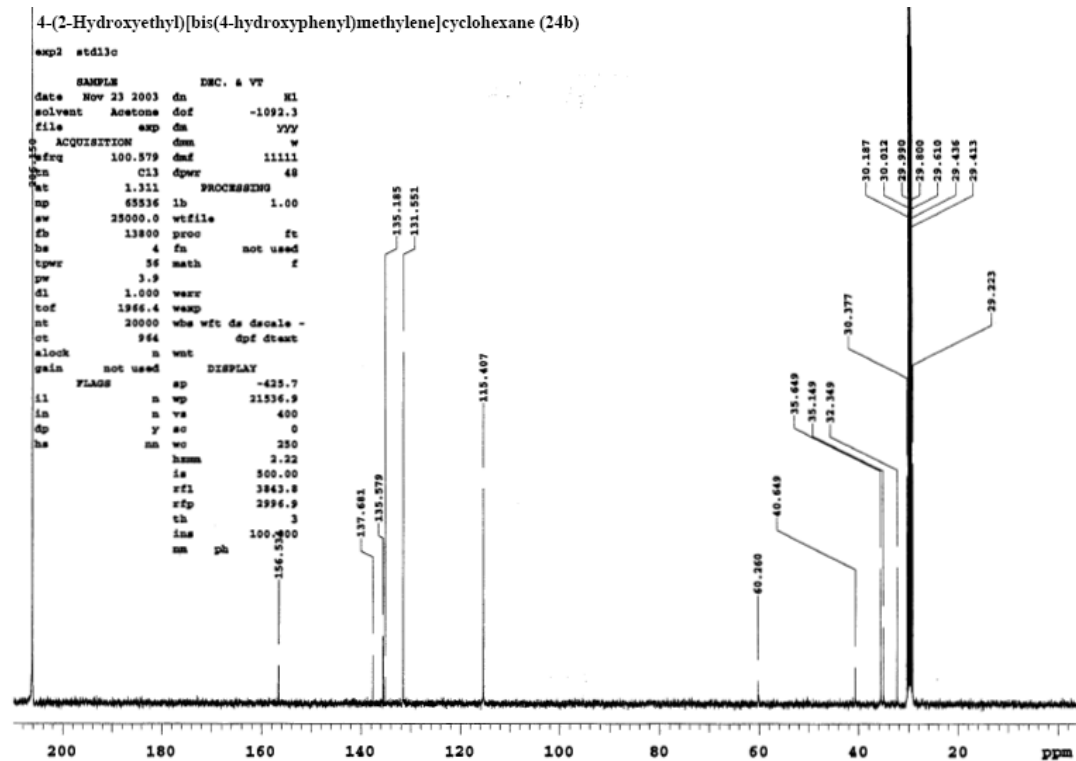


4-(2-Hydroxyethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (24b).

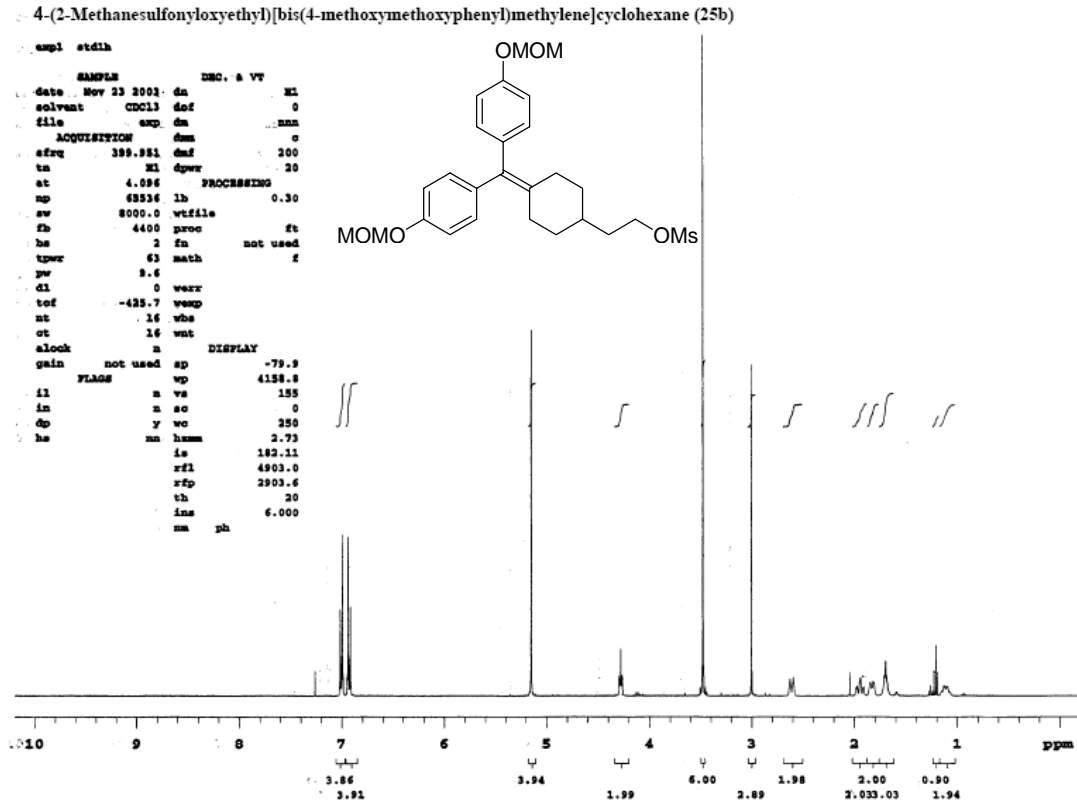
¹H NMR (400 MHz, acetone-d₆)



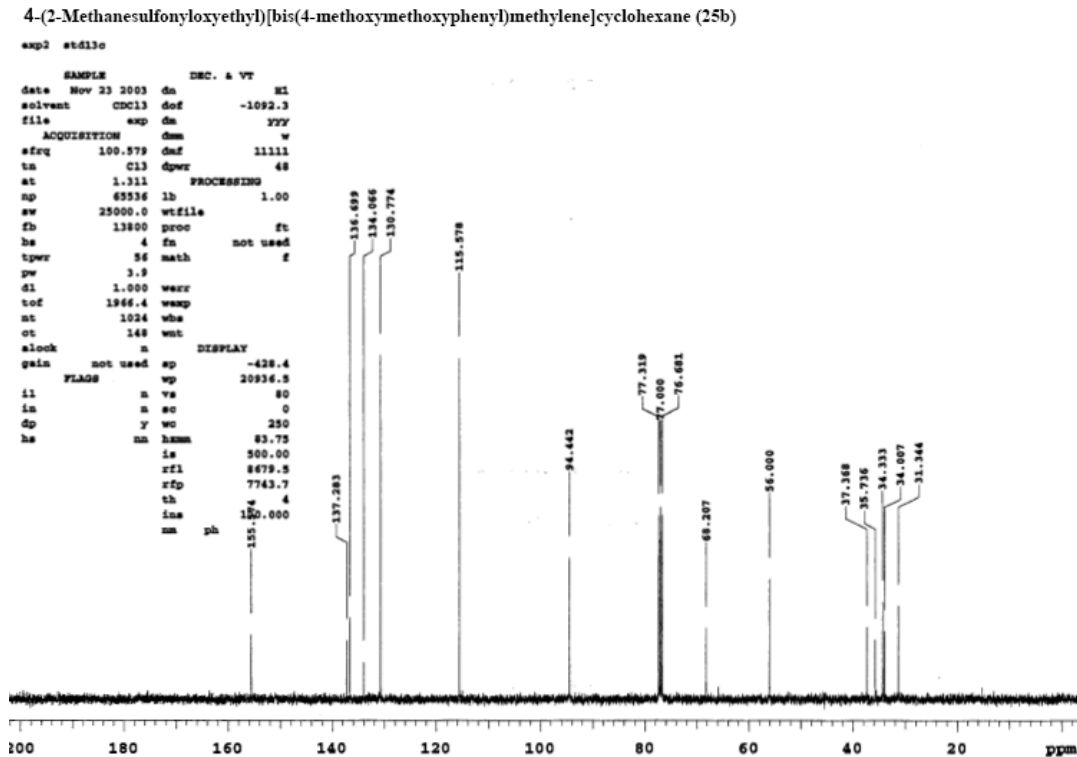
¹³C NMR (100 MHz, acetone-d₆)



4-(2-Methanesulfonyloxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (25b). ¹H NMR (400 MHz, CDCl₃)



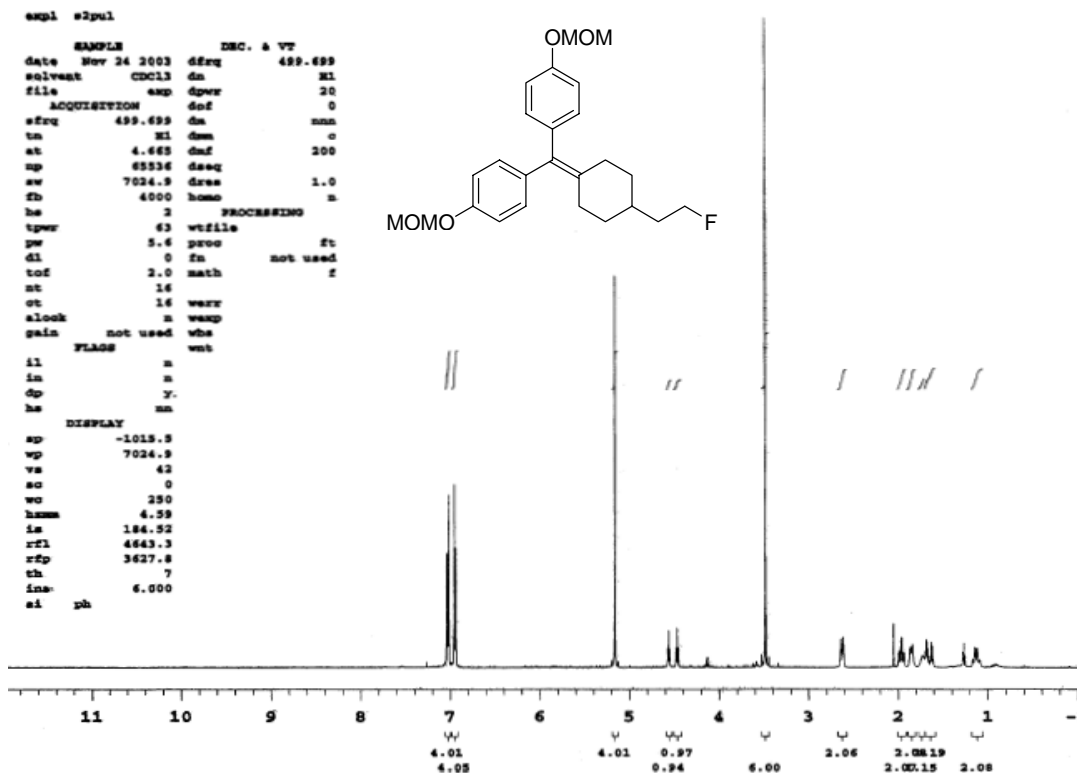
¹³C NMR (100 MHz, CDCl₃)



4-(2-Fluoroethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

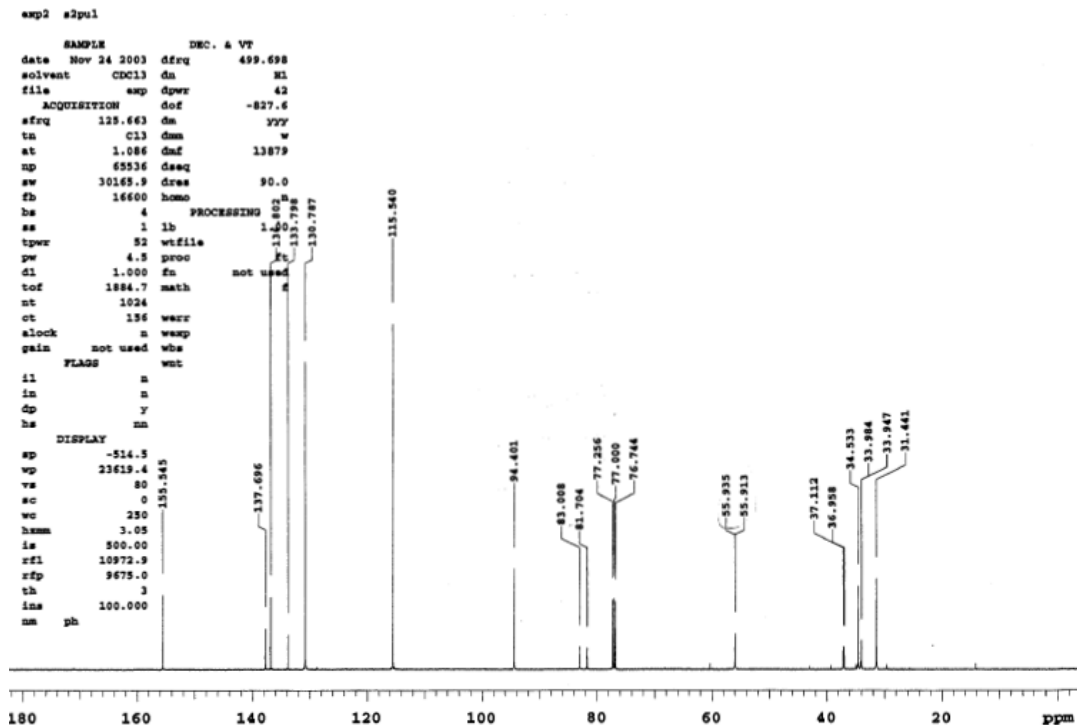
¹H NMR (500 MHz, CDCl₃)

4-(2-Fluoroethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane



¹³C NMR (125 MHz, CDCl₃)

4-(2-Fluoroethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane



4-(2-Fluoroethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (26b).

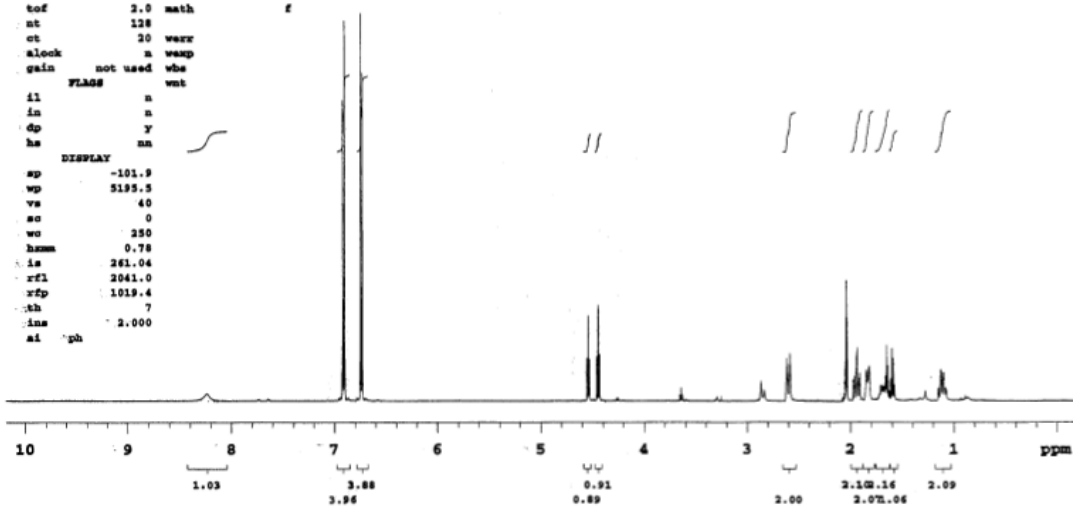
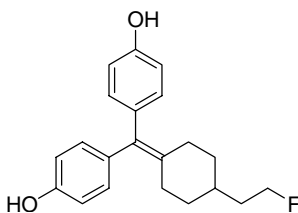
¹H NMR (500 MHz, acetone-*d*₆)

4-(2-Fluoroethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (26b)

exp1 s2pul

```

SAMPLE          DEC. & VT
date Nov 25 2003 dfrq 499.702
solvent Acetone dn 31
file           exp dpwr 30
ACQUISITION    dof 0
sfrq 499.702 dn nnn
tn 31 dnm 0
at 4.665 daf 200
sp 65536 dseq
sw 7024.9 dres 1.0
fb 4000 homo n
bs 2 PROCESSING
tpwr 63 wfile
pw 5.4 proc ft
dl 0 fn not used
tof 2.0 math f
nt 128
ct 20 warr
alock n warr
gain not used wbs
FLAGS          wnt
il n
in n
dp y
hs nn
DISPLAY
sp -101.9
wp 5193.5
vs 40
sc 0
sm 350
hmm 0.78
is 261.04
rfl 2041.0
rfp 1019.4
th 7
ins 2.000
al ph
    
```



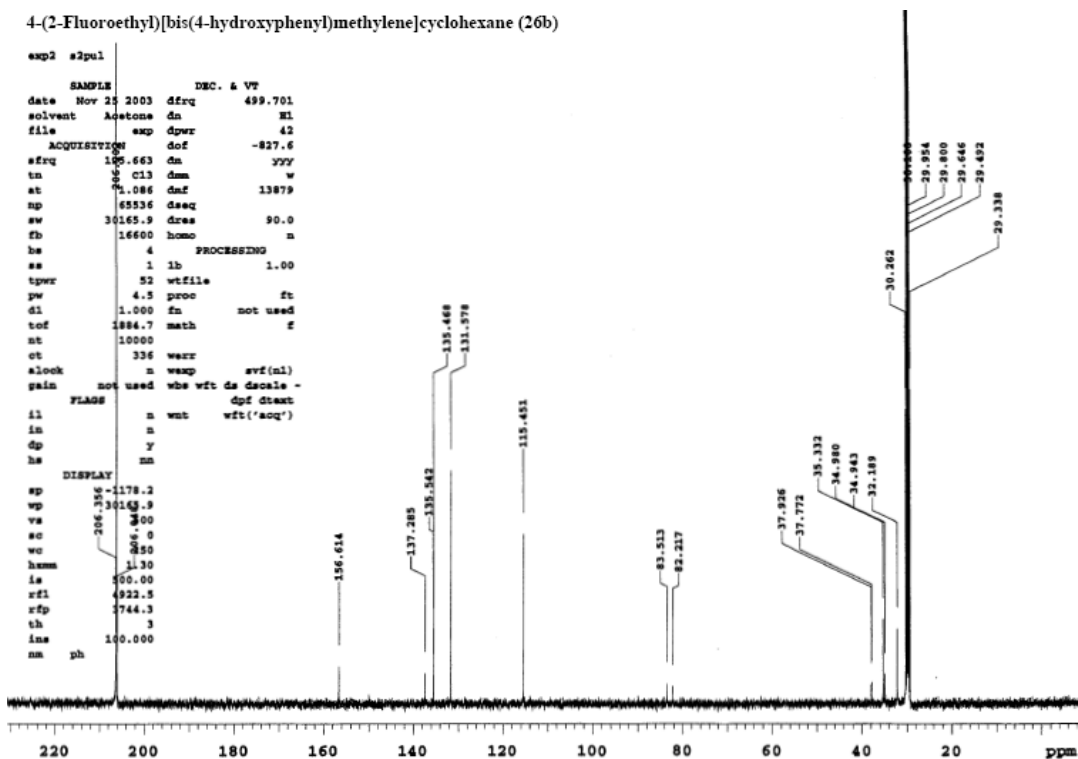
¹³C NMR (125 MHz, acetone-*d*₆)

4-(2-Fluoroethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (26b)

exp2 s2pul

```

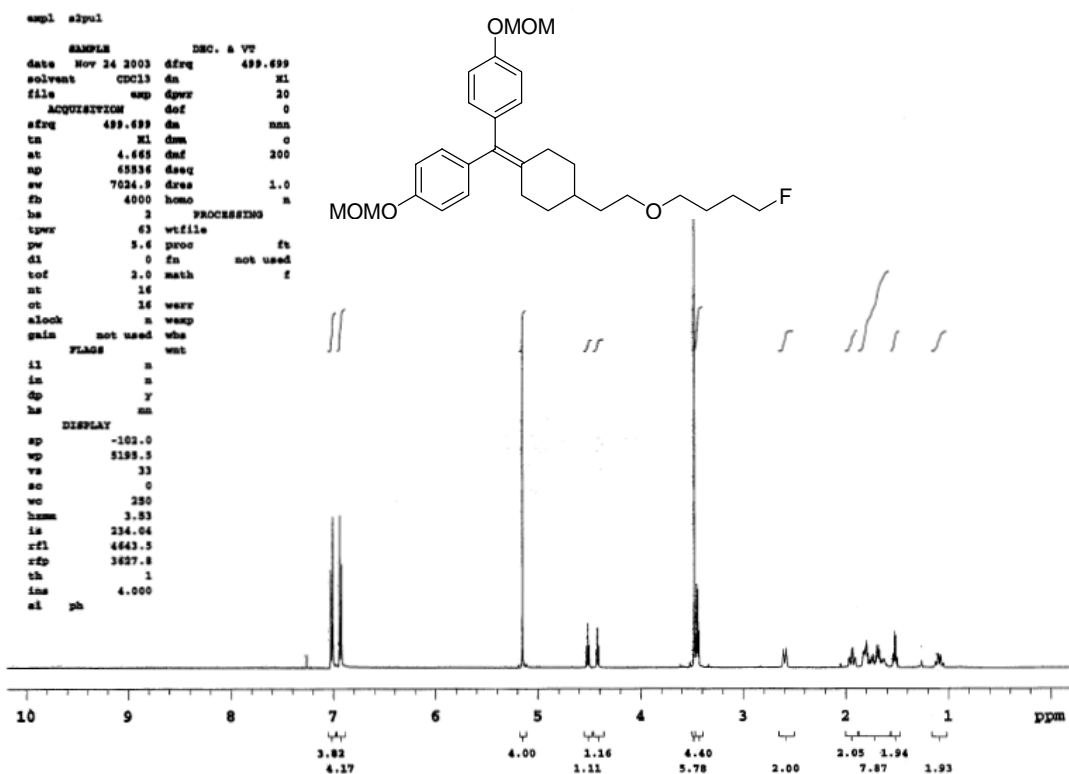
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date Nov 25 2003 dfrq 499.701
solvent Acetone dn 31
file           exp dpwr 42
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sfrq 100.663 dn yyy
tn 31 dnm w
at 4.086 daf 13879
sp 65536 dseq
sw 30165.9 dres 90.0
fb 16600 homo n
bs 4 PROCESSING
es 1 lb 1.00
tpwr 52 wfile
pw 4.5 proc ft
dl 1.000 fn not used
tof 1884.7 math f
nt 10000
ct 336 warr
alock n warr svf(ml)
gain not used wbs wft ds dscale -
FLAGS          dpt dstat
il n
in n
dp y
hs nn
DISPLAY
sp -1178.2
wp 30165.9
vs 300
sc 0
sm 850
hmm 1.30
is 500.00
rfl 4922.5
rfp 2744.3
th 3
ins 100.000
na ph
    
```



4-[2-(4-Fluorobutoxy)ethyl][bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

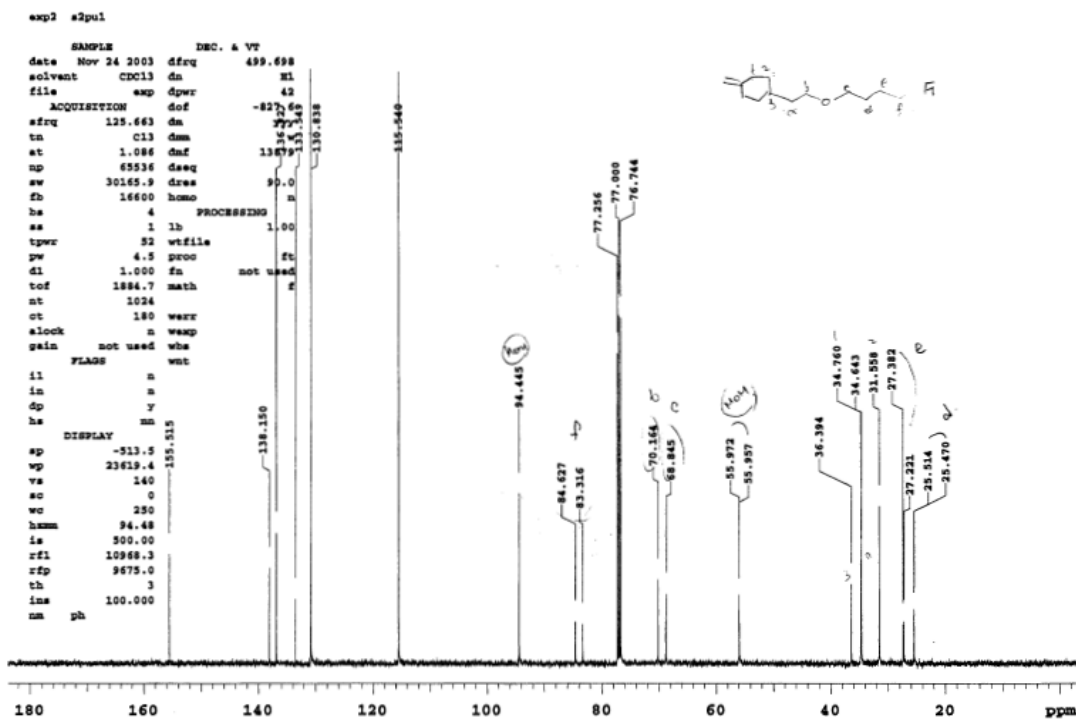
¹H NMR (500 MHz, CDCl₃)

4-[2-(4-Fluorobutoxy)ethyl][bis(4-methoxymethoxyphenyl)methylene]cyclohexane



¹³C NMR (125 MHz, CDCl₃)

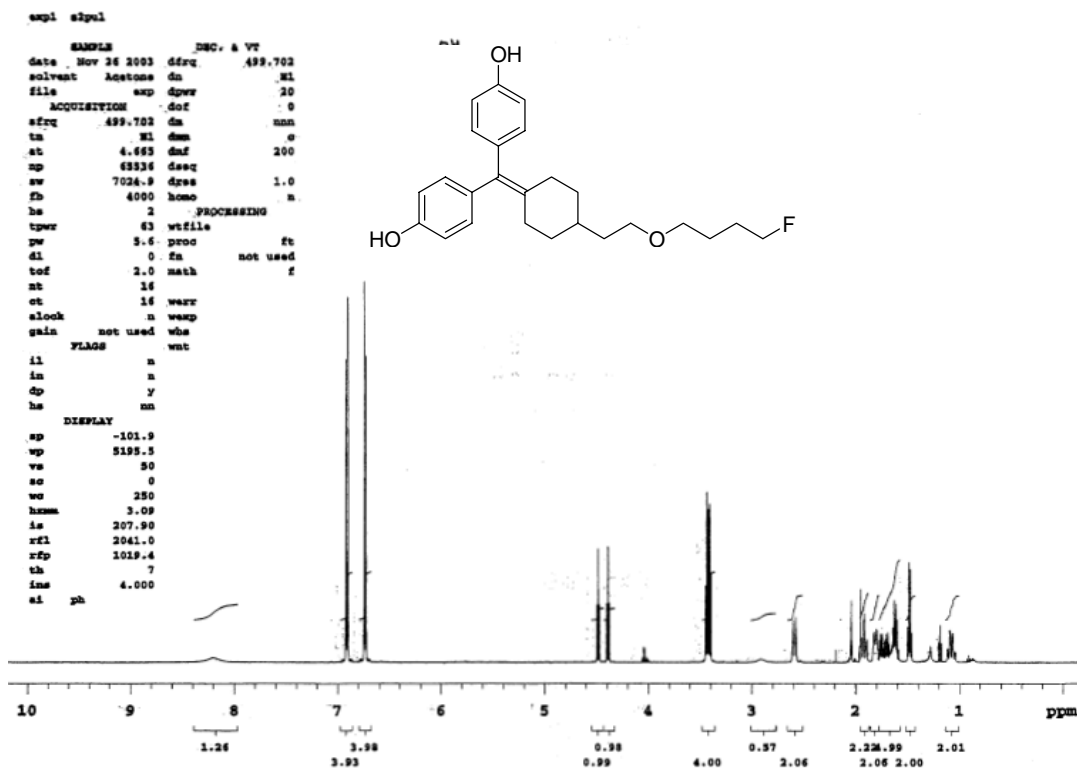
4-[2-(4-Fluorobutoxy)ethyl][bis(4-methoxymethoxyphenyl)methylene]cyclohexane



4-[2-(4-Fluorobutoxy)ethyl][bis(4-hydroxyphenyl)methylene]cyclohexane (28).

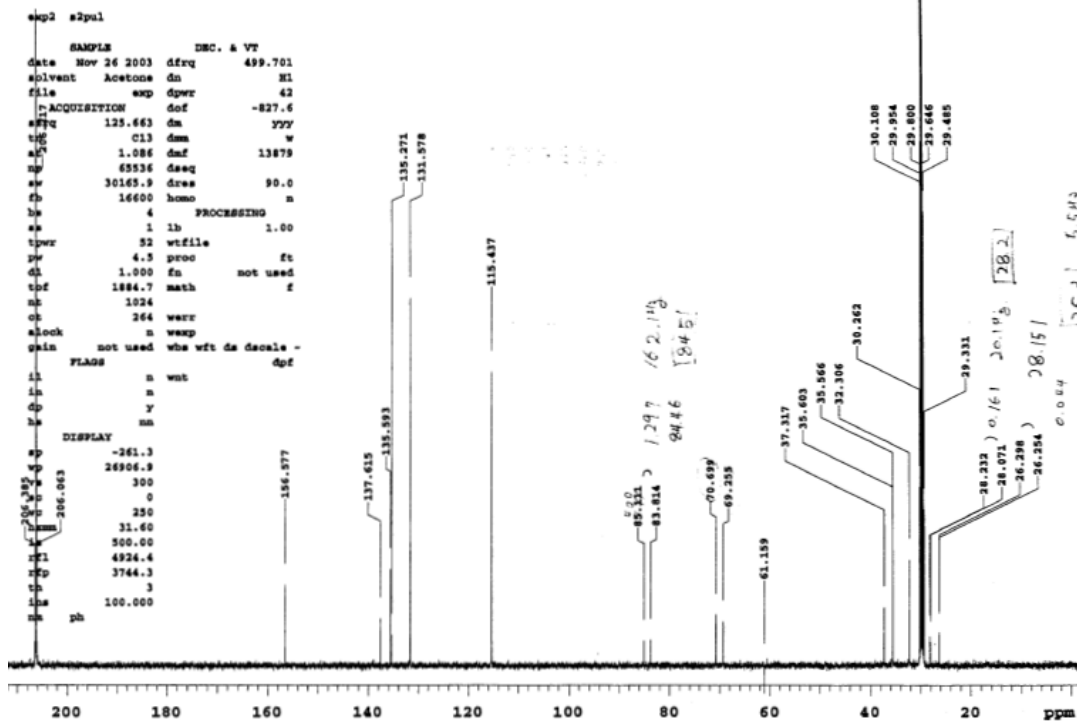
¹H NMR (500 MHz, acetone-d₆)

4-[2-(4-Fluorobutoxy)ethyl][bis(4-hydroxyphenyl)methylene]cyclohexane (28)



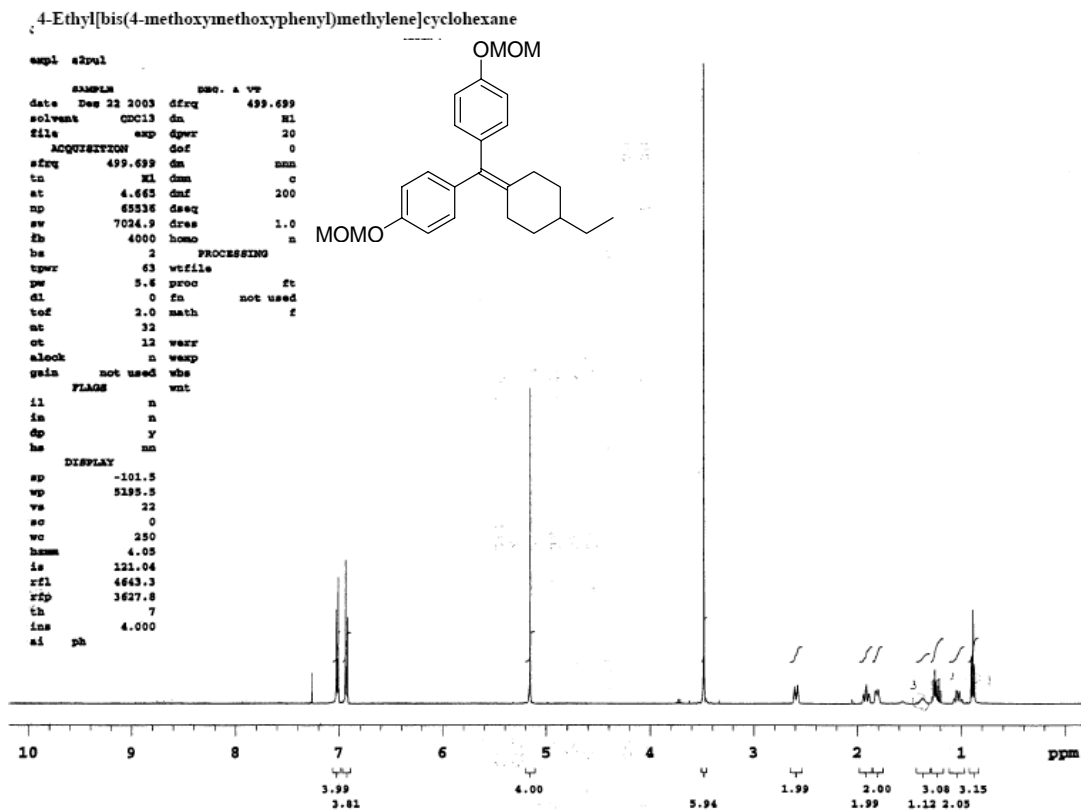
¹³C NMR (125 MHz, acetone-d₆)

4-[2-(4-Fluorobutoxy)ethyl][bis(4-hydroxyphenyl)methylene]cyclohexane (28)

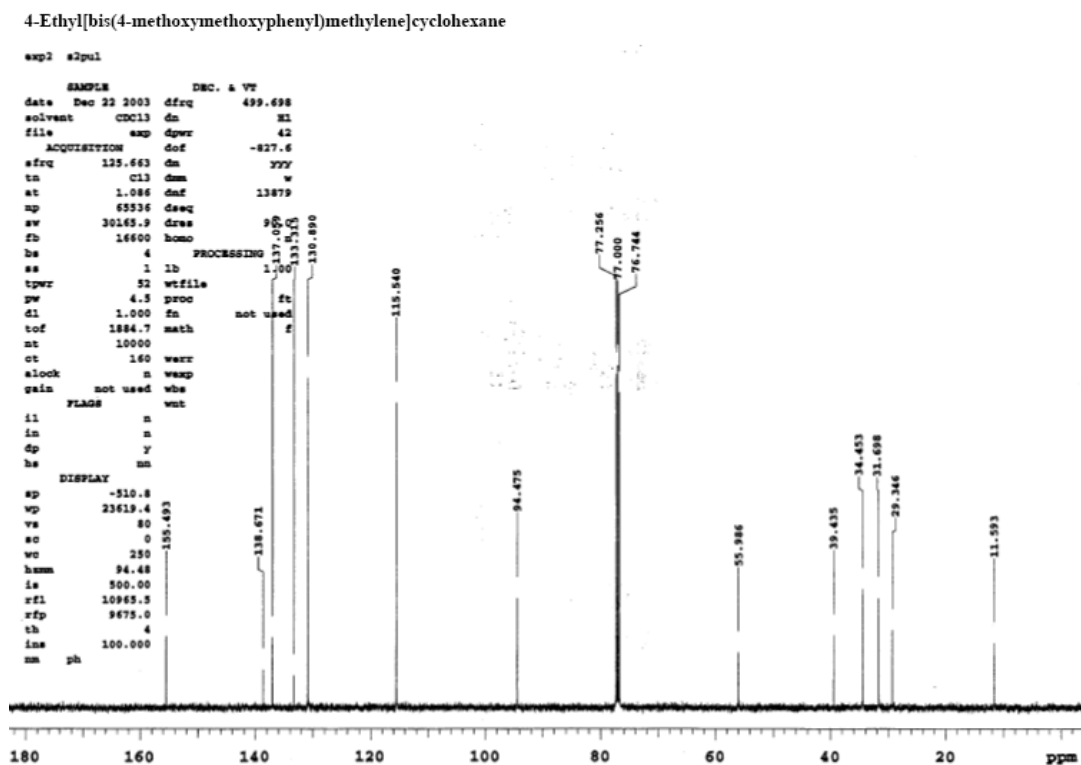


4-Ethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

¹H NMR (500 MHz, CDCl₃)

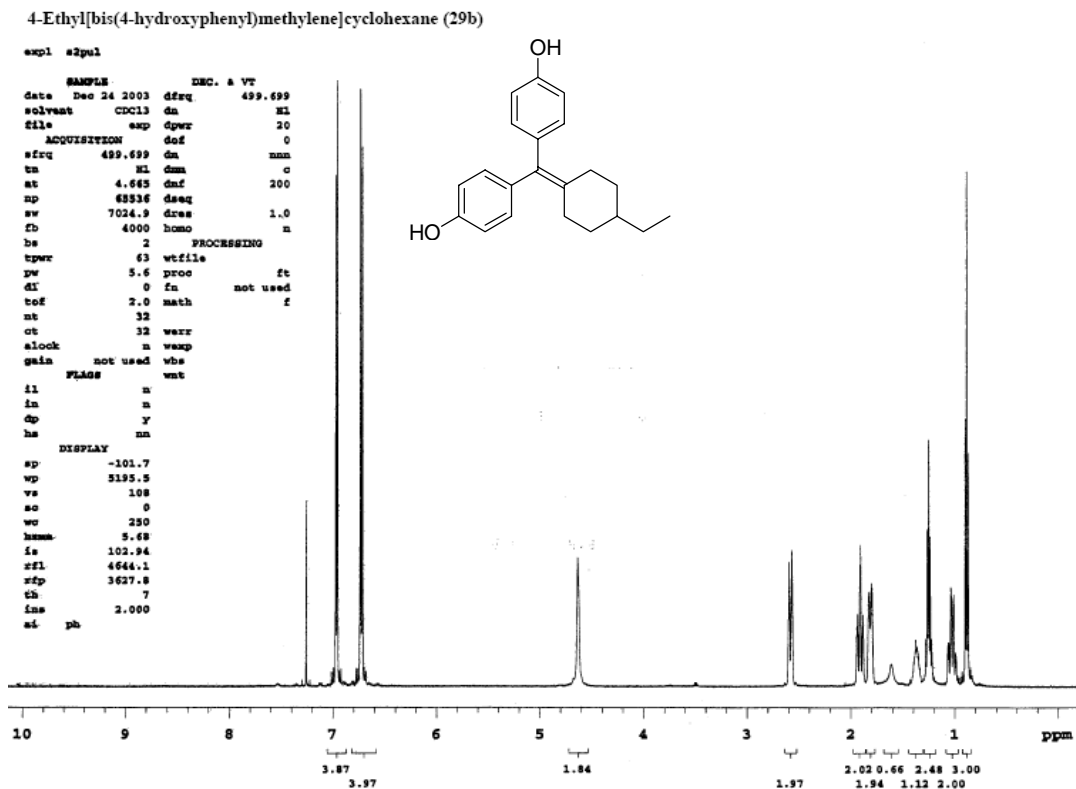


¹³C NMR (125 MHz, CDCl₃)

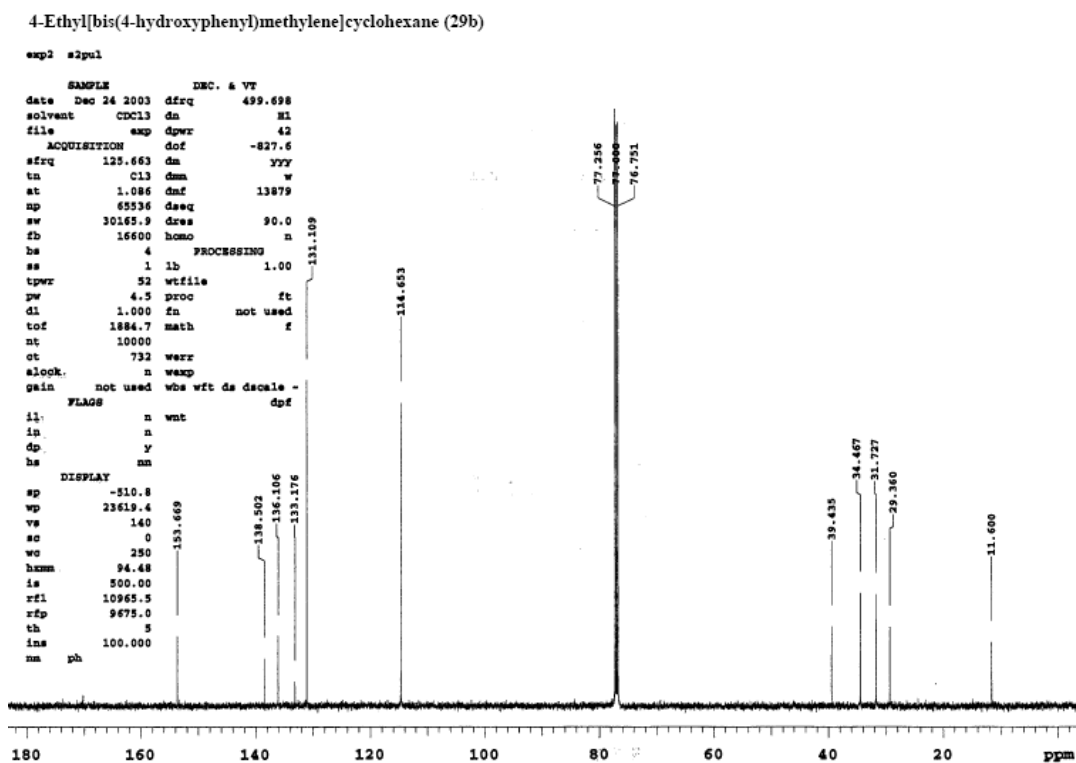


4-Ethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (29b).

¹H NMR (500 MHz, CDCl₃)



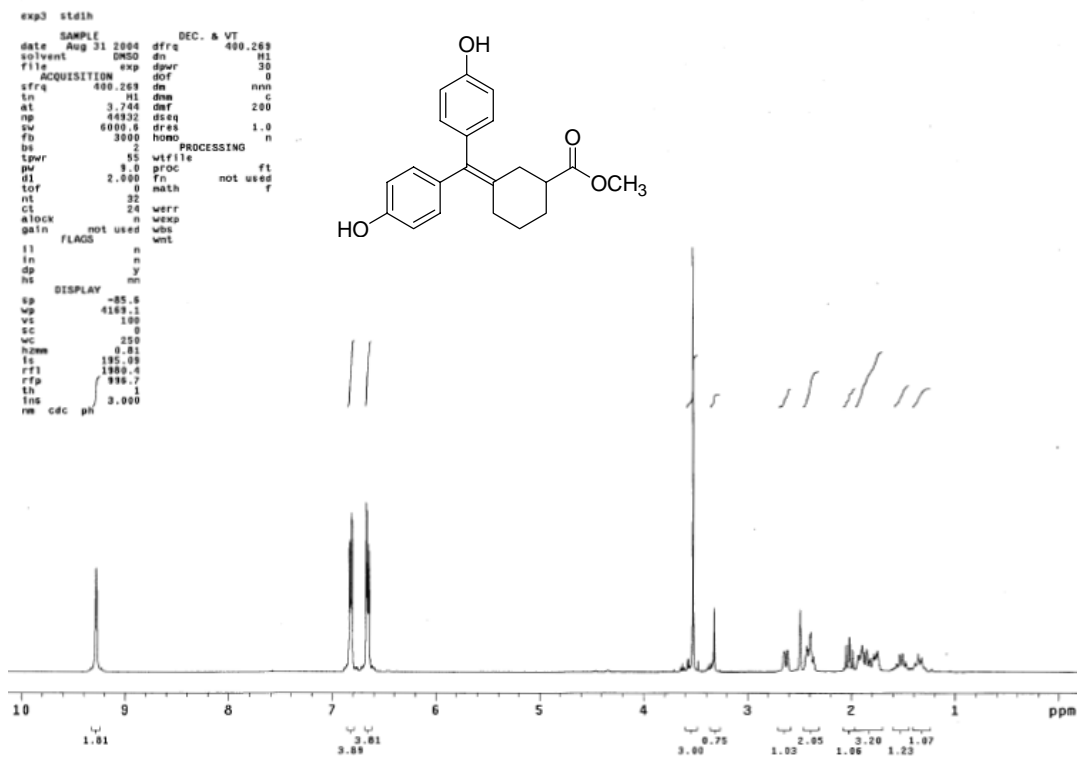
¹³C NMR (125 MHz, CDCl₃)



Methyl 3-[Bis(4-hydroxyphenyl)methylene]cyclohexanecarboxylate (30a).

^1H NMR (400 MHz, acetone- d_6)

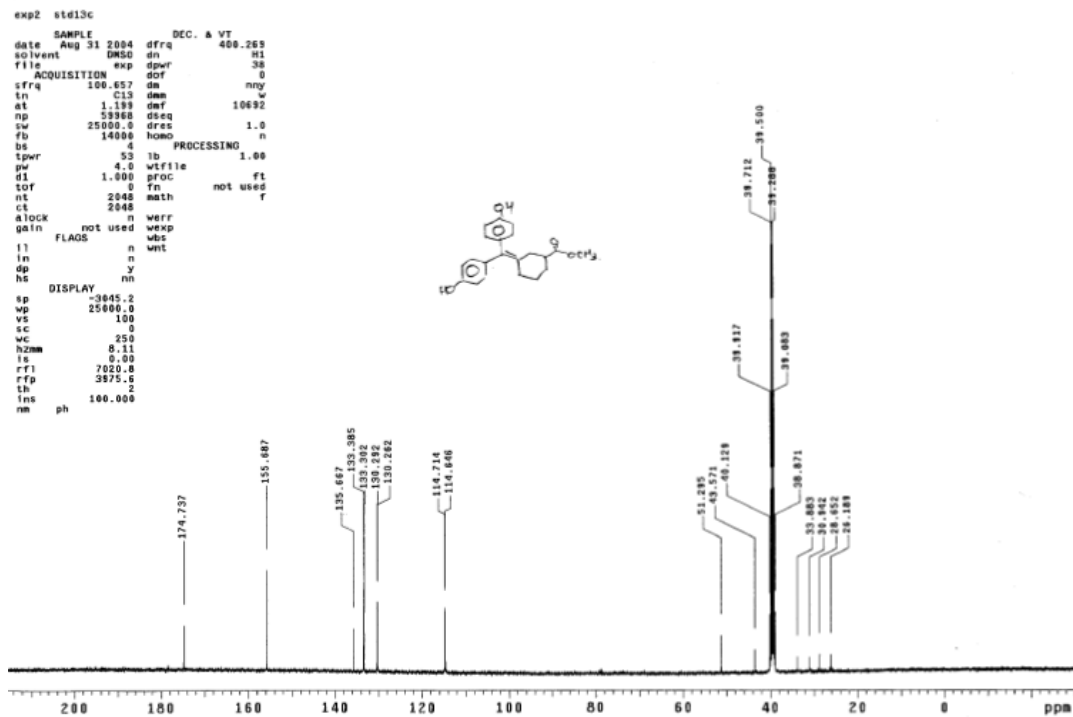
Methyl 3-[Bis(4-hydroxyphenyl)methylene]cyclohexanecarboxylate (30a)



^{13}C NMR

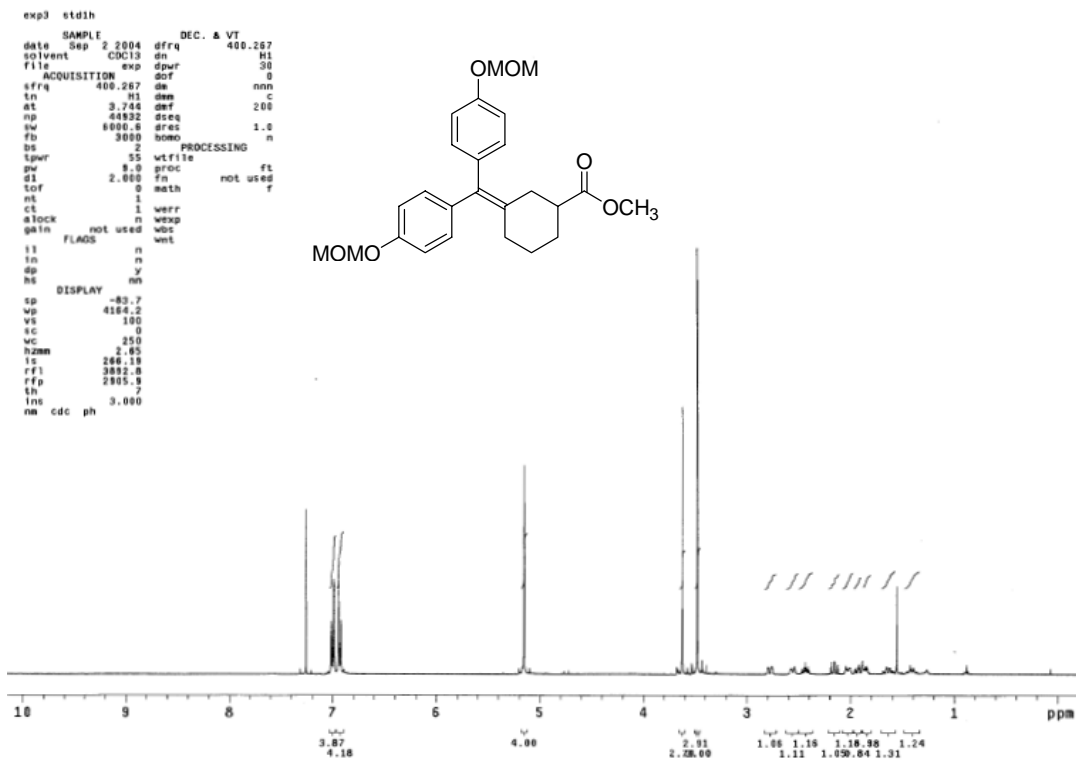
(100 MHz, acetone- d_6)

Methyl 3-[Bis(4-hydroxyphenyl)methylene]cyclohexanecarboxylate (30a)



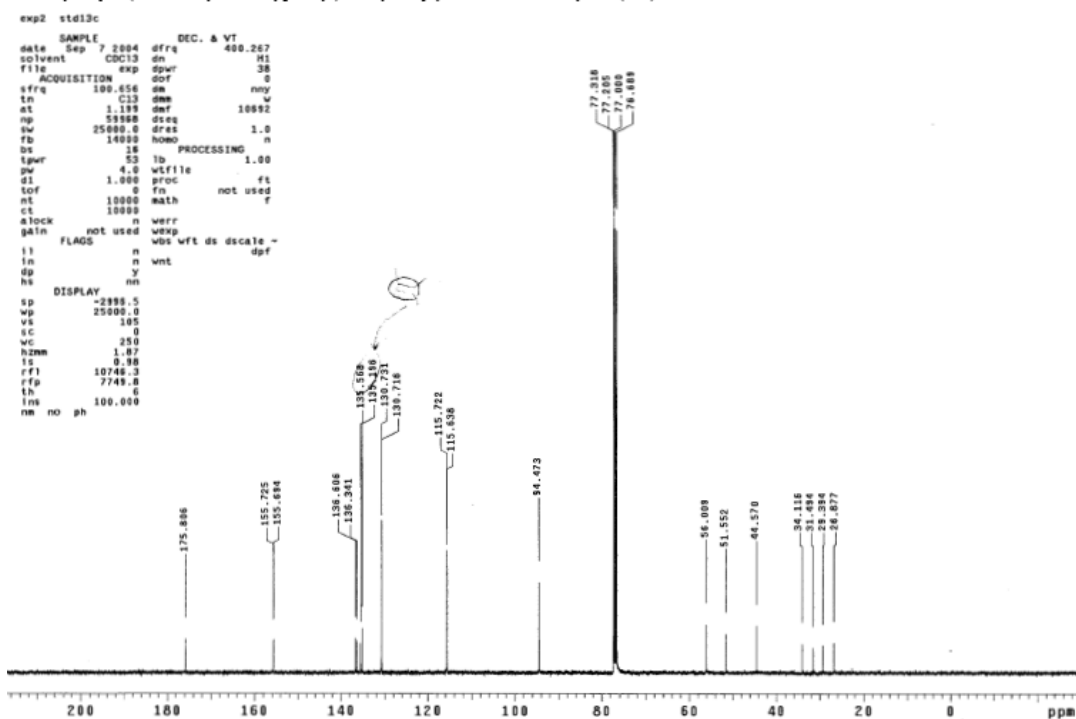
Methyl 3-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexanecarboxylate (33a).
¹H NMR (400 MHz, CDCl₃)

Methyl 3-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexanecarboxylate (33a)



¹³C NMR (100 MHz, CDCl₃)

Methyl 3-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexanecarboxylate (33a)



3-Hydroxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34a).

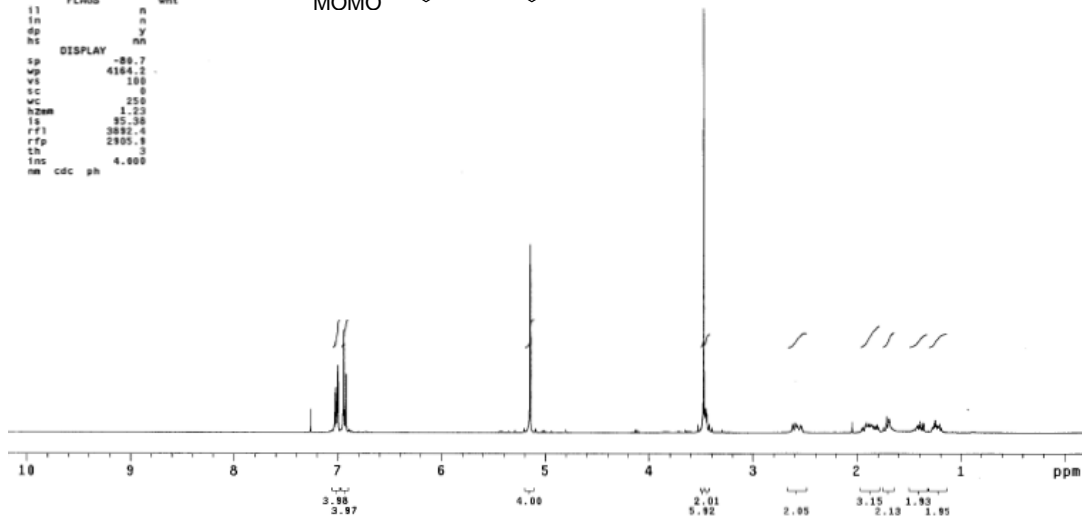
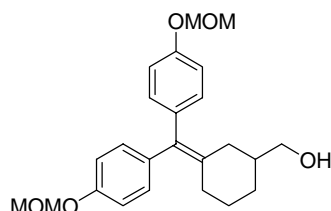
^1H NMR (400 MHz, CDCl_3)

3-Hydroxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34a)

exp3 stdih

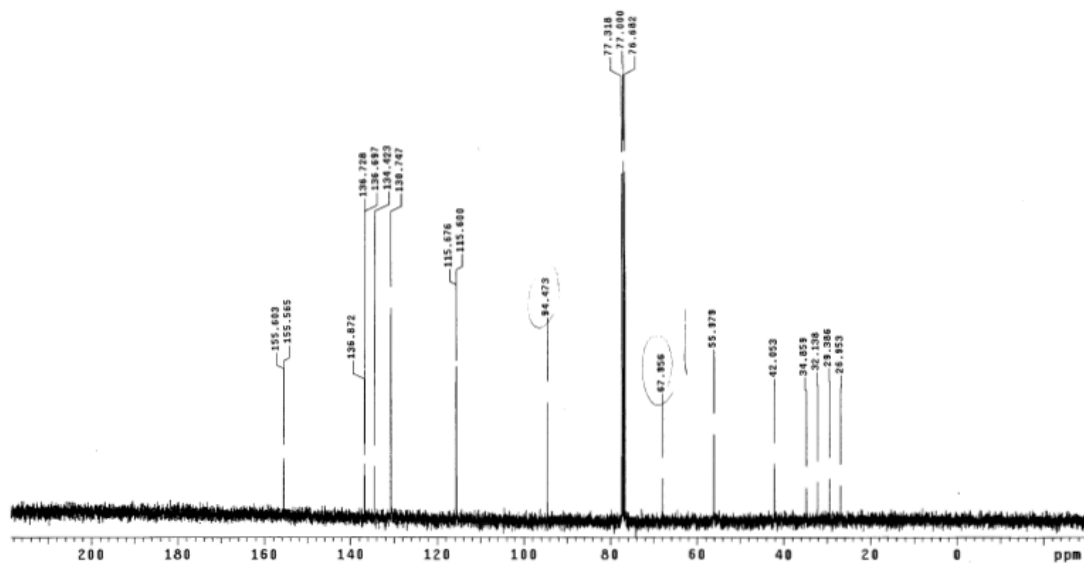
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SAMPLE          DEC. & VT
date Sep 6 2004 09:44:27
solvent CDCl3   dn      H1
file          exp 0001  30
ACQUISITION    dof      0
sfrq 400.267   de       nm
tn      H1      dm       C
at      3.744   df       200
np      44532   dseg     1.0
sw      6000.0  dres     1.0
fp      3000    homo     n
bs      2
tpwr 55        wfile
sw      8.0     dproc
d1      2.000   fn      not used
tof      0     math
nt      36
ct      12     wfft
slock   n     wexp
gain    not used  wds
        not used  wnt
ii      n
in      n
ep      y
hs      m
DISPLAY -80.7
wp      4164.2
vs      100
tc      0
wc      250
h2am   1.23
is      85.38
rf1     3882.4
rfp     2905.8
sh      3
ins     4.000
me cdc ph
    
```



^{13}C NMR (100 MHz, CDCl_3)

3-Hydroxymethyl[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34a)



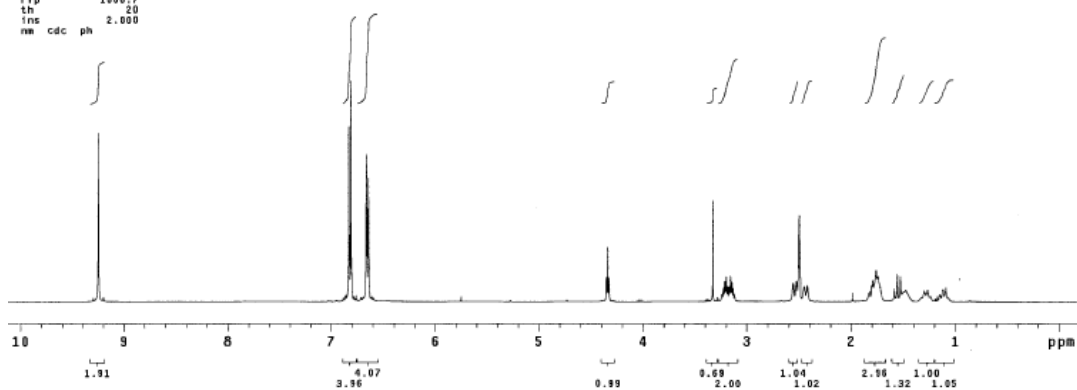
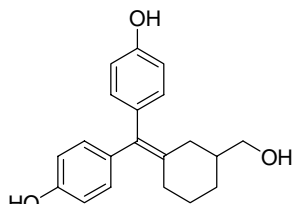
3-Hydroxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (35a)

¹H NMR (400 MHz, DMSO-d₆)

3-Hydroxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (35a)

```

expl std1h
SAMPLE
date Sep 8 2004 dfrq 400.269
solvent DMSO dn H1
file exp dpwr 38
ACQUISITION exp dof 0
sfrq 400.269 de nnn
tn H1 dm C
at 3.744 def 200
np 44532 dseq 1.0
sw 6000.6 dres 1.0
fb 3000 homo n
bs 2 PROCESSING
tpwr 55 wfile ft
pw 8.0 proc not used
d1 2.000 fn f
tof 0 math
nt 16 wefr
ct 16 wefr
alock n wepp
gain not used wbs
FLAGS n wnt
n1 n
in n
dp y
hs nn
DISPLAY
sp -86.7
wp 4164.2
vs 50
sc 0
wc 250
hzam 2.91
ls 273.44
rf1 1866.7
rfp 1800.7
th 20
ims 2.000
nm cdc ph
  
```

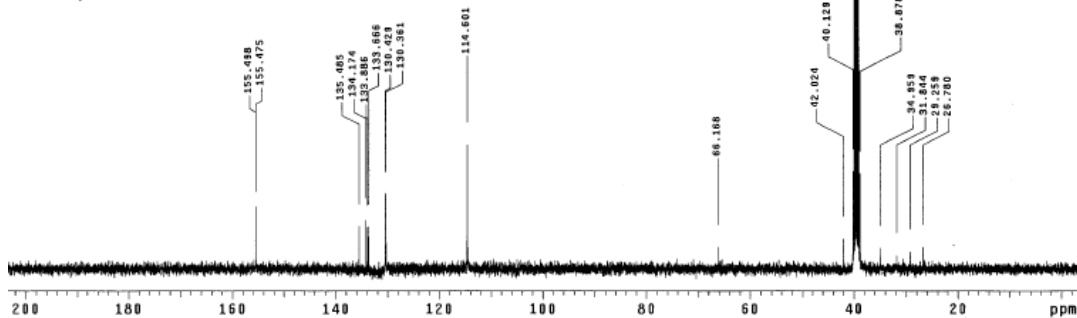


¹³C NMR (100 MHz, DMSO-d₆)

3-Hydroxymethyl[bis(4-hydroxyphenyl)methylene]cyclohexane (35a)

```

expl std13c
SAMPLE
date Sep 8 2004 dfrq 400.269
solvent DMSO dn H1
file exp dpwr 38
ACQUISITION exp dof 0
sfrq 100.657 de nny
tn C13 dm w
at 1.193 def 10692
np 59868 dseq 1.0
sw 25000.0 dres 1.0
fb 14000 homo n
bs 4 PROCESSING
tpwr 53 lb wfile 1.00
pw 4.0 proc not used
d1 1.000 fn f
tof 0 math
nt 2000 wefr
ct 832 wepp
alock n wepp
gain not used wbs
FLAGS n wnt
n1 n
in n
dp y
hs nn
DISPLAY
sp -397.7
wp 20925.8
vs 150
sc 0
wc 250
hzam 7.54
ls 0.49
rf1 7820.0
rfp 3975.5
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ims 100.000
nm no ph
  
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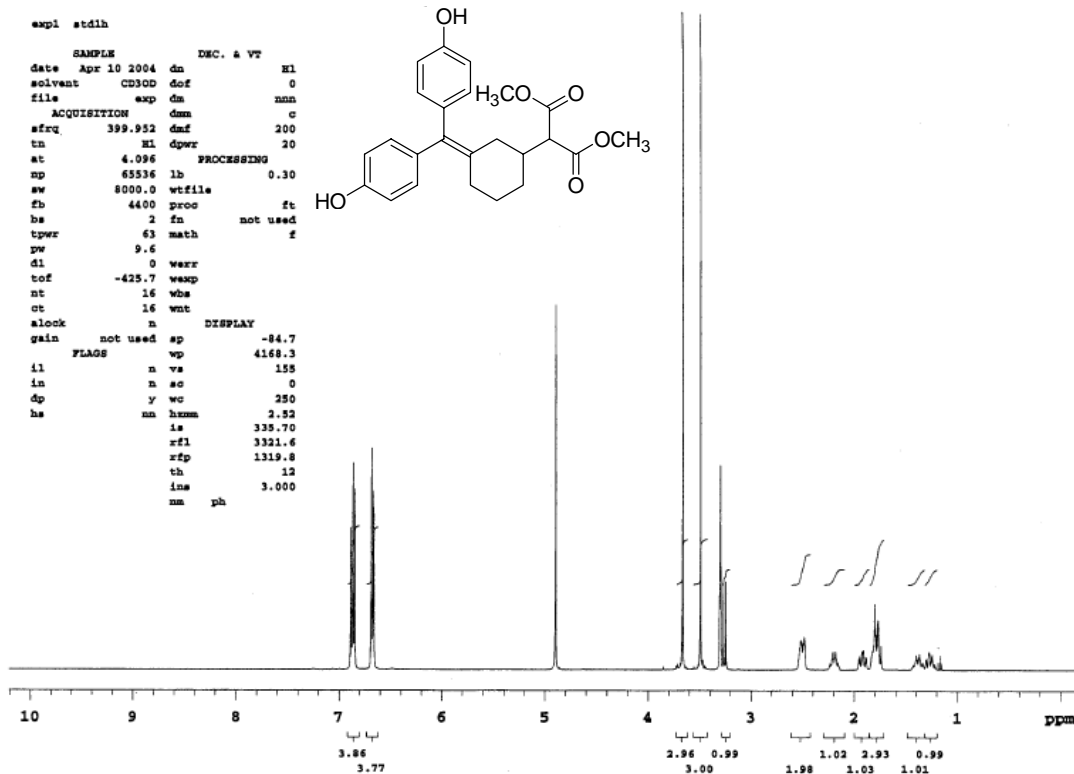
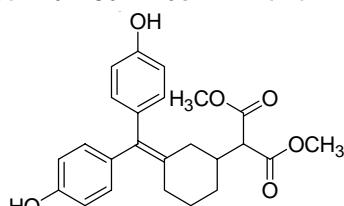
Dimethyl 2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}malonate (30b).

¹H NMR (400 MHz, methanol-*d*₄)

Dimethyl 2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}malonate (30b)

exp1 std1h

SAMPLE		DEC. & VT	
date	Apr 10 2004	dn	HL
solvent	CD3OD	dof	0
file	exp	dm	nmn
ACQUISITION		dms	
sfrq	399.952	dmsf	200
tn	HL	dpwr	20
at	4.096	PROCESSING	
np	65536	lb	0.30
sw	8000.0	wtfile	
fb	4400	proc	ft
bs	2	fn	not used
tpwr	63	math	f
pw	9.6		
dl	0	warr	
tof	-425.7	wexp	
nt	16	wba	
ct	16	wnt	
alock	n	DISPLAY	
gain	not used	sp	-84.7
FLAGS		wp	4168.3
il	n	vs	155
in	n	sc	0
dp	y	wc	250
hs	nn	hnm	2.52
		ls	335.70
		rfl	3321.6
		xrp	1319.8
		th	12
		lms	3.000
		nm	ph

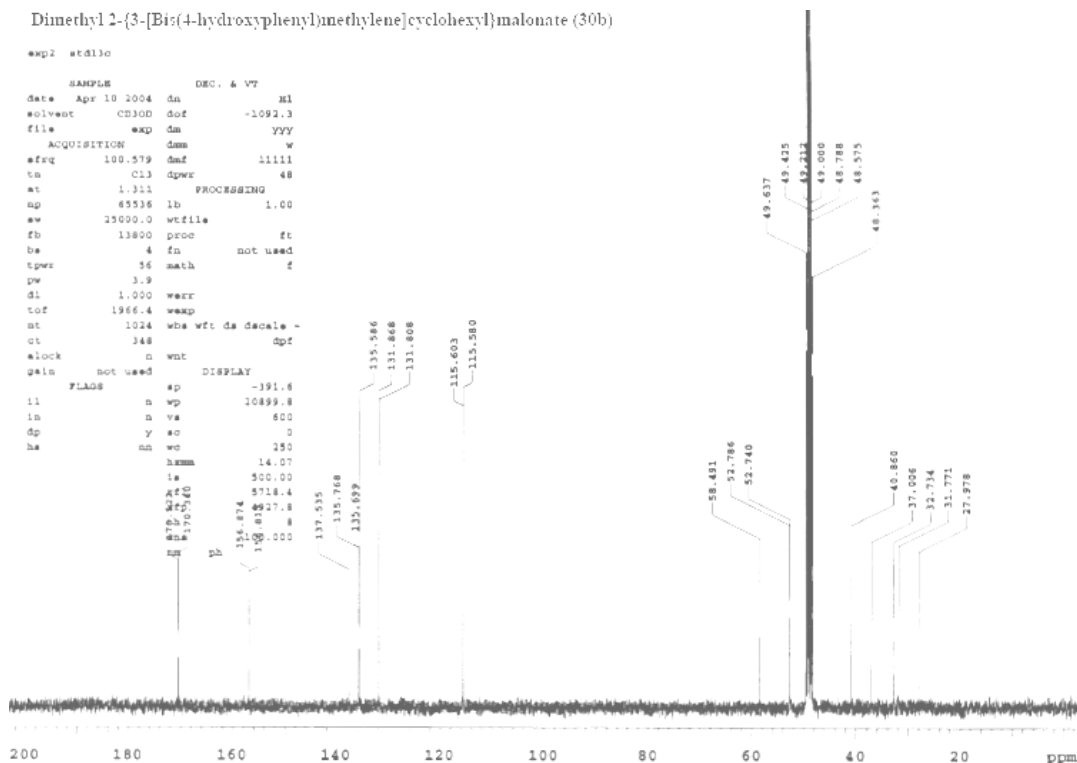


¹³C NMR (100 MHz, methanol-*d*₄)

Dimethyl 2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}malonate (30b)

exp2 std13c

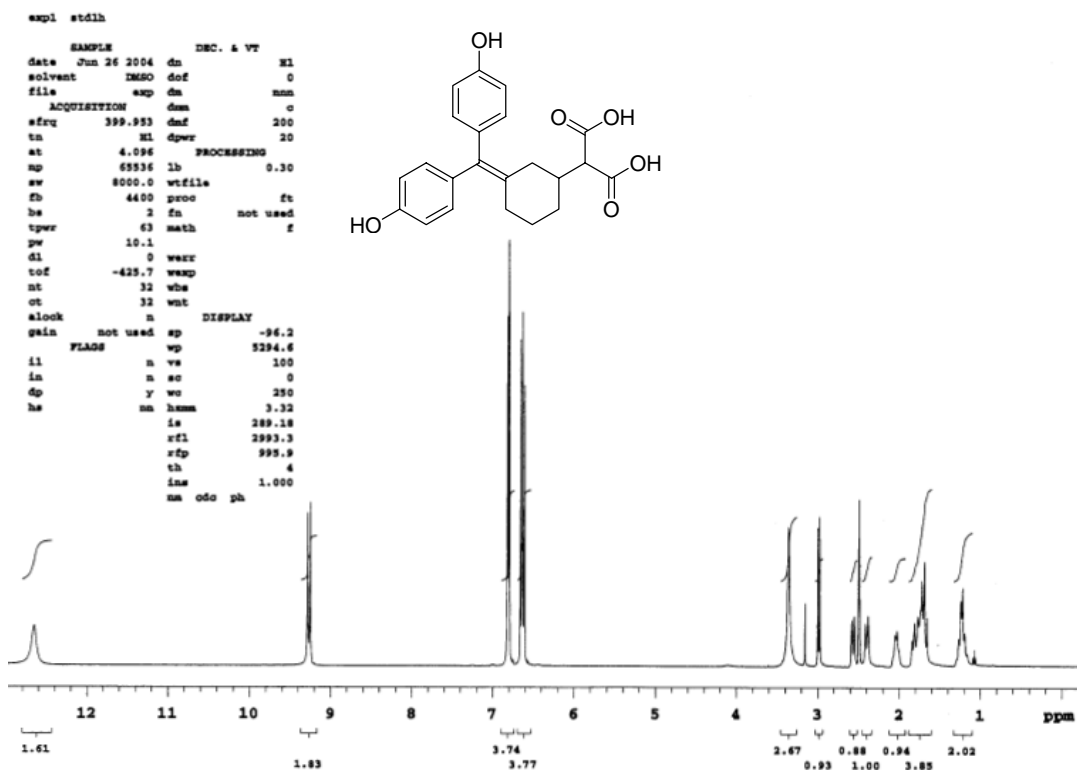
SAMPLE		DEC. & VT	
date	Apr 10 2004	dn	HL
solvent	CD3OD	dof	-1092.3
file	exp	dm	yyy
ACQUISITION		dms	
sfrq	100.579	dmsf	11111
tn	C13	dpwr	48
at	1.311	PROCESSING	
np	65536	lb	1.00
sw	25000.0	wtfile	
fb	13800	proc	ft
bs	4	fn	not used
tpwr	56	math	f
pw	3.9		
dl	1.000	warr	
tof	1966.4	wexp	
nt	1024	wba	wf: ds decale -
ct	348	wnt	dpf
alock	n	DISPLAY	
gain	not used	sp	-191.6
FLAGS		wp	10899.8
il	n	vs	600
in	n	sc	0
dp	y	wc	250
hs	nn	hnm	14.07
		ls	500.00
		ie	5718.4
		rfl	5718.4
		xrp	1000.000
		th	1000.000
		lms	1000.000
		nm	ph



2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}malonic acid (31).

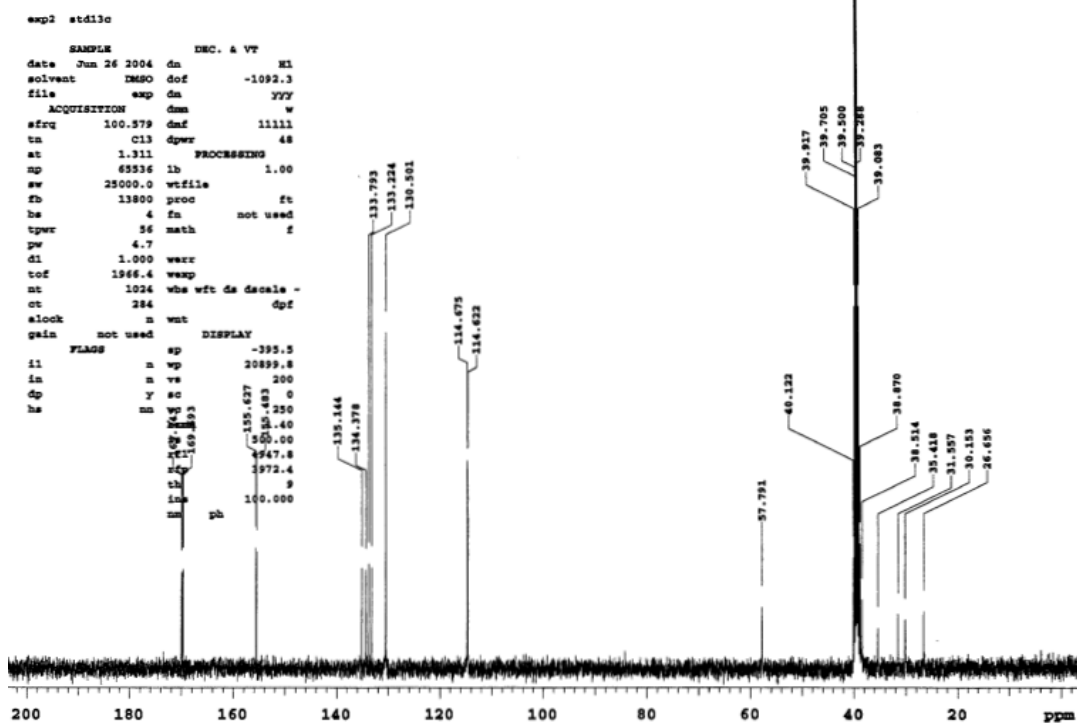
¹H NMR (400 MHz, DMSO-d₆)

2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}malonic acid (31)



¹³C NMR (100 MHz, DMSO-d₆)

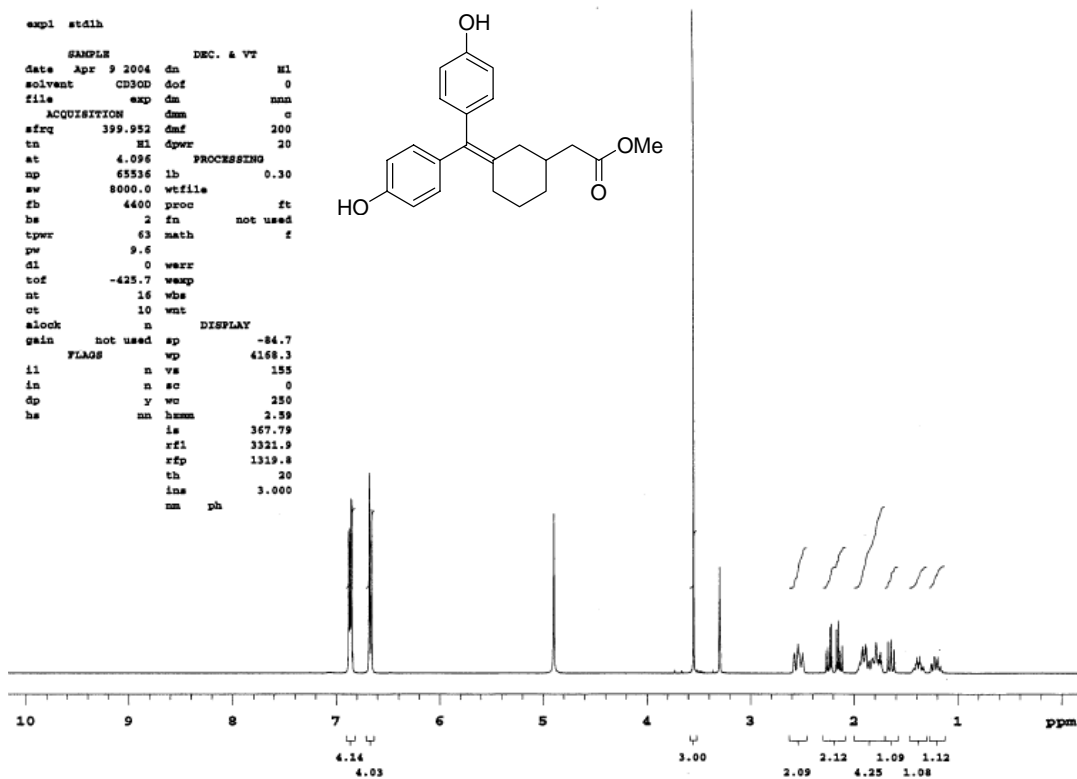
2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}malonic acid (31)



Methyl 2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}acetate (32).

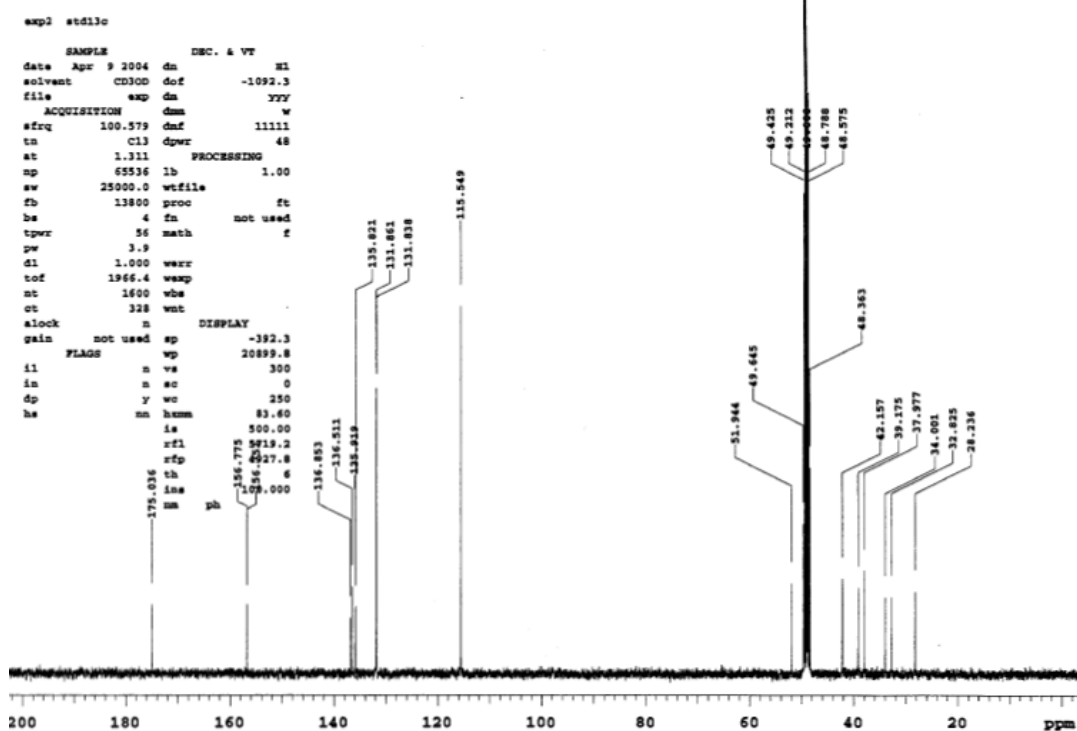
¹H NMR (400 MHz, methanol-d₄)

Methyl 2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}acetate (32)



¹³C NMR (100 MHz, methanol-d₄)

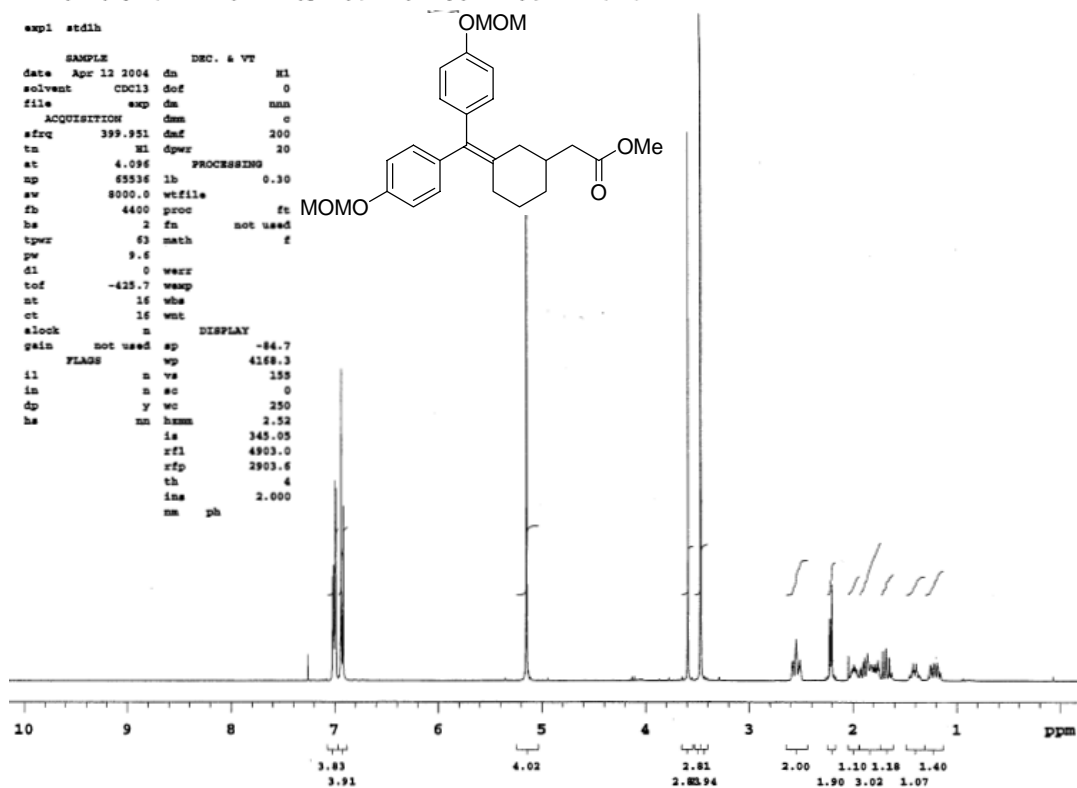
Methyl 2-{3-[Bis(4-hydroxyphenyl)methylene]cyclohexyl}acetate (32)



Methyl 2-{3-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexyl}acetate (33b).

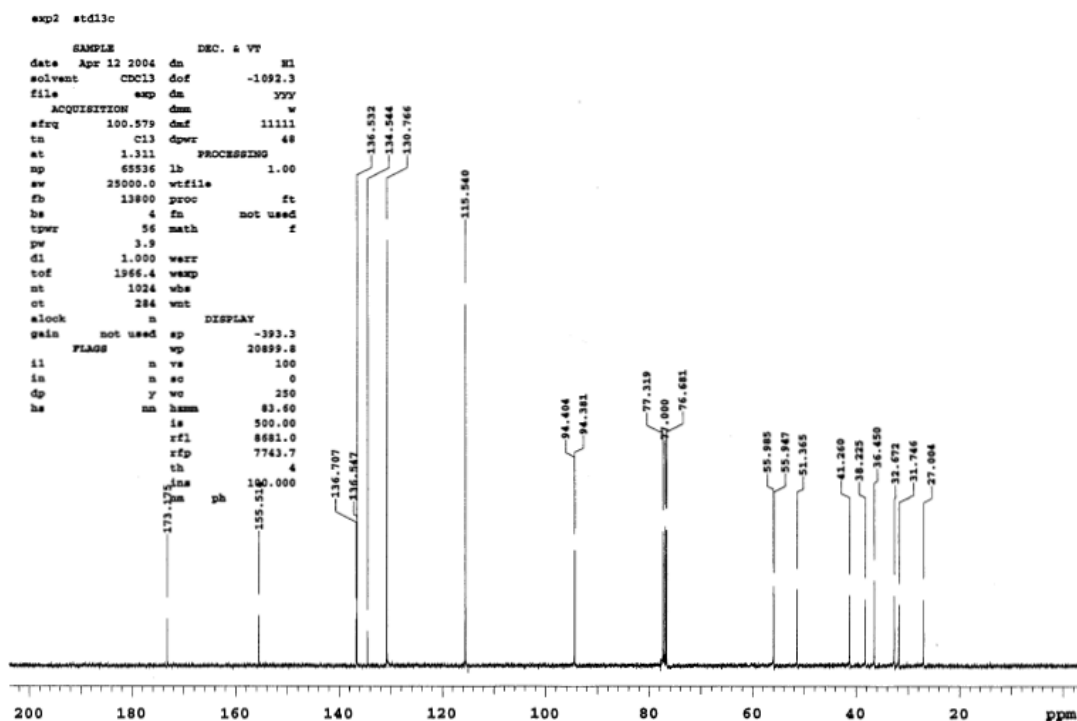
¹H NMR (400 MHz, CDCl₃)

Methyl 2-{3-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexyl}acetate (33b)



¹³C NMR (100 MHz, CDCl₃)

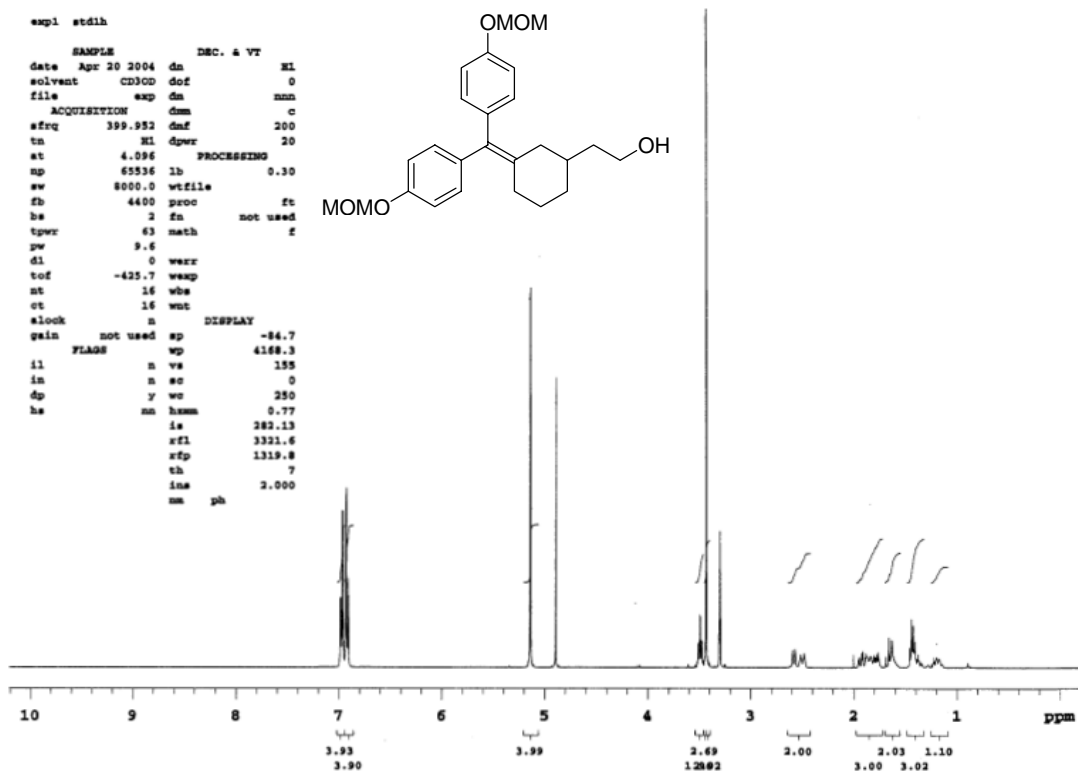
Methyl 2-{3-[Bis(4-methoxymethoxyphenyl)methylene]cyclohexyl}acetate (33b)



3-(2-Hydroxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34b).

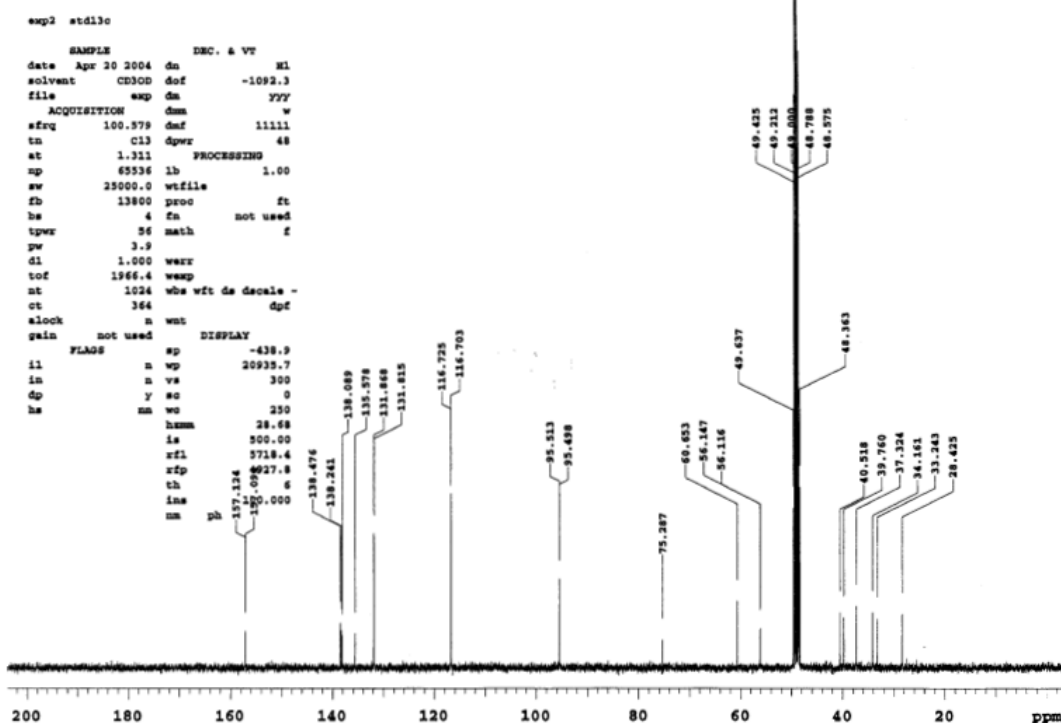
¹H NMR (400 MHz, methanol-*d*₄)

3-(2-Hydroxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34b)



¹³C NMR (100 MHz, methanol-*d*₄)

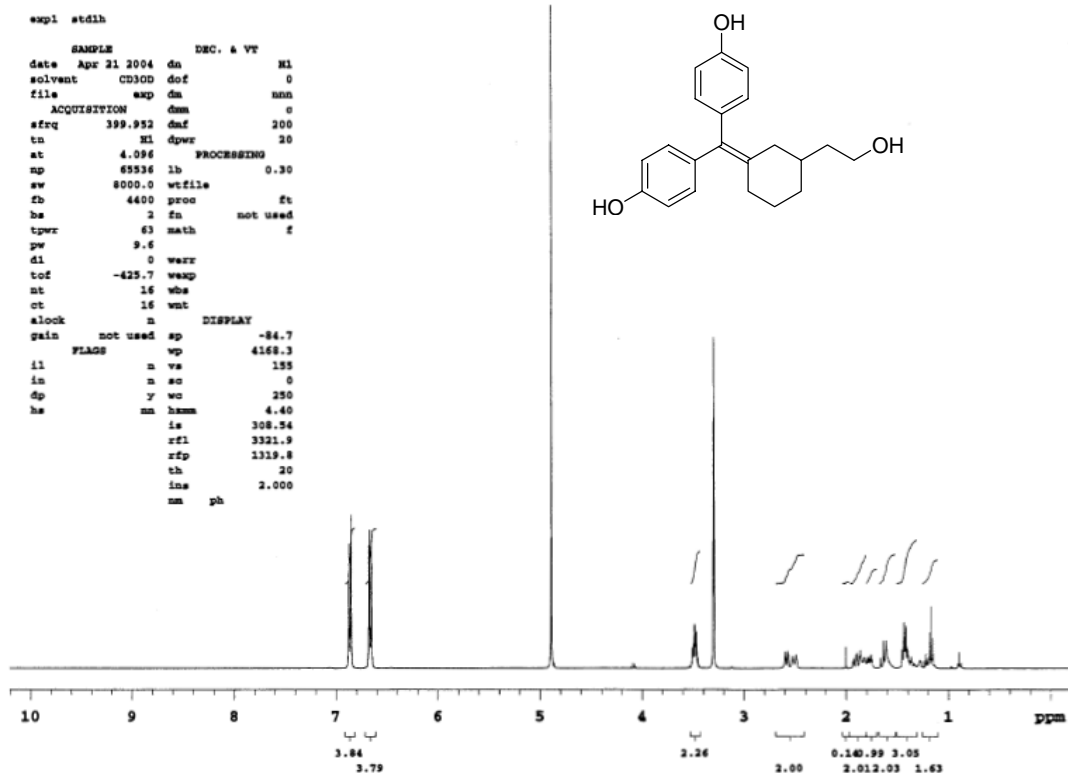
3-(2-Hydroxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34b)



3-(2-Hydroxyethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (35b).

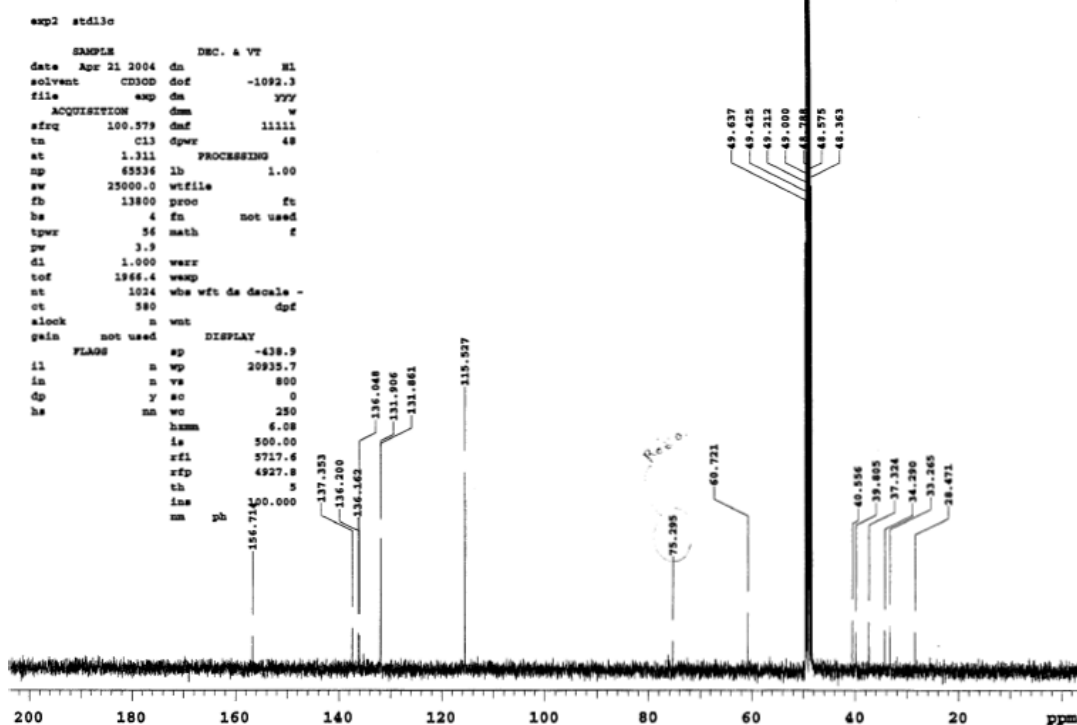
¹H NMR (400 MHz, methanol-d₄)

3-(2-Hydroxyethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (35b)



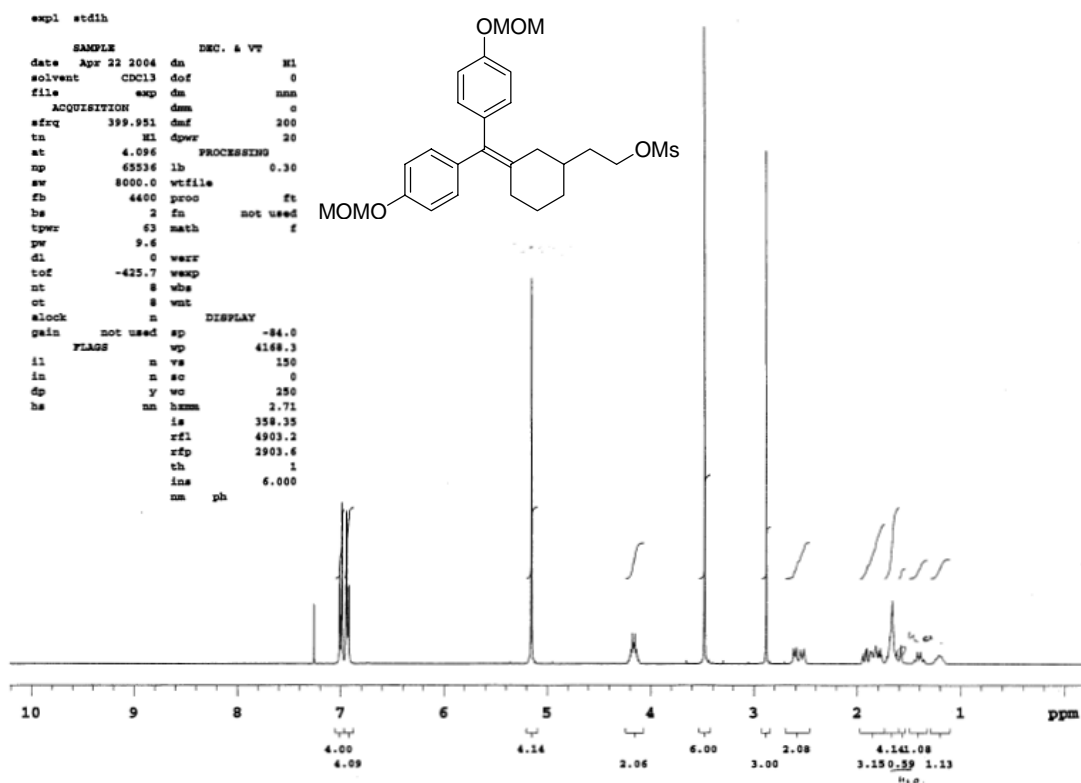
¹³C NMR (100 MHz, methanol-d₄)

3-(2-Hydroxyethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (35b)



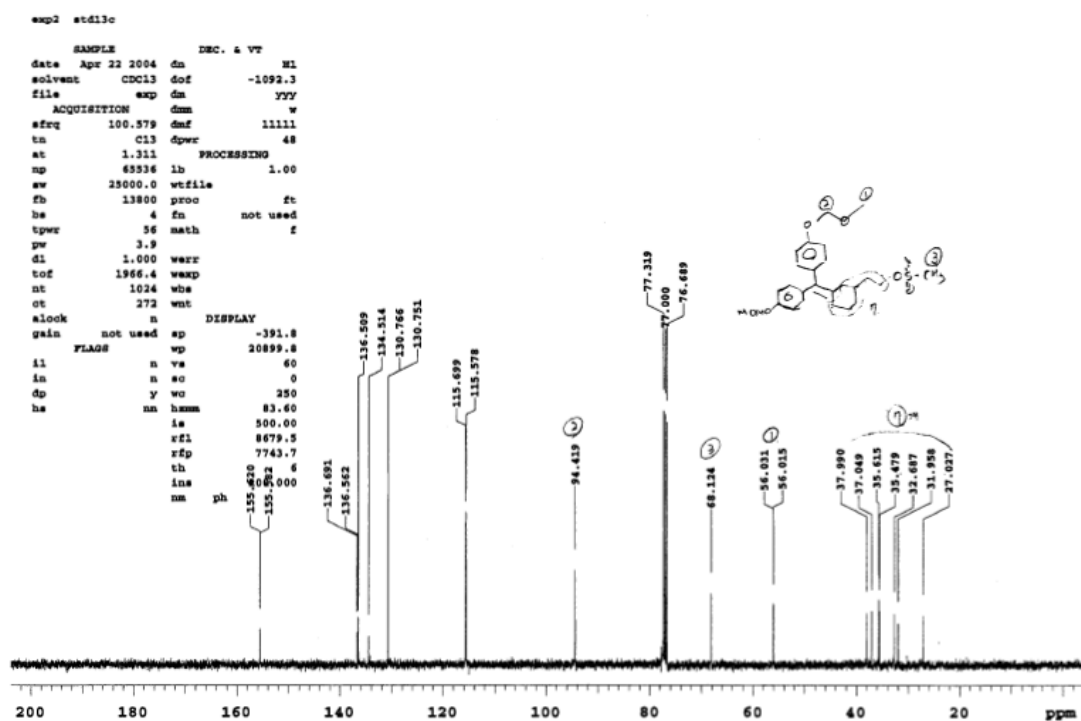
3-(2-Methanesulfonyloxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (36b). ^1H NMR (400 MHz, CDCl_3)

3-(2-Methanesulfonyloxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (36b)



^{13}C NMR (100 MHz, CDCl_3)

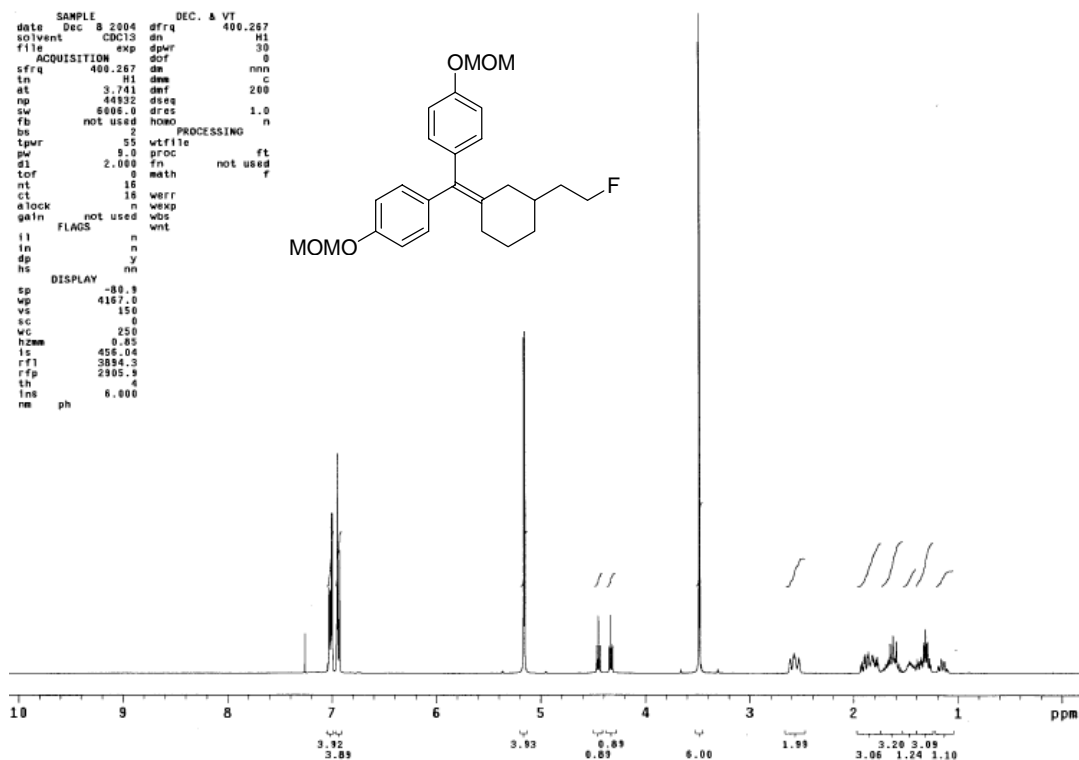
3-(2-Methanesulfonyloxyethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (36b)



3-(2-Fluoroethyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

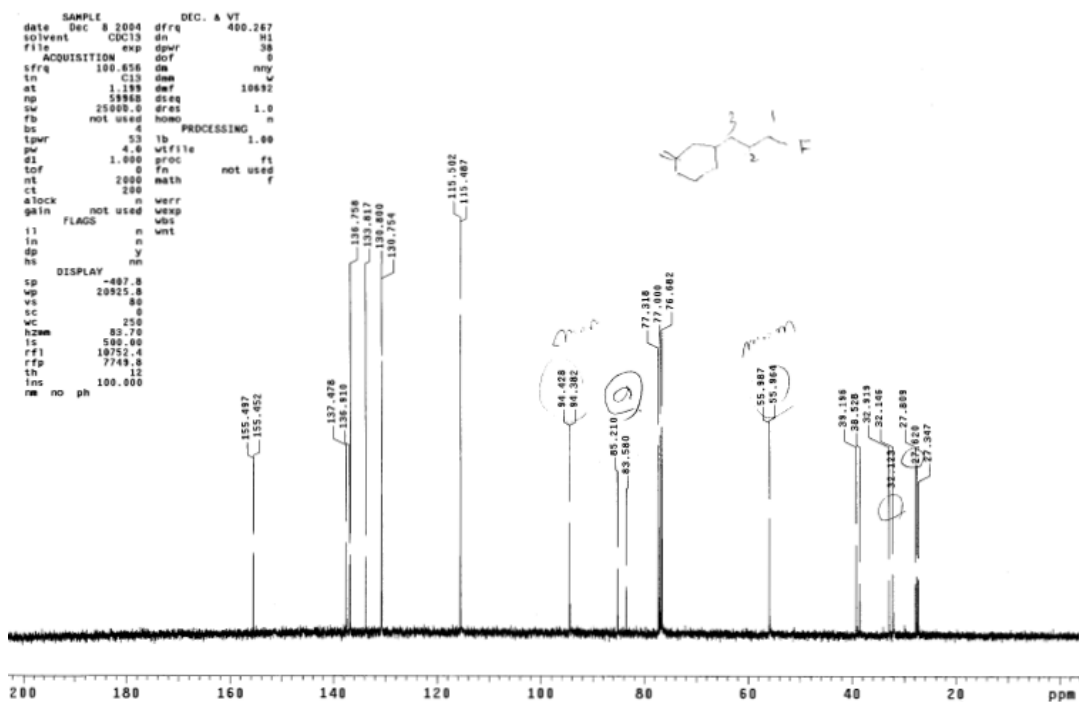
¹H NMR (400 MHz, CDCl₃)

3-(3-Fluoropropyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.



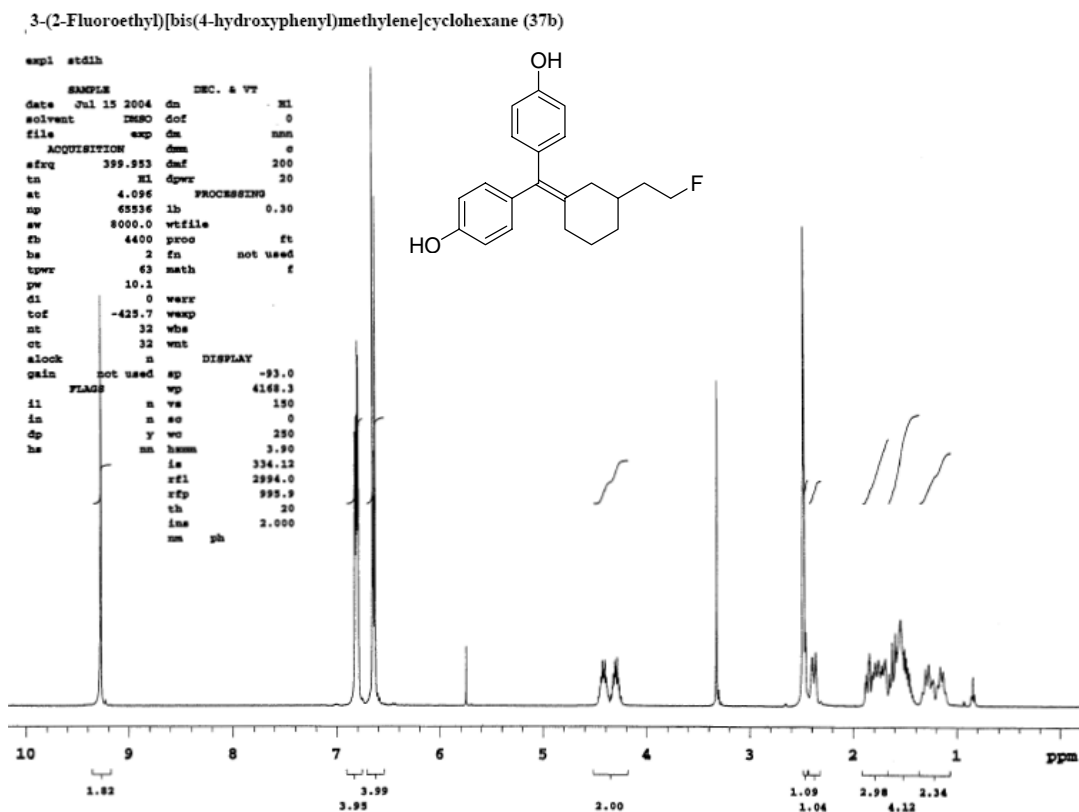
¹³C NMR (100 MHz, CDCl₃)

3-(3-Fluoropropyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

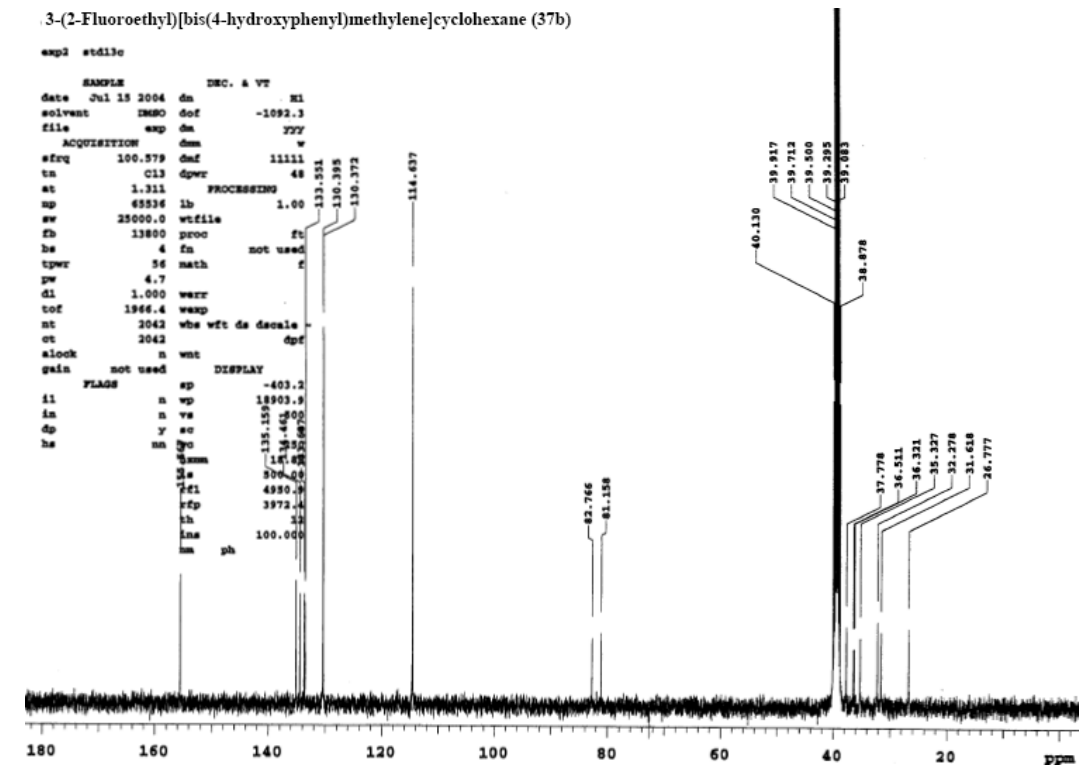


3-(2-Fluoroethyl)[bis(4-hydroxyphenyl)methylene]cyclohexane (37b).

¹H NMR (400 MHz, methanol-d₄)



¹³C NMR (100 MHz, methanol-d₄)

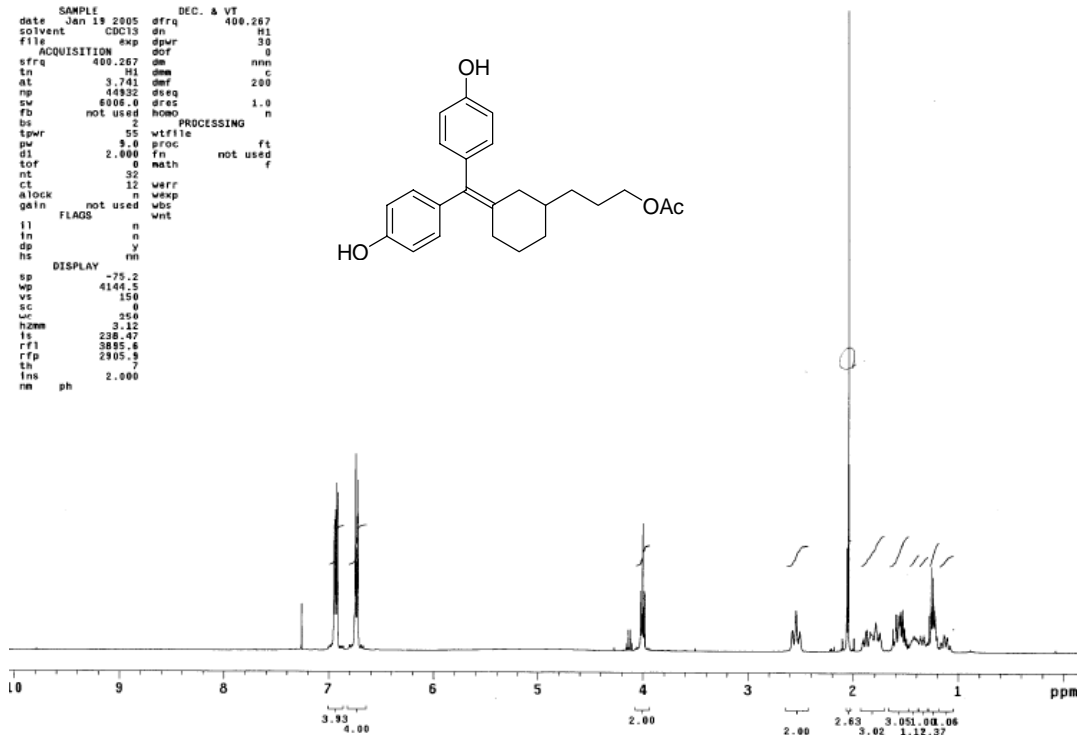
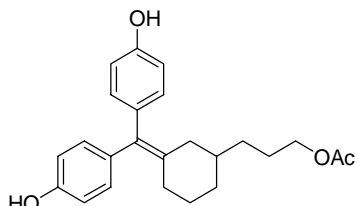


3-(3-Acetoxy-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (30c).
¹H NMR (400 MHz, CDCl₃)

3-(3-Acetoxy-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (30c)

```

exp2 stdih
SAMPLE
date Jan 18 2005 dfrq DEC. & VT 400.267
solvent CDCl3 dn H1
file ACQUISITION exp dpwr 30
sfrq 400.267 dm dof 0
tn H1 dm nnn
at 3.741 dmf 200
np 44932 dseq
sw 6505.0 dres 1.0
fb not used homo n
bs 2 PROCESSING
tpwr 55 wfile
pw 3.0 proc ft
d1 2.000 fn not used
tof 0 math f
nt 32
ct 12 werr
alock n wbp
gain not used wbs
flags n wnt
f1 n
f2 n
dp y
hs nm
DISPLAY
sp -75.2
wp 4144.5
vs 150
sc 0
wc 250
hznm 3.12
fs 238.47
rf1 3895.6
rfp 2305.5
th 7
lms nm ph 2.000
    
```

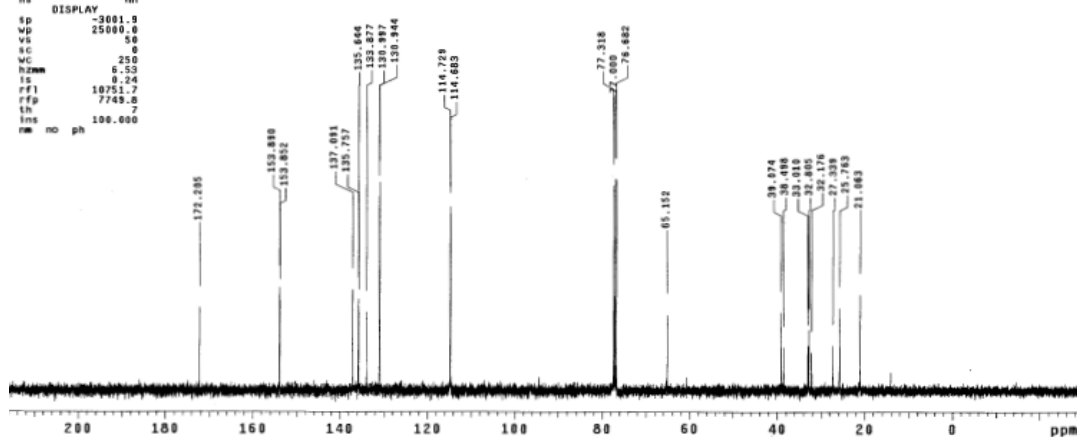


¹³C NMR (100 MHz, CDCl₃)

3-(3-Acetoxy-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (30c)

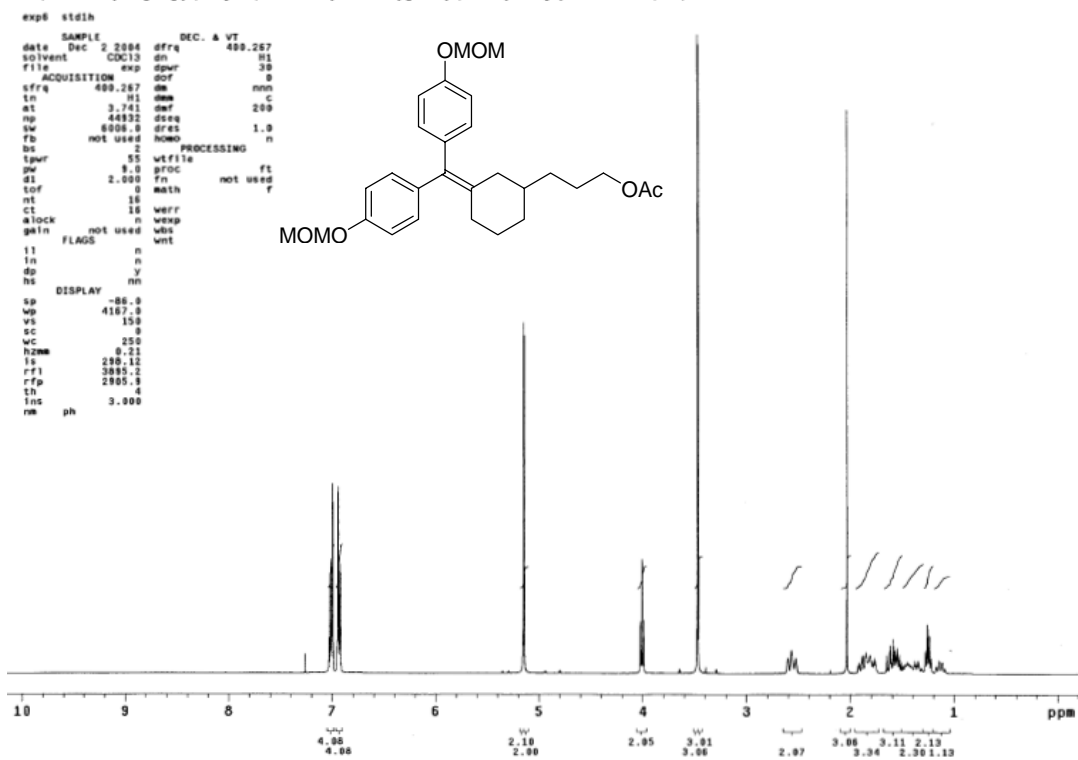
```

exp1 std13c
SAMPLE
date Jan 18 2005 dfrq DEC. & VT 400.267
solvent CDCl3 dn H1
file ACQUISITION exp dpwr 30
sfrq 100.626 dm dof 0
tn C13 dm mny
at 1.188 dmf 10692
np 58958 dseq
sw 25000.0 dres 1.0
fb not used homo n
bs 4 PROCESSING
tpwr 53 lb wfile 1.00
pw 4.0 proc ft
d1 1.000 fn not used
tof 0 math f
nt 1824
ct 300
alock n werr
gain not used wbp
flags n wbs wft bc ds dsca-
f1 n wnt le dpf
f2 n
dp y
hs nm
DISPLAY
sp -3001.9
wp 25000.0
vs 50
sc 0
wc 250
hznm 6.53
fs 8.24
rf1 10751.7
rfp 7743.0
th 7
lms nm no ph 100.000
    
```



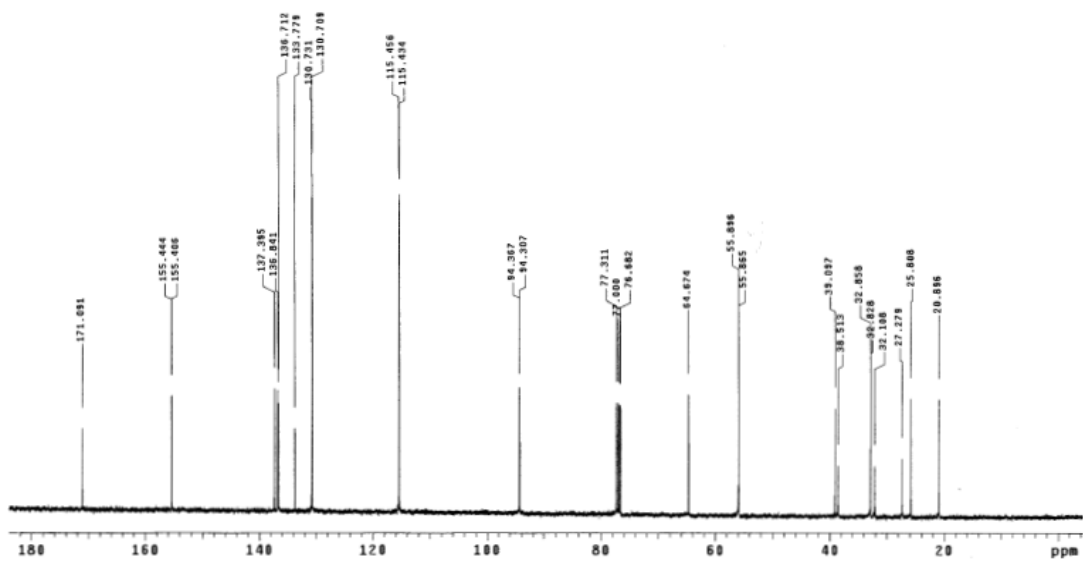
3-(3-Acetoxy-*n*-propyl)-1-[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (33c).
¹H NMR (400 MHz, CDCl₃)

3-(3-Acetoxy-*n*-propyl)-1-[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (33c)



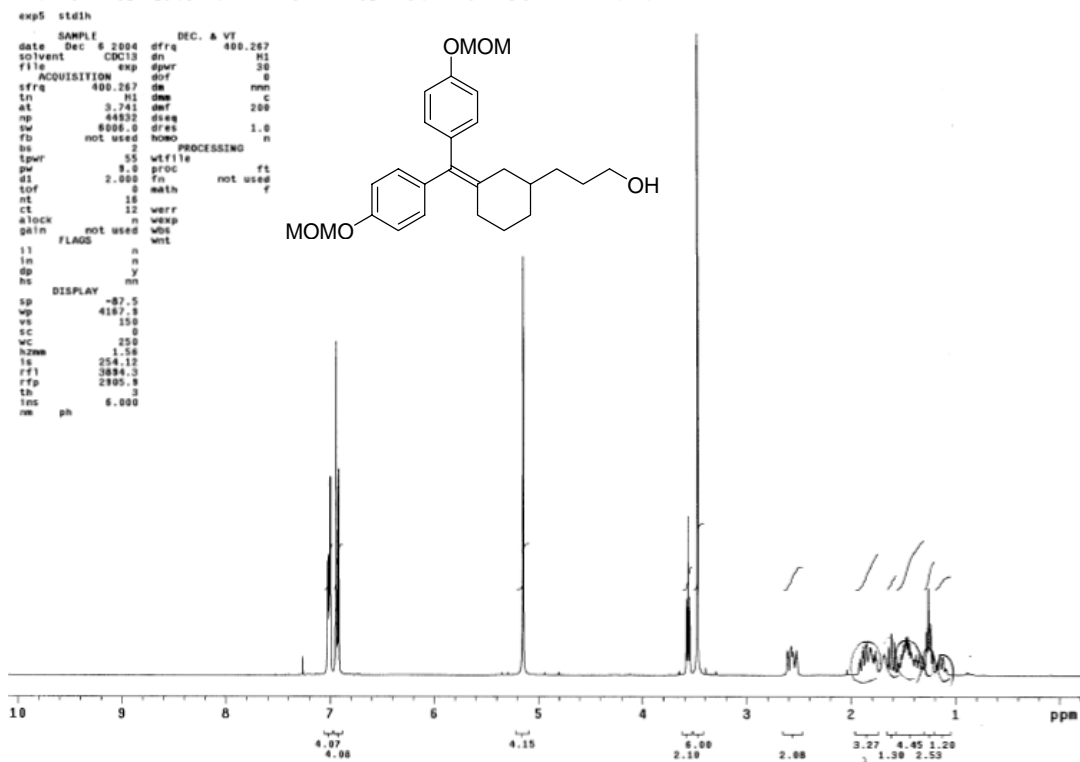
¹³C NMR (100 MHz, CDCl₃)

3-(3-Acetoxy-*n*-propyl)-1-[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (33c)



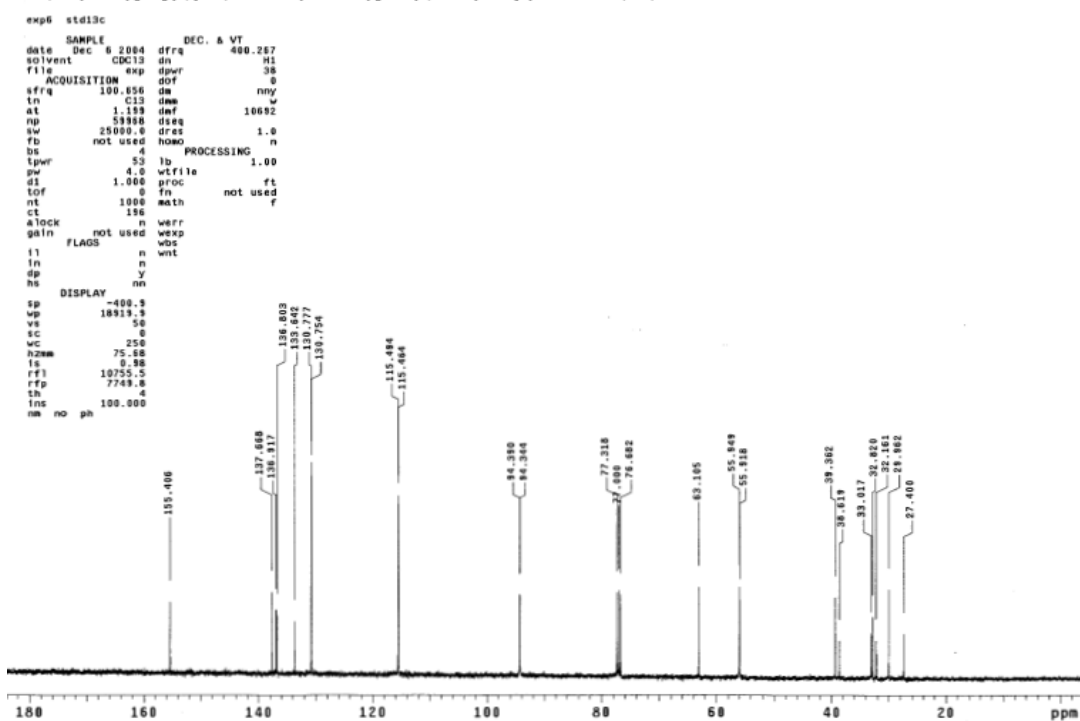
3-(3-Hydroxypropyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34c).
¹H NMR (400 MHz, CDCl₃)

3-(3-Hydroxypropyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34c)



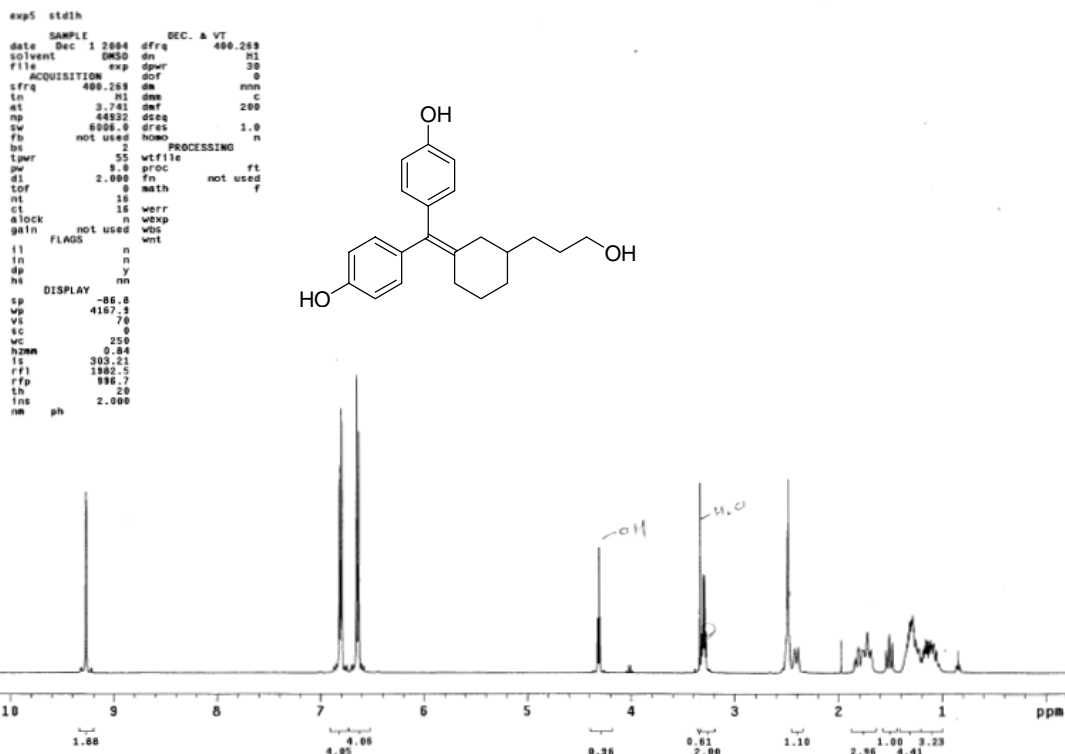
¹³C NMR (100 MHz, CDCl₃)

3-(3-Hydroxypropyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane (34c)



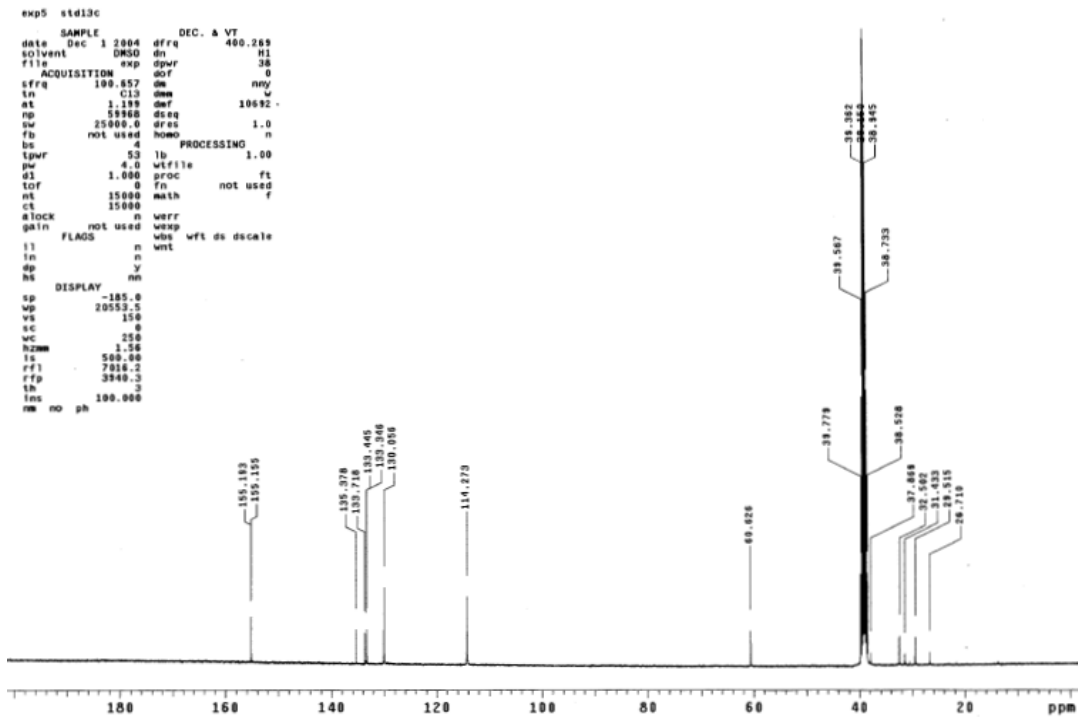
3-(3-Hydroxy-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (35c).
¹H NMR (400 MHz, DMSO-*d*₆)

3-(3-Hydroxy-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (35c)



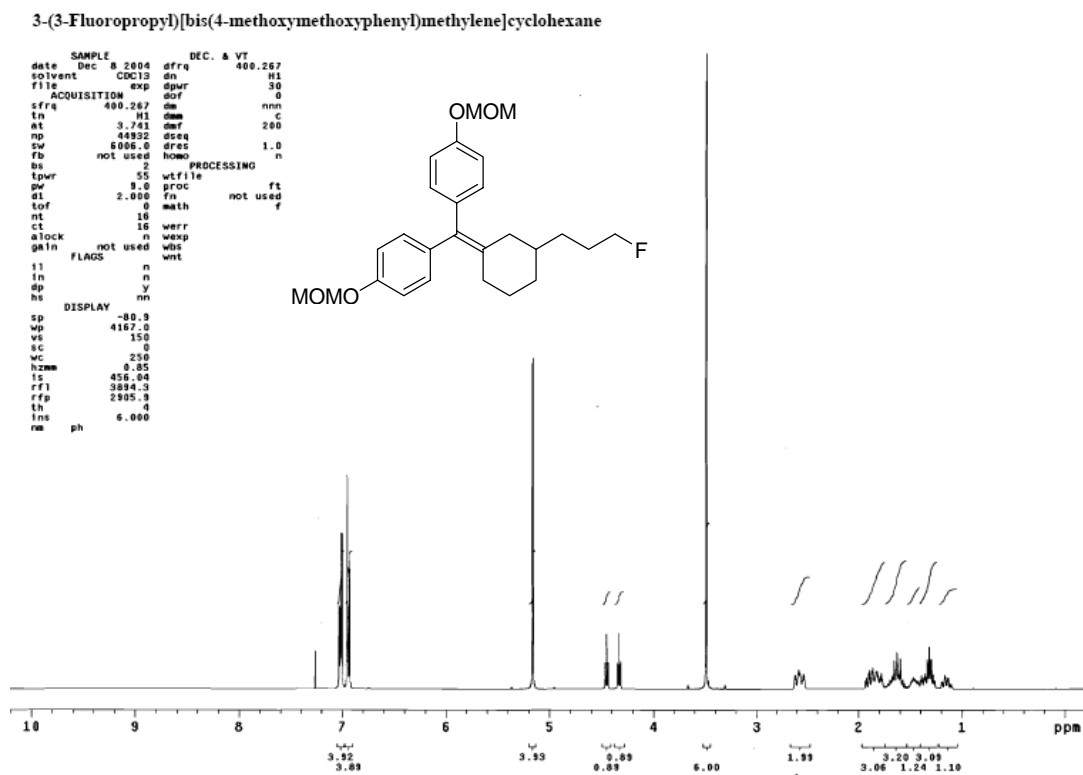
¹³C NMR (100 MHz, DMSO-*d*₆)

3-(3-Hydroxy-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (35c)

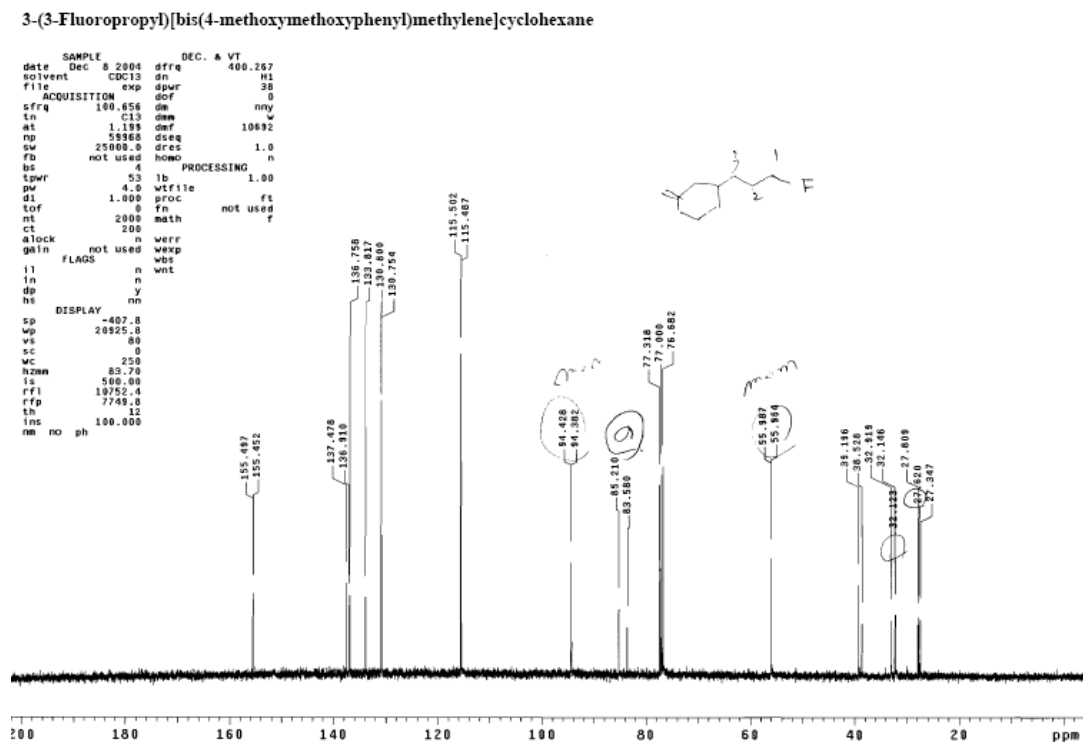


3-(3-Fluoropropyl)[bis(4-methoxymethoxyphenyl)methylene]cyclohexane.

¹H NMR (400 MHz, CDCl₃)



¹³C NMR (100 MHz, CDCl₃)



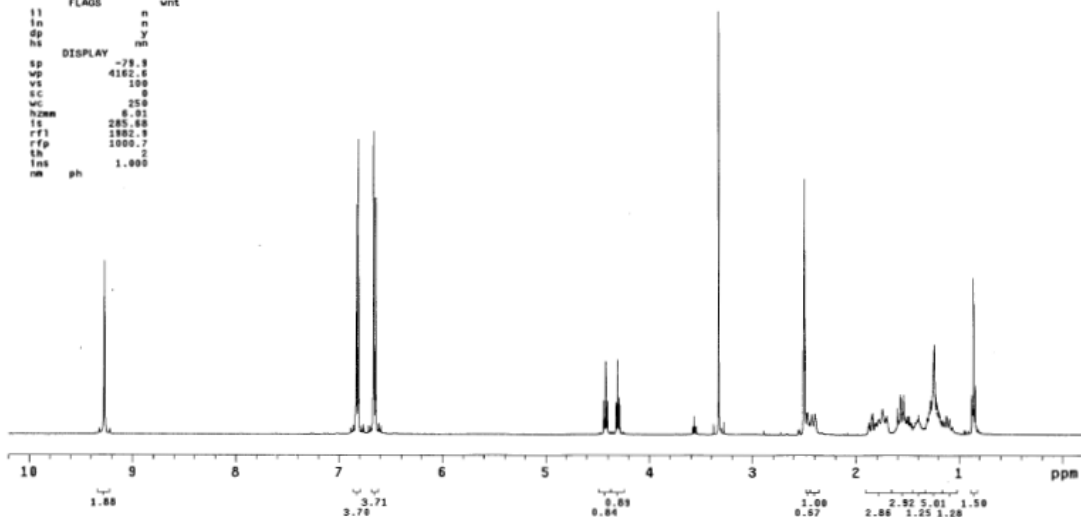
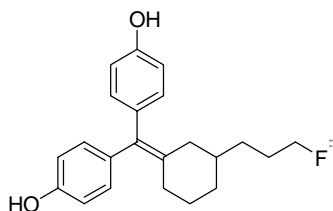
3-(3-Fluoro-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (37c).

¹H NMR (400 MHz, DMSO-*d*₆)

3-(3-Fluoro-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (37c)

```

exp4 std1h
SAMPLE
date Jul 13 2005 dfrq 400.269 DEC. & VT
solvent DMSO dn H1
file
ACQUISITION exp dpwr 30
sfrq 400.269 dn nmx
tn H1 dm C
nt 3.743 dmf 200
np 44932 dseq
sw 6006.0 dres 1.0
fb not used homo n
bs 2
tpwr 55 wtfite
pw 8.0 proc ft
d1 2.000 fn not used
tof 0 math f
nt 36
ct 16 verr
alock not used n wexp
gain not used wbc wnt
ll
in n
sp DISPLAY -79.9
wp 4182.4
vs 100
sc 0
wc 250
hzmm 6.01
ls 285.48
rf1 1892.9
rfp 1000.7
ln 2
ins ph 1.000
nm
    
```

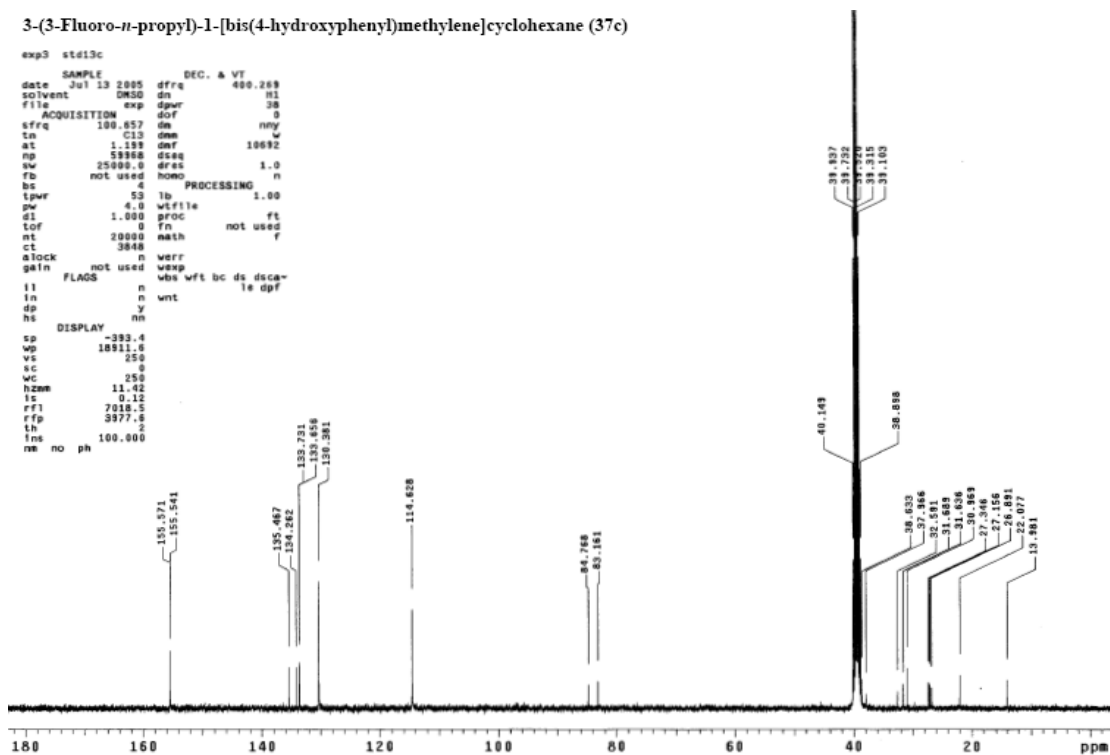


¹³C NMR (100 MHz, acetone-*d*₆)

3-(3-Fluoro-*n*-propyl)-1-[bis(4-hydroxyphenyl)methylene]cyclohexane (37c)

```

exp3 std13c
SAMPLE
date Jul 13 2005 dfrq 400.269 DEC. & VT
solvent DMSO dn H1
file
ACQUISITION exp dpwr 30
sfrq 100.657 dn nmy
tn C13 dm 10092
nt 1.193 dmf
np 59368 dseq
sw 25000.0 dres 1.0
fb not used homo n
bs 6
tpwr 53 lb PROCESSING 1.00
pw 4.0 wtfite
d1 1.000 proc ft
tof 0 fn not used
nt 20000 math
ct 3848
alock not used n verr
gain not used wexp
ll
in n
sp DISPLAY -393.4
wp 18911.6
vs 250
sc 0
wc 250
hzmm 11.42
ls 0.12
rf1 7019.5
rfp 3977.6
ln 2
ins no ph 100.000
nm
    
```



3 . HPLC purity data for compounds (37b and 37c)

37b was detected at 250 nm wavelength and **37c** at 254 nm wavelength.

Room temperature					
Compd.	Column and Condition	Pressure	Flow late	Retention time (min)	Purity (%)
37b	Alltech silica 5 μ (250X4.6 mm) 97% EtOAc/3% IPA	540 psi	1 ml/min	9.95	>95%
	Phenomenex LUNA C8(2) 5 μ (150X4.6 mm) 50% CH ₃ CN/50% H ₂ O	1168 psi	1 ml/min	11.8	>95%
37c	Alltech Econosil silica 10 μ (250X10 mm) 100% EtOAc	1.9 MPa	3 ml/min	7.25	>95%
	RS Tech OP C18-51002546 (250X4.6 mm) 70% CH ₃ CN/30% H ₂ O	9.2 MPa	1 ml/min	9.55	>95%

HPLC trace of 37b

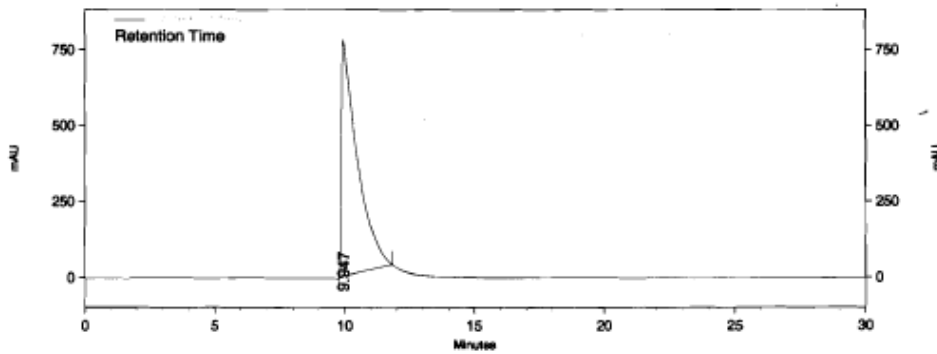
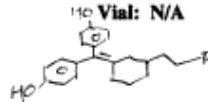
Normal Phase

Alltech .. Alltima Silica 5µ
Lot No AT0167
part No 8817) Length 250mm

Area Percent Report Serial No. 01021121, ID 4.6mm Page 1 of 1
Data File: D:\Jay\Data\cyclofenil\Jay_3-FEC_after_dry_normal_97%EA_3%IPA_1.dat
Acquired: 7/17/2004 11:33:18 AM Printed: 07/17/2004
02:00:48 PM

540PSI

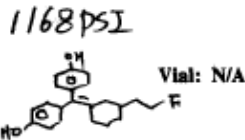
Analyst: System
Sample ID: Jay_3-FEC_after_dry_normal_97%EA_3%IPA
Injection Volume: 0 20µL



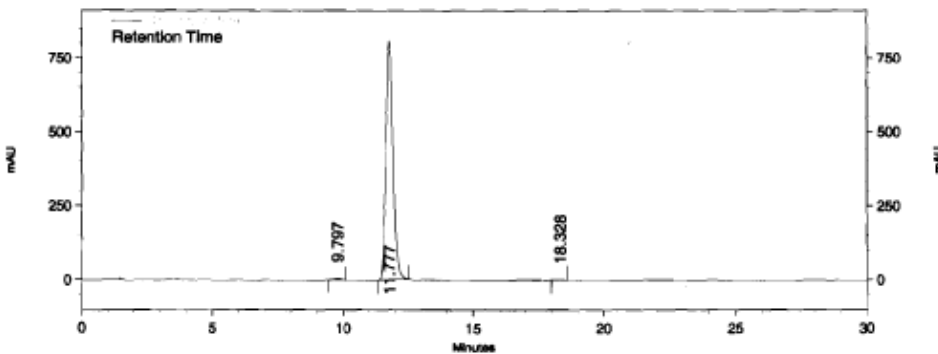
Reverse Phase

phenomenex P/No 00F-4249-EO
LUNA 5µ C8(2)
150 x 4.6mm
S/No 303799

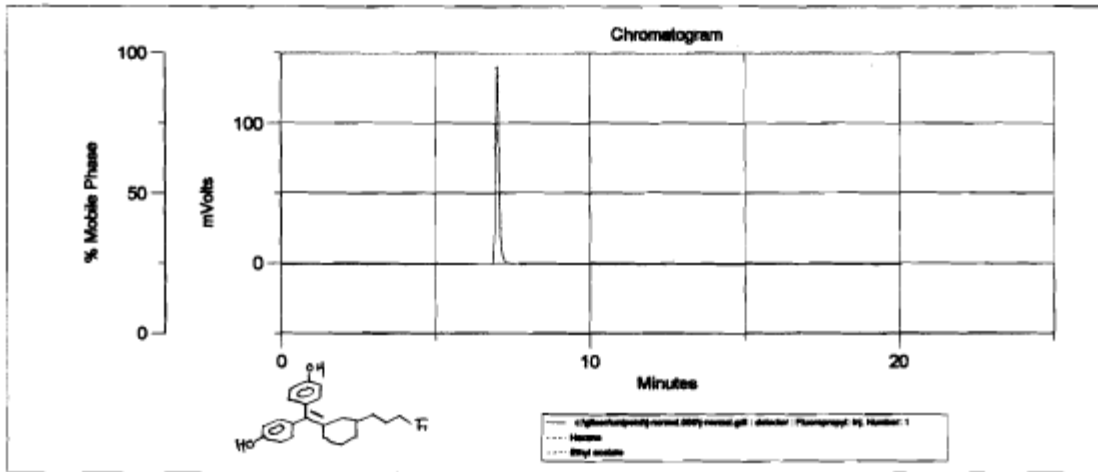
Area Percent Report Page 1 of 1
Data File: D:\Jay\Data\cyclofenil\Jay_3-FEC_after_dry_reverse_50%ACN_50%H2O_1.dat
Acquired: 7/16/2004 1:16:19 AM Printed: 07/16/2004
01:56:05 AM



Analyst: System
Sample ID: Jay_3-FEC_after_dry_reverse_50%ACN_50%H2O
Injection Volume: 0 20µL



HPLC trace of 37c
Normal Phase

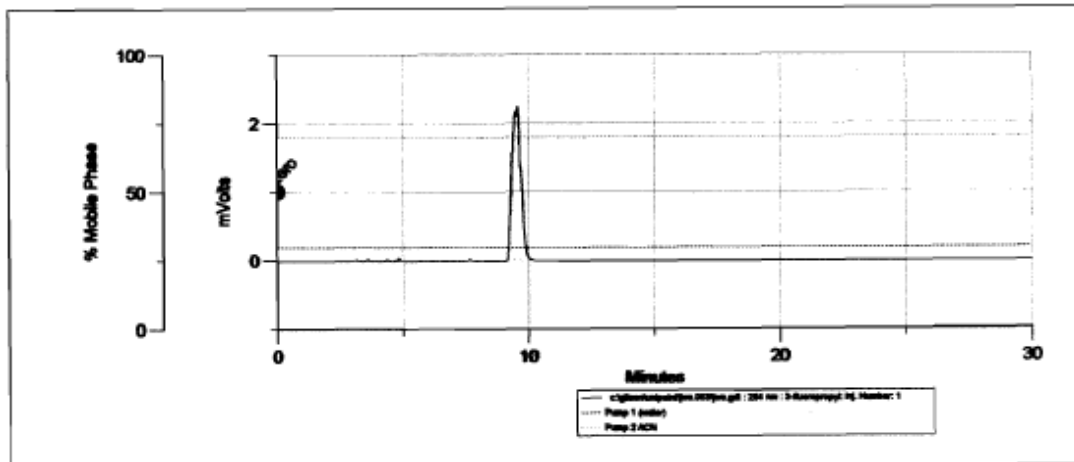


Column status

Alltech
Normal phase
Cat. No.: Econosil Silica 10 μ
250mm x 10 mm

1.9 Mpa
100% EA
3ml/min.

Reverse Phase



Column status

RS tech
reverse phase
Cat. No. OP C18-51002546
250 mm X 4.6 mm

70% CH₃CN
30% H₂O

9.2 Mpa.

flow 1ml/min

70% CH₃CN 30% H₂O

flow rate: 1ml/min

