

Supporting Information

A New Look at Boron Enolate Chemistry: Aminative C-C Bond Formation Using Diaminoboron enolate with Aldehyde

Michinori Suginome,* Lars Uehlin, Akihiko Yamamoto, and Masahiro Murakami*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, and PRESTO, Japan Science and Technology Corporation (JST), Sakyo-ku, Kyoto 606-8501, Japan

Contents

1. General
2. Preparation of boron enolates
3. Aminative alkylation of aldehydes
4. ^1H and ^{13}C NMR spectra of new compounds

1. General

All reactions were performed in drybox or using Schlenk technique under a nitrogen atmosphere with magnetic stirring. ^1H NMR spectra were recorded on a Varian Mercury-400 (400 MHz) or Varian GEMINI-2000 (300 MHz) spectrometer using CDCl_3 as solvent and tetramethylsilane as internal standard or using C_6D_6 as solvent and internal standard. ^{13}C NMR spectra were recorded on a Varian GEMINI-2000 spectrometer at 75.45 MHz with CDCl_3 as solvent. Chemical shifts of the ^{13}C NMR spectra were measured relative to CDCl_3 (77.0 ppm). ^{11}B NMR spectra were recorded on a Varian Mercury-400 spectrometer at 128.48 MHz with C_6D_6 as solvent. Chemical shifts of the ^{11}B NMR spectra were measured relative to $\text{BF}_3\cdot\text{Et}_2\text{O}$ (0 ppm). High resolution mass (FAB) spectra were recorded on a JEOL JMS-700 spectrometer.

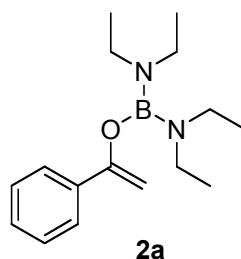
Anhydrous solvents were purchased from Kanto Chemical Co. Aldehydes and ketones were dried over CaH_2 and distilled under Ar. Bis(diamino)chloroboranes were

synthesized according to the literature method.¹

2. Preparation of boron enolates 2a –2e

2.1. General procedure.

To a solution of diisopropylamine (10 mmol) in THF (10 mL) was added *n*-butyllithium (1.6 M in hexane, 6.3 mL, 10 mmol) dropwise at 0 °C. Stirring was continued for 30 min. at 0 °C. To the reaction mixture cooled to -78 °C was added dropwise a solution of ketone (10 mmol) in THF (10 mL). After stirring for 15 min., chlorobis(dialkylamino)borane (10 mmol) was added slowly at -78 °C. The reaction mixture was allowed to warm up to room temperature and stirred further for 3 h. Evaporation of the volatile material followed by addition of hexane (20 mL) to the residue resulted in precipitation of LiCl, which was filtered off. Evaporation of hexane gave essentially pure boron enolate, which can be purified by distillation. Obtained yields varied between 82% and 97%.



1-(1-bis(diethylamino)boryloxyvinyl)benzene (2a) (b.p. 90 °C/ 0.3 mmHg)

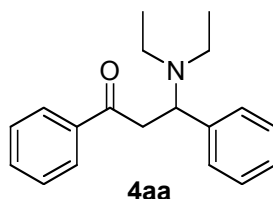
¹H NMR (C₆D₆): δ 0.97 (t, *J* = 7.2 Hz, 12H), 2.90 (q, *J* = 7.2 Hz, 8H), 4.42 (d, *J* = 1.2 Hz, 1H), 4.85 (d, *J* = 1.2 Hz, 1H), 7.05-7.18 (m, 3H) 7.77 (dd, *J* = 7.2 Hz, *J* = 1.2 Hz, 2H). ¹³C NMR (C₆D₆): δ 15.6, 41.1, 87.8, 125.5, 127.9, 128.5, 137.8, 156.9. ¹¹B NMR (C₆D₆): δ = 24.4.

3. Aminative alkylation of aldehydes

¹Chavant, P. Y.; Vaultier M. *J. Organomet. Chem.* **1993**, 455, 37-46. Gerrard, W.; Lappert, M. F.; Pearce, C.A. *J. Chem Soc.* **1957**, 381-386.

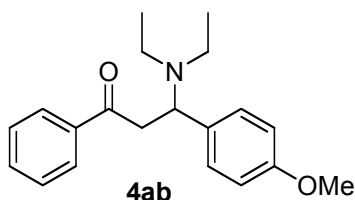
3.1. General procedure.

Boron enolate **2** (0.25 mmol) was dissolved in THF or DMF (0.5 mL). Aldehyde (0,50 mmol) was then added, and the mixture was stirred at 50 °C for 5 h in THF or for 1.5 to 2 h in DMF. To the reaction mixture were added ice water and, subsequently, *tert*-butyl methyl ether (15 mL). Basic components were extracted three times with hydrochloric acid (0.5 M, 5 mL × 3). The combined acid layers were washed with *tert*-butyl methyl ether (10 ml) and cooled to 0 °C. The pH of the solution was brought to 8 by addition of conc. ammonia solution. The organic material was extracted with *tert*-butyl methyl ether and washed with water (10 mL). Removal of the solvent in vacuo at 0 °C afforded the products as colorless or pale yellow oil.



3-Diethylamino-1,3-diphenyl-propan-1-one (**4aa**)²

¹H NMR (C₆D₆): δ = 0.90 (t, *J* = 7.2 Hz, 6H), 2.22 (dq, *J* = 13.2, 6.8 Hz, 2H), 2.42 (dq, *J* = 13.2, 7.2 Hz, 2H), 3.11 (dd, *J* = 15.6 Hz, *J* = 7.6 Hz, 1H), 3.26 (dd, *J* = 15.6 Hz, *J* = 6.4 Hz, 1H), 4.70 (t, *J* = 7.0 Hz, 1H), 6.98-7.24 (m, 8H), 7.78 (dd, *J* = 6.8, 1.6 Hz, 2H). ¹³C NMR (C₆D₆): δ = 13.9, 41.2, 44.0, 60.5, 127.5, 128.9, 129.0, 130.6, 132.9, 141.8, 199.6.

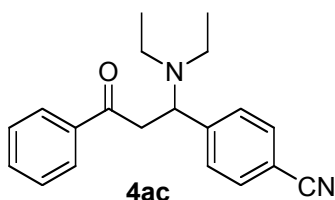


3-Diethylamino-3-(4-methoxy-phenyl)-1-phenyl-propan-1-one (**4ab**)

¹H NMR (C₆D₆): δ 0.98 (t, *J* = 7.2 Hz, 6H), 2.31 (dq, *J* = 13.2, 6.8 Hz, 2H), 2.58 (dq, *J* =

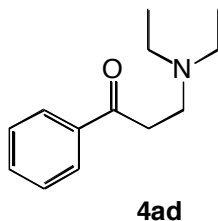
²Hosomi, A.; Yanagi, T.; Hojo, M.; *Tetrahedron Lett.* **1991**, 32, 2371-2374; Clark, J. H.; Cork, D. G.; Gibbs, H. W.; *Perkin Trans. 1* **1983**, 9, 2253-2258; Clark, J. H.; Cork, D. G.; *Chem. Commun.* **1982**, 11, 935-936.

13.2, 7.2 Hz, 2H), 3.38 – 3.50 (m, 2H), 3.76 (s, 3H), 4.52 (t, $J = 7.0$ Hz, 1H), 6.81 (d, $J = 8.8$ Hz, 2H), 7.21 (d, $J = 8.8$ Hz, 2H), 7.45 (t, $J = 8.0$ Hz, 2H), 7.55 (δ , $J = 6.8$ Hz, 1H), 7.91 (dd, $J = 8.4, 1.6$ Hz, 2H). ^{13}C NMR (C_6D_6): δ 13.0, 41.3, 43.2, 55.1, 59.2, 113.3, 128.1, 128.4, 129.4, 130.3, 132.8, 137.5, 158.5, 199.4. IR (neat): 2970, 2834, 1683, 1609, 1511, 1447, 1246, 1179, 1036, 831, 708 cm^{-1} . MS (FAB): m/z (%) 312 (12) $[\text{M}+\text{H}^+]$, 289 (19), 239 (37), 192 (11), 154 (100), 136 (66), 119 (10), 107 (18), 89 (14), 77 (12), 65 (5). HRMS for $\text{C}_{20}\text{H}_{25}\text{O}_2\text{N}\cdot\text{H}^+$: calcd.: 312.1964, found: 312.1964.



4-(3-Diethylamino-3-phenyl-propionyl)-benzonitrile (4ac)

^1H NMR (CDCl_3): δ 0.89 (t, $J = 7.2$ Hz, 6H), 2.36 (dq, $J = 13.2$ Hz, $J = 6.8$ Hz, 2H), 2.52 (dq, $J = 13.2$ Hz, $J = 6.8$ Hz, 2H), 3.41-3.61 (m, 2H), 4.60 (dd, $J = 8.0, 5.6$ Hz, 1H), 7.41-7.57 (m, 8H) 7.89 (dd, $J = 7.2, 1.6$ Hz, 2H). ^{13}C NMR (CDCl_3): δ 13.0, 39.7, 43.4, 59.3, 110.6, 118.9, 127.9, 128.7, 129.0, 131.9, 133.3, 136.9, 147.2, 198.5. IR (neat): 2970, 2811, 2229, 1683, 1607, 1385, 1206, 1065, 841, 691 cm^{-1} . MS (FAB): m/z (%) 307 (31) $[\text{M}+\text{H}^+]$, 277 (5), 234 (5), 187 (100), 159 (4), 135 (4), 105 (39), 89 (6), 77 (8). HRMS for $\text{C}_{20}\text{H}_{23}\text{ON}_2\cdot\text{H}^+$: calcd.: 307.1810, found: 307.1810.

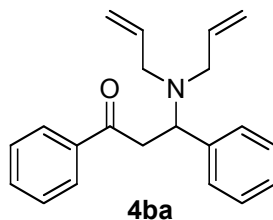


3-(Diethylamino)-1-phenylpropan-1-one (4ad)³

^1H NMR (C_6D_6): δ 1.05 (t, $J = 7.2$ Hz, 6H), 2.57 (q, $J = 7.2$ Hz, 2H), 2.91 (dd, $J = 8.4$ Hz, $J = 6.4$ Hz, 2H), 3.14 (dd, $J = 8.0, 6.8$ Hz, 2H), 7.45 (dt, $J = 6.8, 1.2$ Hz, 2H), 7.53 (t, $J = 6.0$

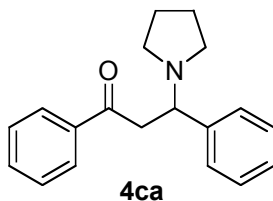
³ Rochin, C.; Babet, O.; Dunogues, J.; Duboudin, F. *Synthesis* **1986**, 8, 667-668.

Hz, 1H), 7.96 (dt, $J = 6.8, 1.2$ Hz, 2H). ^{13}C NMR (C_6D_6): δ 11.7, 36.3, 46.9, 47.8, 128.1, 128.6, 133.8, 137.1, 199.9.



3-Diallylamino-1,3-diphenyl-propan-1-one (4ba)

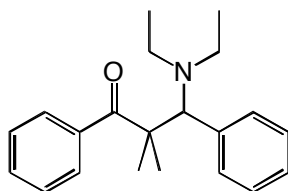
^1H NMR (C_6D_6): δ 2.73 (dd, $J = 14.4$ Hz, $J = 7.6$ Hz, 2H), 3.09 (dd, $J = 15.6$ Hz, $J = 7.2$ Hz, 1H), 3.15 – 3.20 (m, 2H), 3.31 (dd, $J = 15.6$ Hz, $J = 7.6$ Hz, 1H), 4.77 (t, $J = 7.2$ Hz, 1H), 4.93 – 5.10 (m, 4H), 5.67 – 5.76 (m, 2H), 6.99–7.18 (m, 7H), 7.34 (d, $J = 7.6$ Hz, 1H), 7.77 (dd, $J = 6.8$ Hz, $J = 1.8$ Hz, 2H). ^{13}C NMR (C_6D_6): $\delta = 42.7, 54.7, 61.2, 118.3, 128.9, 129.9, 130.0, 130.1, 130.3, 138.0, 138.9, 141.2, 199.2$. IR (film): 3080, 2813, 1686, 1580, 1493, 1449, 1285, 996, 919, 702 cm^{-1} . MS (FAB): m/z (%) 306 (89) $[\text{M}+\text{H}^+]$, 289 (17), 264 (20), 186 (100), 154 (92), 136 (54), 105 (52), 96 (39), 89 (10). HRMS for $\text{C}_{21}\text{H}_{24}\text{ON}\cdot\text{H}^+$: calcd.: 306.1858, found: 306.1856.



1,3-Diphenyl-3-pyrrolidin-1-yl-propan-1-one (4ca)⁴

^1H NMR (C_6D_6): δ 1.47 (brm, 4H), 2.34 (brm, 4H), 3.12 (dd, $J = 16.0, 6.8$ Hz, 1H), 3.35 (dd, $J = 16.0, 6.0$ Hz, 1H), 4.13 (t, $J = 6.4$ Hz, 1H), 6.91–7.12 (m, 6H), 7.41 (d, $J = 8.0$ Hz, 1H), 7.77 (dd, $J = 6.8, 1.8$ Hz, 2H). ^{13}C NMR (C_6D_6): δ 24.0, 46.2, 52.7, 65.9, 127.7, 128.7, 128.9, 132.9, 138.3, 144.2, 197.8.

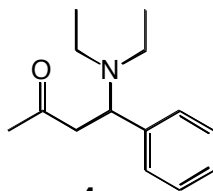
⁴Kinastowski, S.; Grabarkiewicz-Szczesna, J.; Kosteci, M.; *Pol. J. Chem.* **1980**, 9, 1697-1706.



4da

3-Diethylamino-2,2-dimethyl-1,3-diphenylpropan-1-one (4da)

^1H NMR (CDCl_3): δ 0.82 (t, $J = 7.2$ Hz, 6H), 1.05 (s, 3H), 1.38 (s, 3H), 2.21 (dq, $J = 13.2$, 6.8 Hz, 2H), 2.61 (dq, $J = 13.2$, 7.2 Hz, 2H), 4.33 (s, 1H), 7.17-7.33 (m, 8H), 7.51 (dd, $J = 6.8$, 1.6 Hz, 2H). ^{13}C NMR (CDCl_3): δ 12.5, 22.9, 27.1, 45.2, 52.8, 71.2, 110.9, 118.8, 127.0, 127.7, 127.8, 130.1, 130.6, 138.8, 199.2. IR (neat): 2968, 2931, 2815, 1697, 1493, 1468, 1382, 1057, 756, 700 cm^{-1} . MS (FAB): m/z (%) 310 (43) $[\text{M}+\text{H}^+]$, 289 (17), 188 (6), 163 (48), 154 (100), 136 (58), 105 (18), 89 (10), 77 (9). HRMS for $\text{C}_{21}\text{H}_{28}\text{ON}\cdot\text{H}^+$: calcd.: 310.2171, found: 310.2171.

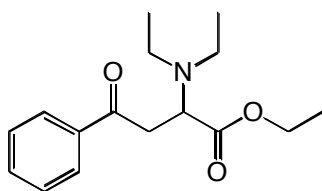


4ea

4-(diethylamino)-4-phenylbutan-2-one (4ea)⁵

^1H NMR (CDCl_3): δ 1.01 (t, $J = 6.9$ Hz, 6H), 2.10 (s, 3H), 2.26 (dq, $J = 13.2$, 7.2 Hz, 2H), 2.60 (dq, $J = 14.7$, 7.2 Hz, 2H), 2.79 (dd, $J = 15.0$, 7.5 Hz, 1H), 3.01 (dd, $J = 15.0$, 6.9 Hz, 1H), 4.33 (t, $J = 7.5$ Hz, 1H), 7.23 – 7.33 (m, 5H). ^{13}C NMR (CDCl_3): δ 13.1, 30.4, 43.2, 46.5, 59.6, 127.1, 128.1, 128.3, 139.9, 207.9.

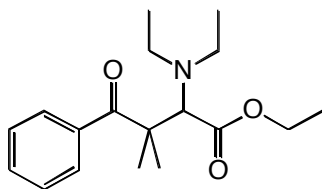
⁵ Clark, J. H.; Cork, D. G., *Chem. Commun.* **1982**, 11, 635-636.



4ae

Ethyl 2-(diethylamino)-4-oxo-4-phenylbutanoate (4ae)

^1H NMR (C_6D_6): δ 1.05 (t, $J = 7.2$ Hz, 6H), 1.28 (t, $J = 7.2$ Hz, 3H), 2.56 (dq, $J = 12.8$, 6.8 Hz, 2H), 2.67 (dq, $J = 12.8$, 7.2 Hz, 2H), 3.31 (dd, $J = 17.6$, 4.8 Hz, 1H), 3.57 (dd, $J = 17.6$, 8.4 Hz, 1H), 4.15-4.19 (m, 3H), 7.47 (t, $J = 8.0$ Hz, 2H), 7.53-7.59 (m, 1H), 7.97 (dd, $J = 8.8$, 1.6 Hz, 2H). ^{13}C NMR (C_6D_6): δ 13.9, 14.3, 38.7, 45.1, 58.7, 60.4, 128.1, 128.6, 133.1, 137.0, 172.4, 199.6. IR (neat): 2964, 2858, 1698, 1636, 1470, 1397, 1260, 1065, 801, 699 cm^{-1} . MS (FAB): m/z (%) 278 (90) [$\text{M}+\text{H}^+$], 204 (100), 158 (46), 154 (29), 136 (19), 105 (28), 77 (8), 56 (7). HRMS for $\text{C}_{16}\text{H}_{24}\text{O}_3\text{N}\cdot\text{H}^+$: calcd.: 278.1756, found: 278.1749.



4de

Ethyl 2-(diethylamino)-3,3-dimethyl-4-oxo-4-phenylbutanoate (4de)

^1H NMR (C_6D_6): δ 1.05 (t, $J = 7.2$ Hz, 6H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.34 (s, 6H), 2.57 (dq, $J = 13.2$, 7.2 Hz, 2H), 2.68 (dq, $J = 13.2$, 6.8 Hz, 2H), 4.06 (s, 1H), 4.09-4.20 (m, 2H), 7.37-7.40 (m, 3H), 7.53 (dd, $J = 7.6$ Hz, $J = 1.6$ Hz, 2H). ^{13}C NMR (C_6D_6): δ 14.1, 14.4, 20.8, 26.2, 47.4, 60.1, 69.3, 127.1, 127.9, 129.9, 140.6, 172.4, 197.8. IR (film): 2971, 2933, 1723, 1679, 1466, 1382, 1198, 1069, 963, 758, 700 cm^{-1} . MS (FAB): m/z (%) 306 (20) [$\text{M}+\text{H}^+$], 289 (9), 232 (12), 158 (100), 154 (48), 136 (37), 120 (6), 105 (18), 89 (7), 73 (34), 56 (5). HRMS for $\text{C}_{18}\text{H}_{28}\text{O}_3\text{N}\cdot\text{H}^+$: calcd.: 306.2069, found: 306.207.

Reaction of boron enolate 5 with benzaldehyde. (Table 2)

Reactions were carried out according to the general procedure. The compounds **7a** and **7b**

were reported in the literature.⁶

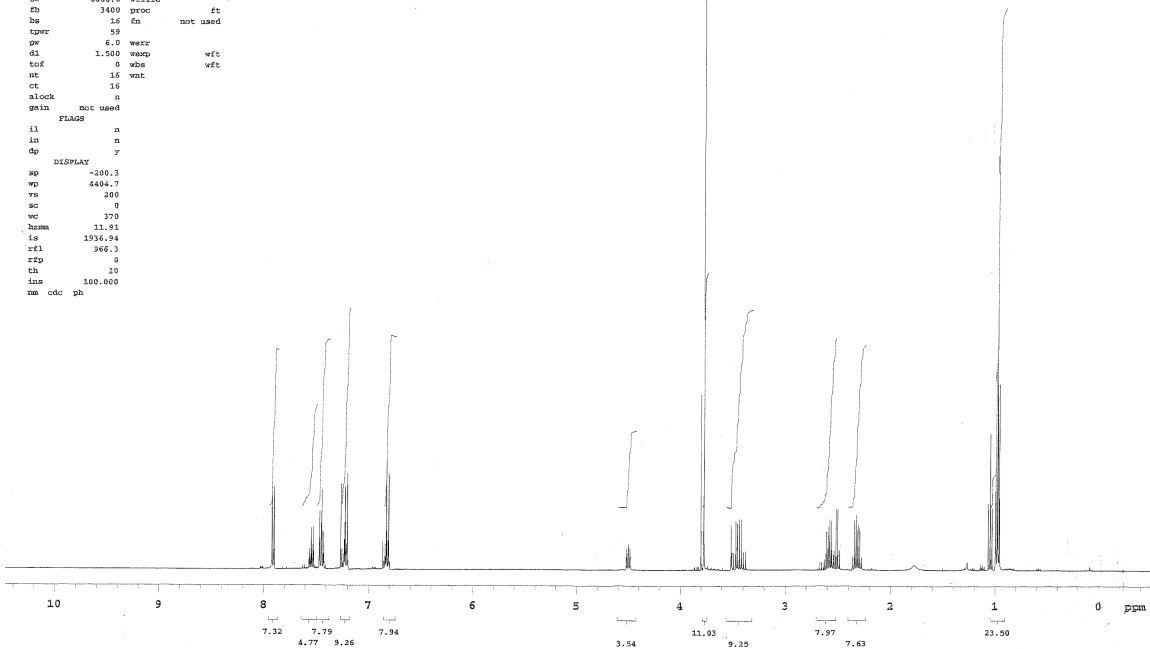
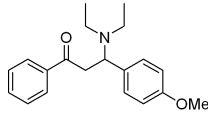
Crossover experiment using boron enolate 2b and 2e. (Scheme 2)

Boron enolate **2b** (40.0 mg, 0.125 mmol) was dissolved in DMF-*d*⁷ (0.6 mL). Boron enolate **2e** (26.5 mg, 0.125 mmol) was added and the mixture was heated for 2 h at 50 °C. ¹H NMR data showed no formation of boron enolates other than **2b** and **2e**. Benzaldehyde (52 μl, 0.5 mmol) was added and the mixture was stirred for 2 h at 50 °C. To the yellow solution cooled to room temperature were added ice water (3 ml) and *t*-butyl methyl ether (15 ml). Basic substances were extracted three times with 5 ml 0.5 N hydrochloric acid. The combined acidic aqueous layers were washed with 10 ml *t*-butyl methyl ether, cooled to 0 °C, and adjusted to pH 9 by addition of conc. ammonia solution. Organic material was extracted with *t*-butyl methyl ether and washed with 10 ml water. Removal of the solvent in vacuo at 0 °C yielded 51 mg of a product mixture containing **4aa** and **4ea** in a ratio of 1:1.38. Yield: **4aa**: 69 %, **4ea**: 95 % .

⁶ **7a**: Arend, M.; Nikolaus, R. *Angew. Chem.* **1995**, *107*, 2861. **7b**: Seebach, D.; C. Betschart; M. Schiess, *Helv. Chim. Acta.* **1984**, *67*, 1593.

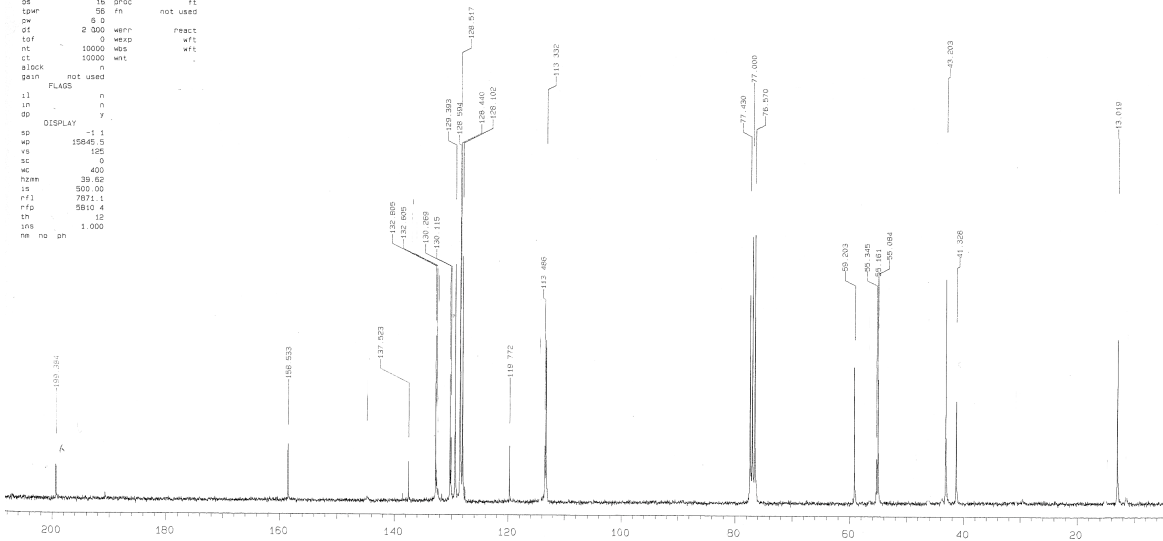
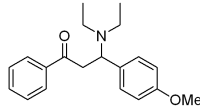
STANDARD 1H OBSERVE

```
exp1 st1h
SAMPLE DEC: 4 VP
date Jun 18 2003 dfrq 400.446
solvent CDCl3 dn H1
file exp d1w 30
ACQUISITION dof 0
sfrq 400.446 dn mm
tn 81 dn c
at 3.500 dnd 300
no 42043 PROCESSING
sw 6006.0 wfile
fd 3400 proc ft
bs 16 fn not used
tqwr 59
pw 6.0 warr
d1 1.500 warr wft
tuf 0 wbe wft
nt 16 wnt
ct 16
alock n
gain not used
FLAGS
il n
in n
dp 7
DISPLAY
sp -200.3
wp 4404.7
vs 200
sc 0
wc 370
hnm 11.91
is 1336.04
rfl 266.3
rfp 0
lh 10
ins 100.000
me cdc ph
```

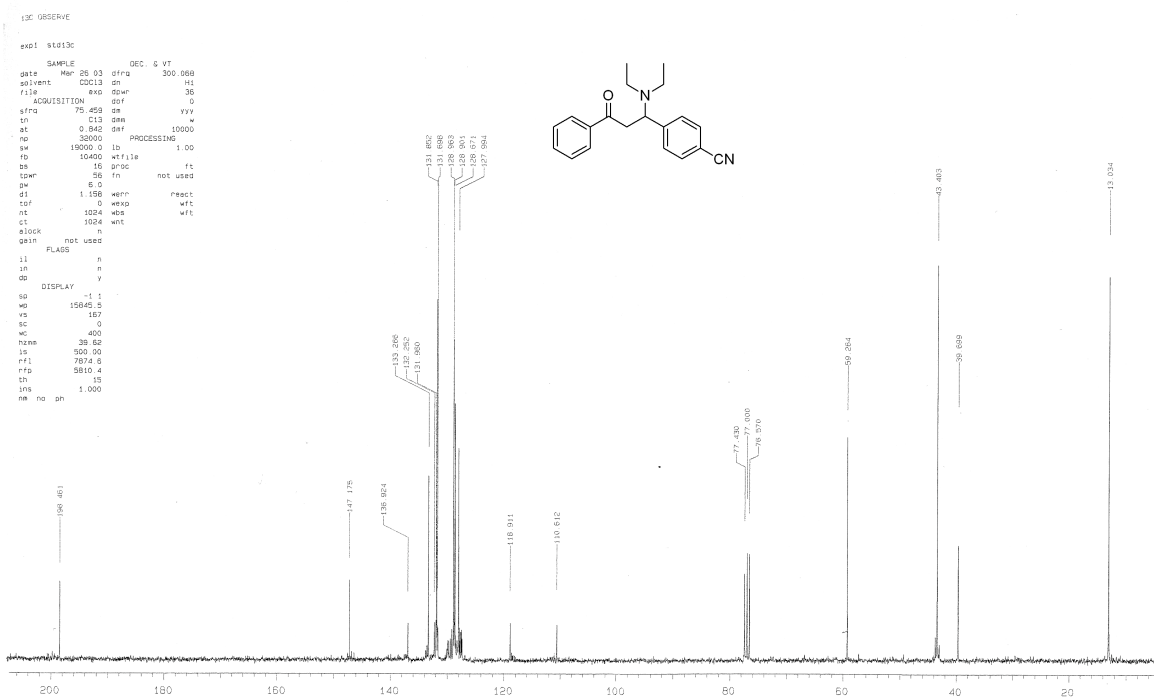
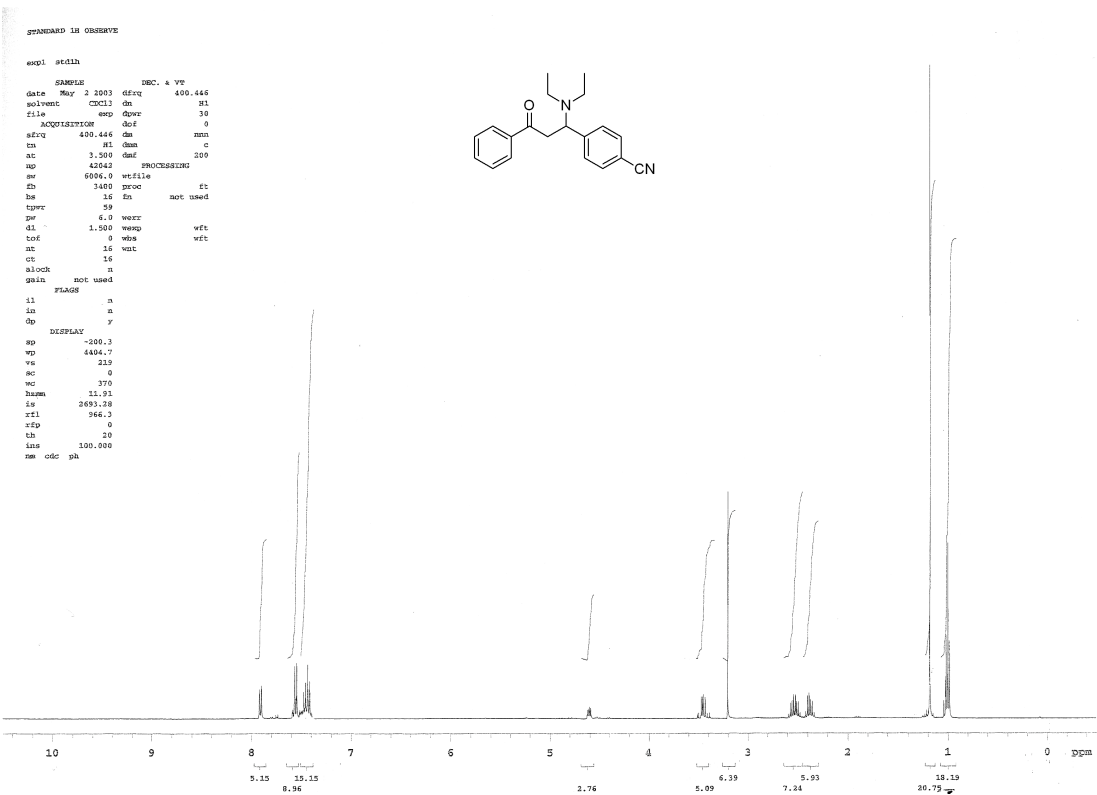


13C OBSERVE

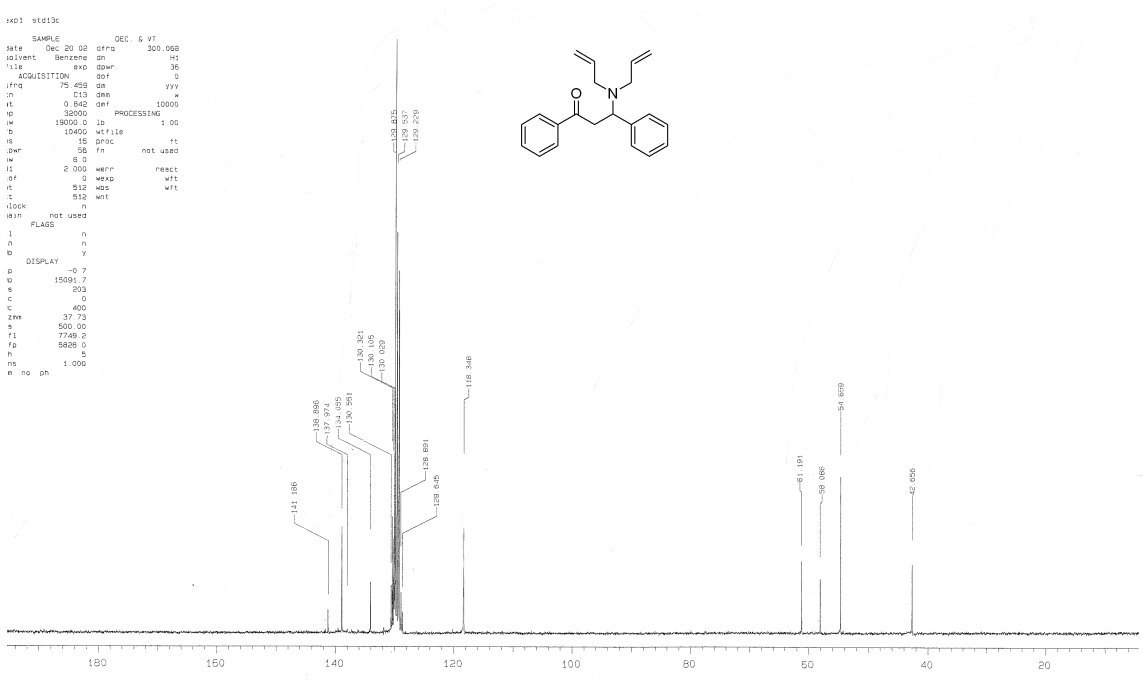
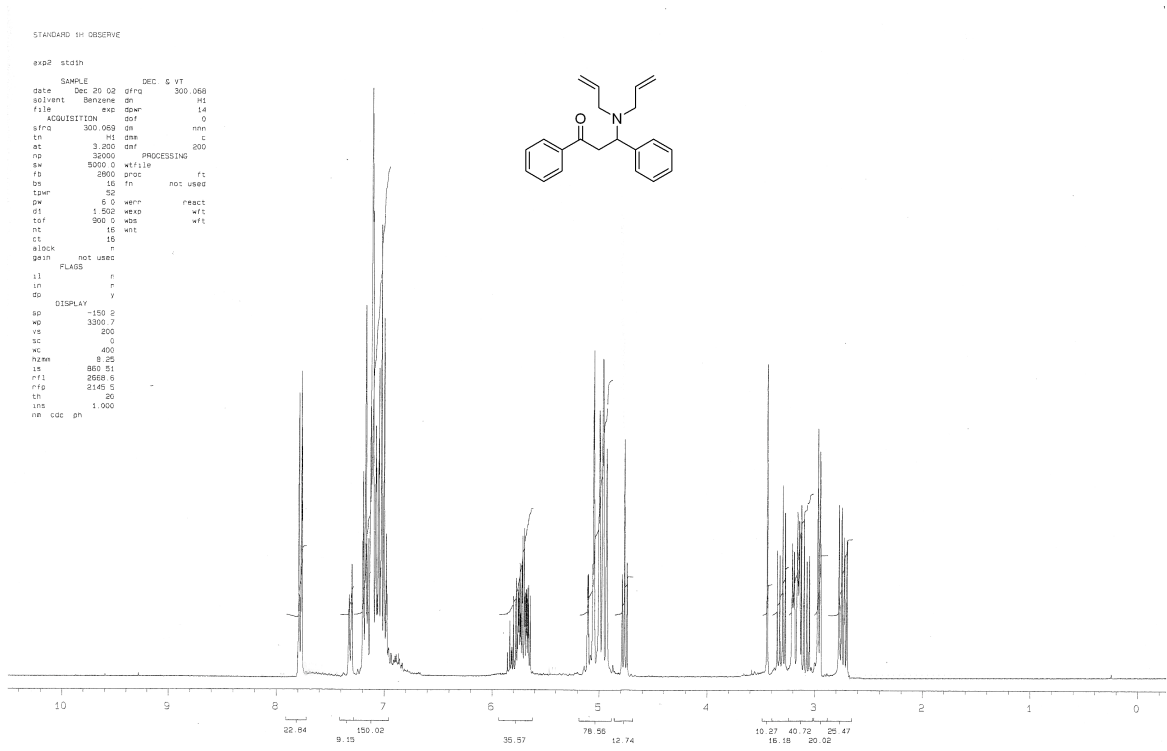
```
exp1 st13c
SAMPLE DEC: 6 VT
date Jun 18 03 dfrq 300.068
solvent CDCl3 dn H1
file exp d1w 30
ACQUISITION dof 0
sfrq 75.400 dn yyy
tn 81 dn c
at 0.842 dnd 30000
no 30000 PROCESSING
sw 19000.0 lb 1.00
fd 10400 wfile
ds 16 dnd ft
pw 6.0 warr not used
d1 2.000 warr react
tuf 0 wbe wft
nt 10000 wnt
ct 10000
alock n
gain not used
FLAGS
il n
in n
dp 7
DISPLAY
sp -1.1
wp 15845.5
vs 100
sc 0
wc 400
hnm 39.62
is 900.00
rfl 7871.1
rfp 5810.4
lh 12
ins 1.000
me no an
```



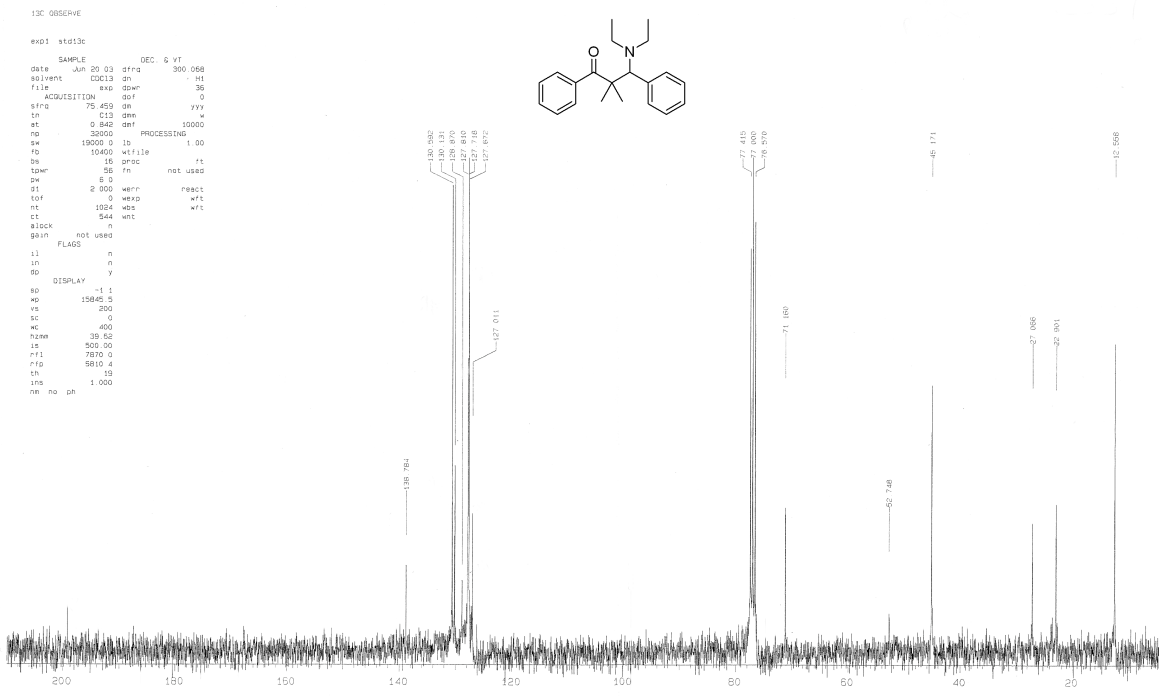
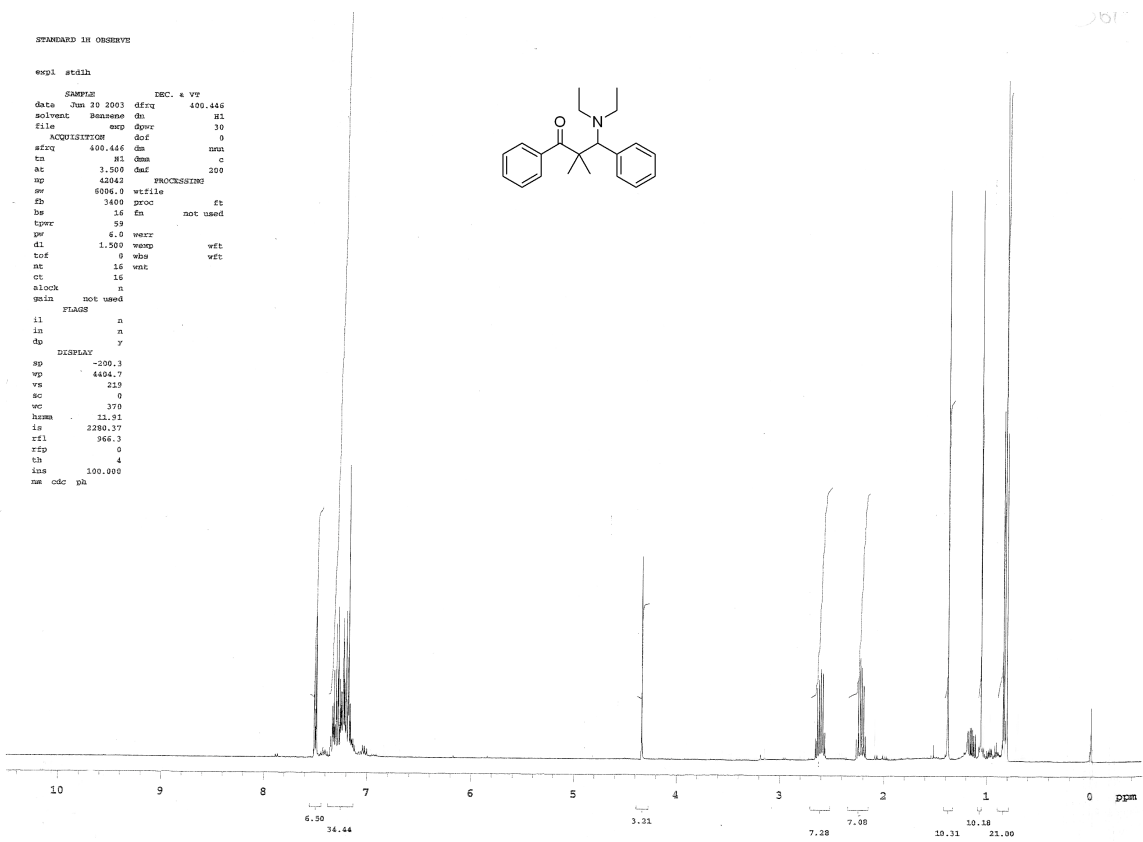
¹H and ¹³C NMR spectra of 4ab



^1H and ^{13}C NMR spectra of 4ac



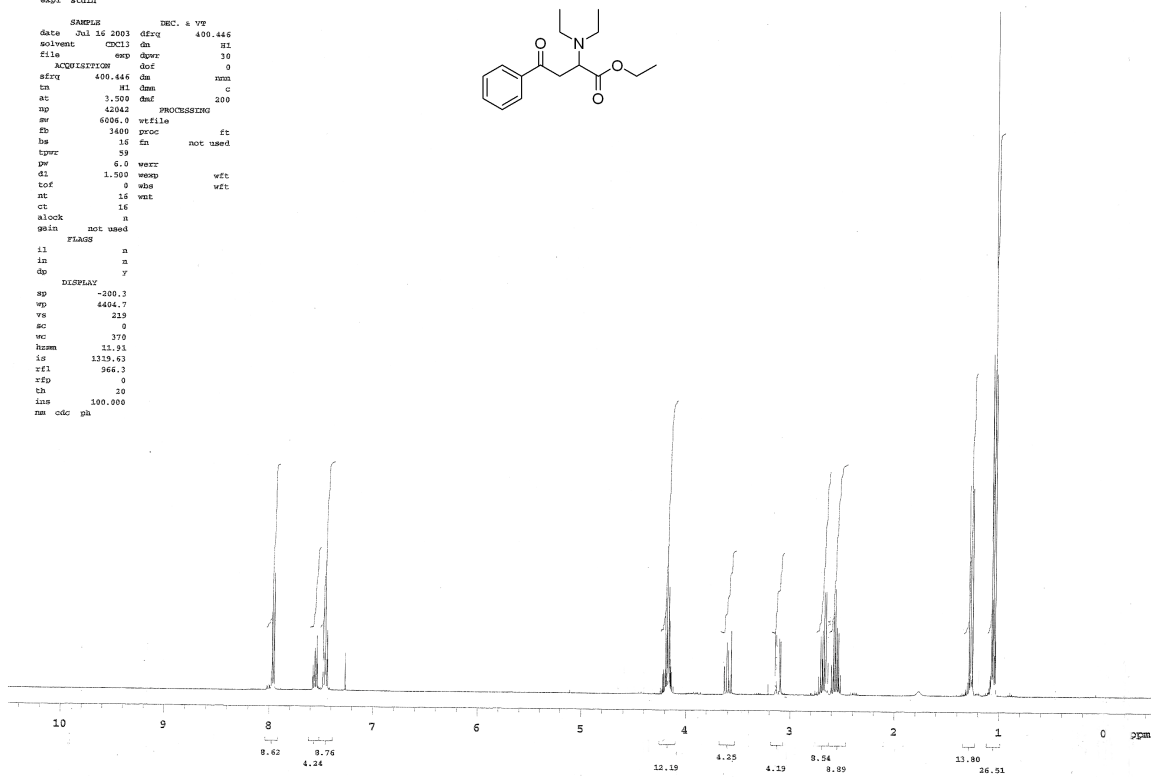
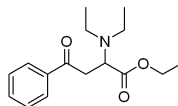
¹H and ¹³C NMR spectra of 4ba



¹H and ¹³C NMR spectra of 4da

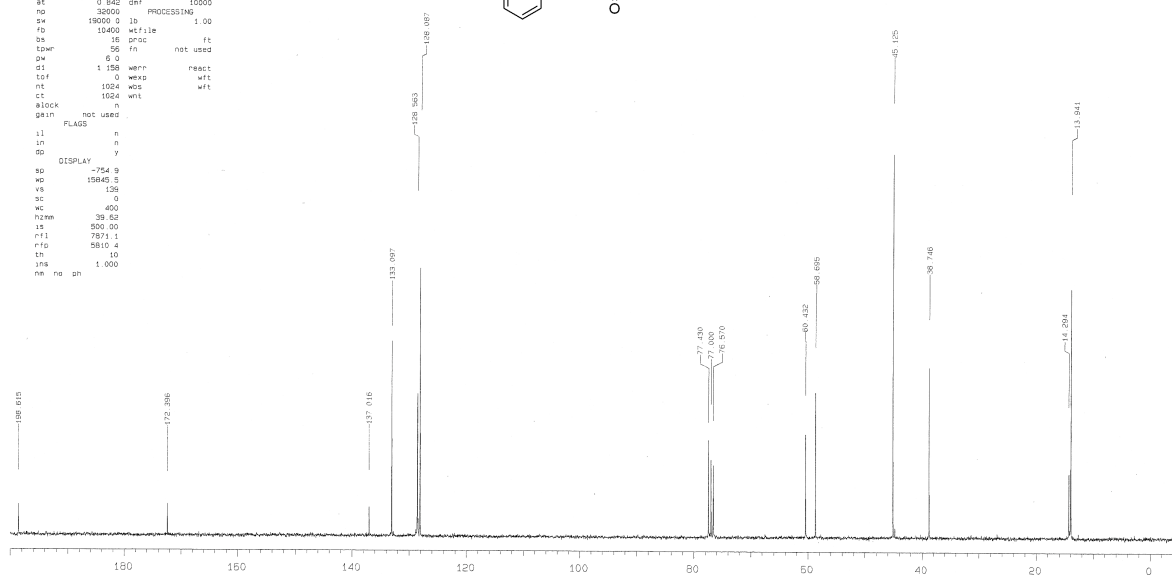
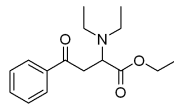
STANDARD IN OBSERVE

```
expl stdih
SAMPLE
date Jul 16 2003 dExq DEC. & VT 400.446
solvent CDCl3 dm H1
file exp dprw 30
ACQUISITION dof 0
sfreq 400.446 dm mm
tm H1 dm c
at 3.500 daf 200
ap 42042
nr 4006.0 wfile PROCESSING
rb 3400 proc ft
bs 16 fm not used
tprc 59
pw 6.0 werr
d1 1.500 wexp wft
tcf 9 wde wft
nt 16 wft
ct 16
alock n
dwin not used
FLAGS
ll n
in n
dp y
DISPLAY
sp -200.3
wp 4454.7
rs 219
sc 0
vc 370
hzmm 11.91
is 1319.63
rf1 344.3
rf2 0
sh 10
lms 100.000
nm odc ph
```



13C OBSERVE

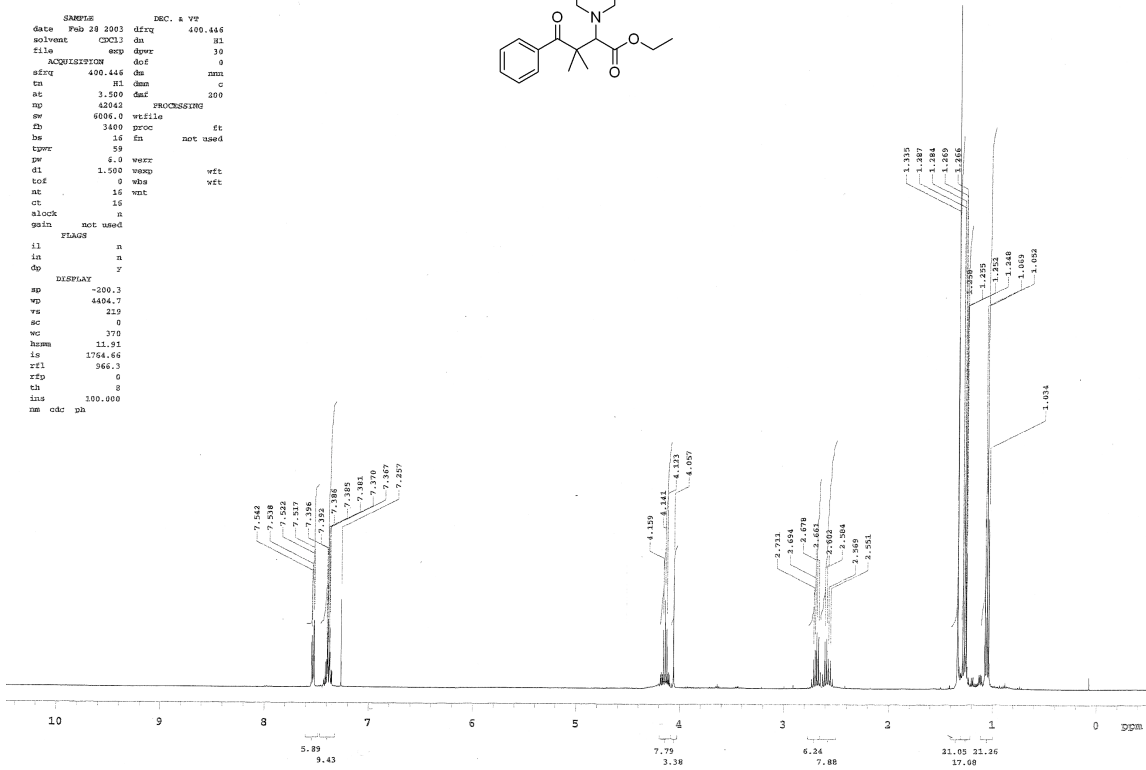
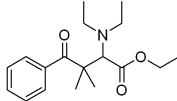
```
expl stdic
SAMPLE
date Jul 16 03 dprw DEC. & VT 300.058
solvent CDCl3 dm H1
file exp dprw 30
ACQUISITION dof 0
sfreq 75.459 dm H1
tm C13 dm H1
at 0.842 dmf 10000
nr 30000 PROCESSING
rb 19000.0 id 1.00
tprc 10400 wfile
pw 6.0
d1 1.158 werr react
tcf 0 wexp wft
nt 1024 wds wft
ct 1024
alock n
dwin not used
FLAGS
ll n
in n
dp y
DISPLAY
sp -754.9
wp 15849.5
rs 158
sc 0
vc 400
hzmm 38.63
is 500.00
rf1 7871.1
rf2 5810.4
sh 10
lms 1.000
nm no ph
```



¹H and ¹³C NMR spectra of 4ae

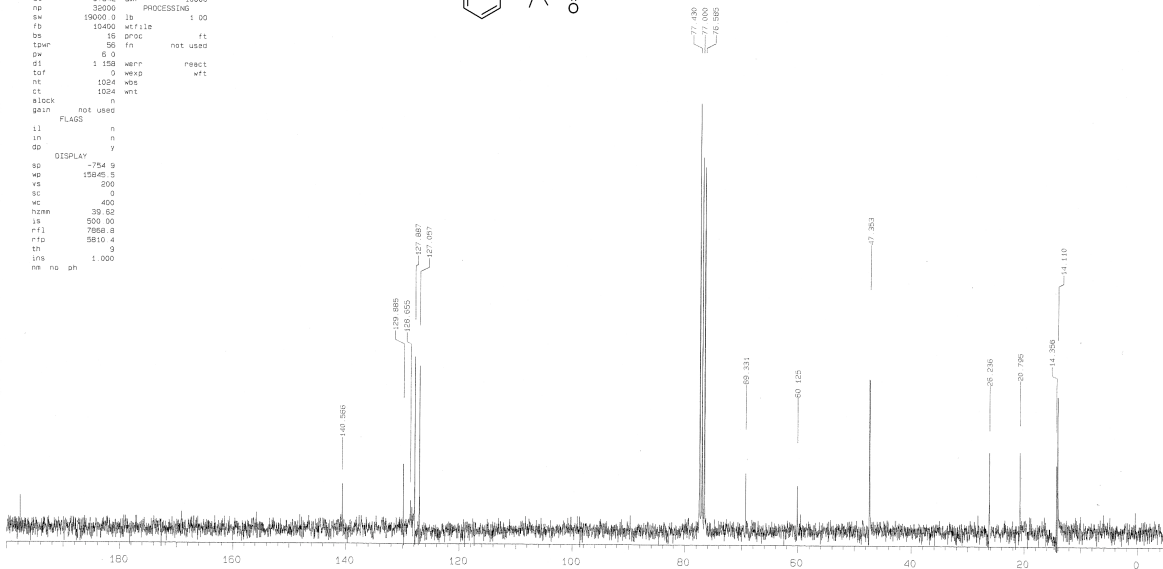
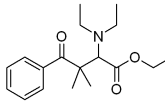
STANDARD IN OBSERVE

expt st01h
SAMPLE DEC. & Yr
date Feb 28 2003 dfrq 400.446
solvent CDCl3 dm H1
file exp dprvr 30
ACQUISITION dof 0
sfrq 400.446 dm mm
tn H1 dm c
at 3.500 dm 200
pp 42042 PROCESSING
sw 6006.0 wtfile
th 3400 proc Et
bs 16 fn not used
tprc 59
sw 6.0 wscr
ot 1.500 wscr wt
tof 0 wba wt
at 16 wnt wt
ct 16
block n
gain not used
FLAGS n
il n
in n
dp 7
DISPLAY 7
sp -200.3
wp 4404.7
vs 210
sc 0
wc 370
hzmn 11.91
is 1764.66
rl 966.3
rfd 0
th 8
lms 100.000
ne cdc ph



13C OBSERVE

expt st01c
SAMPLE DEC & Yr
date Jul 17 03 dfrq 300.008
solvent CDCl3 dm H1
file exp dprvr 38
ACQUISITION dof 0
sfrq 75.459 dm vvy
tn C13 dm
at 0.842 dm 10000
pp 30000 PROCESSING
sw 150000.0 lb 1.00
th 10450 wtfile
bs 15 dproc ft
tprc 56 fn not used
sw 8.0
ot 1.158 wscr react
tof 0 wba wt
at 1024 wnt wt
ct 1024
block n
gain not used
FLAGS n
il n
in n
dp 7
DISPLAY 7
sp -754.9
wp 15849.5
vs 200
sc 0
wc 400
hzmn 39.62
is 500.00
rl 7586.8
rfd 5810.4
th 0
lms 1.000
ne no ph



¹H and ¹³C NMR spectra of 4de