

Selective Tsuji-Trost type C-allylation of hydrazones: A straightforward entry into 4,5-dihydro pyrazoles

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Supporting information:

¹H NMR spectra were recorded on a Brucker Avance 400 MHz spectrometer, using CDCl₃ as solvent. ¹³C NMR spectra were recorded on a 100.6 MHz spectrometer. Chemical shifts are reported in ppm relative to internal TMS. Coupling constant J is quoted in hertz Hz. IR spectra were performed on a Perkin-Elmer FT 1600 spectrometer. High-resolution mass spectra (HRMS) were carried out with JEOL Gemate spectrometer. Melting points (mp) were determined on a Stuart SMP3 apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on silica gel using precoated plates of silica 60 F₂₅₄. Enantiomeric excess (ees) determinations were performed by supercritical fluid chromatography (SFC) analysis on chiral phase.

General procedures:	page 1-2
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General procedure I for Passerini products

A mixture of aldehyde (1.0 equiv), acetic acid (1.0 equiv) and isocyanide (1.0 equiv) was stirred at room temperature for 3 days. The crude is purified by flash chromatography on silica gel.

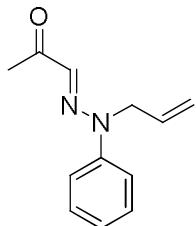
General procedure II for 4,5-dihydro pyrazolylacétamides

To a 0.2 M solution of Passerini adduct **2** (1.0 equiv) in toluene were added the starting hydrazone (1.0 equiv), Cs₂CO₃ (1.0 equiv), Pd (OAc)₂ (0.05 equiv) and dppe (0.05 equiv). The resulting mixture was stirred at 130°C for 15 min under heating (Anton Paar, Monowave 300). The solvent was removed afterwards under reduced pressure and the crude was purified by flash chromatography on silica gel.

General procedure III for 4,5-dihydro pyrazolyl phosphonates

To a 0.2 M solution of phosphonate adduct (1.0 equiv) in toluene were added the starting hydrazone (1.1 equiv), Cs₂CO₃ (1.0 equiv) and Pd(PPh₃)₄ (0.05 equiv). The resulting mixture was stirred at 50°C for 1 h. The solvent was removed afterwards under reduced pressure and the crude was purified by flash chromatography on silica gel.

(E)-1-(2-allyl-2-phenylhydrazono)propan-2-one



$$M=202.110 \text{ g.mol}^{-1}$$

To a 0.2 M solution of (1*E*)-1-(2-phenylhydrazin-1-ylidene)propan-2-one (100 mg, 0.61 mmol) in toluene were added the allyl methyl carbonate (0.07 ml, 0.61 mmol) and the Pd(PPh₃)₄ (36 mg, 0.03 mmol). The resulting mixture was stirred at 50°C for 1 h. The solvent was removed afterwards under reduced pressure and the crude was purified by flash chromatography on silica gel with a gradient Et₂O/EP (20/80 to 40/60) gave the desired product in 64% isolated yield (80 mg, 0.4 mmol).

Aspect: red oil

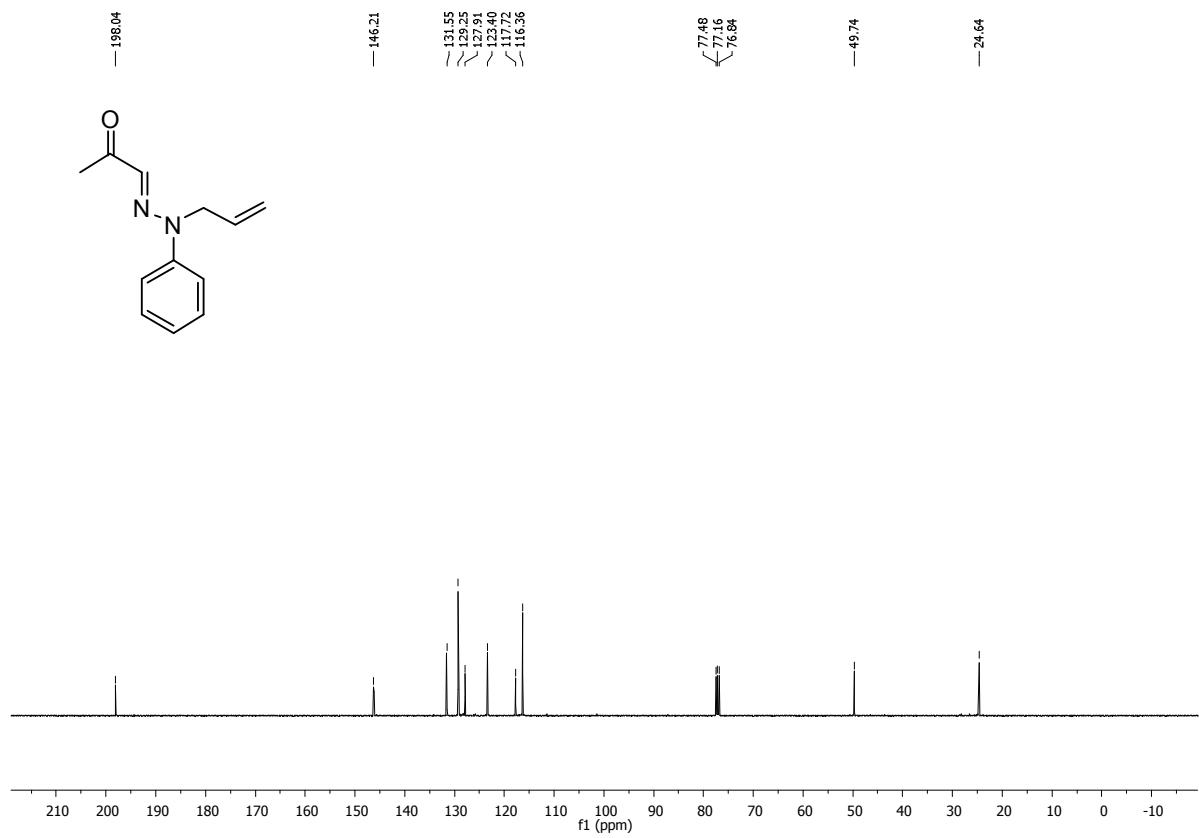
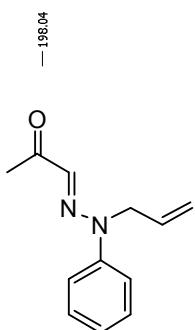
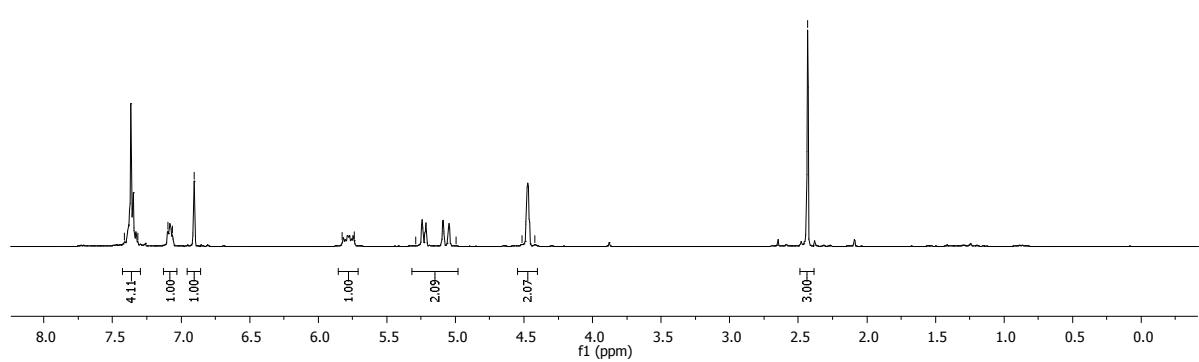
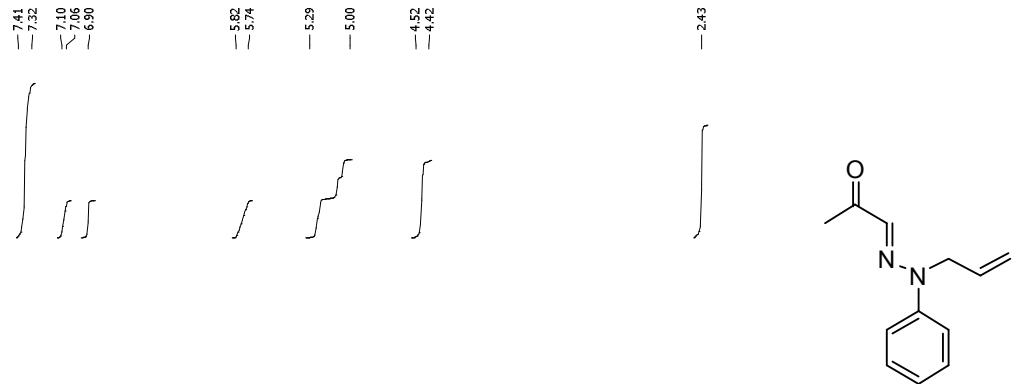
R_f: 0.39 (50:50 diethyl ether / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.42-7.30 (m, 4H), 7.12-7.04 (m, 1H), 6.90 (s, 1H), 5.84-5.71 (m, 1H), 5.29-4.99 (m, 2H), 4.54-4.40 (m, 2H), 2.43 (s, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 198.0, 146.2, 131.5, 129.2, 127.9, 123.4, 117.7, 116.3, 49.7, 24.6.

HRMS: calculated for C₁₂H₁₄N₂O : 202.1106, found 202.1109.

I.R. (thin film): 3069, 3016, 2989, 2257, 1656, 1599, 1541, 1495, 1394, 1357, 1238, 1180, 1007 cm⁻¹.



Laboratoire de Synthèse Organique

10/05/2016

10:32:26

File: EH213
Sample:

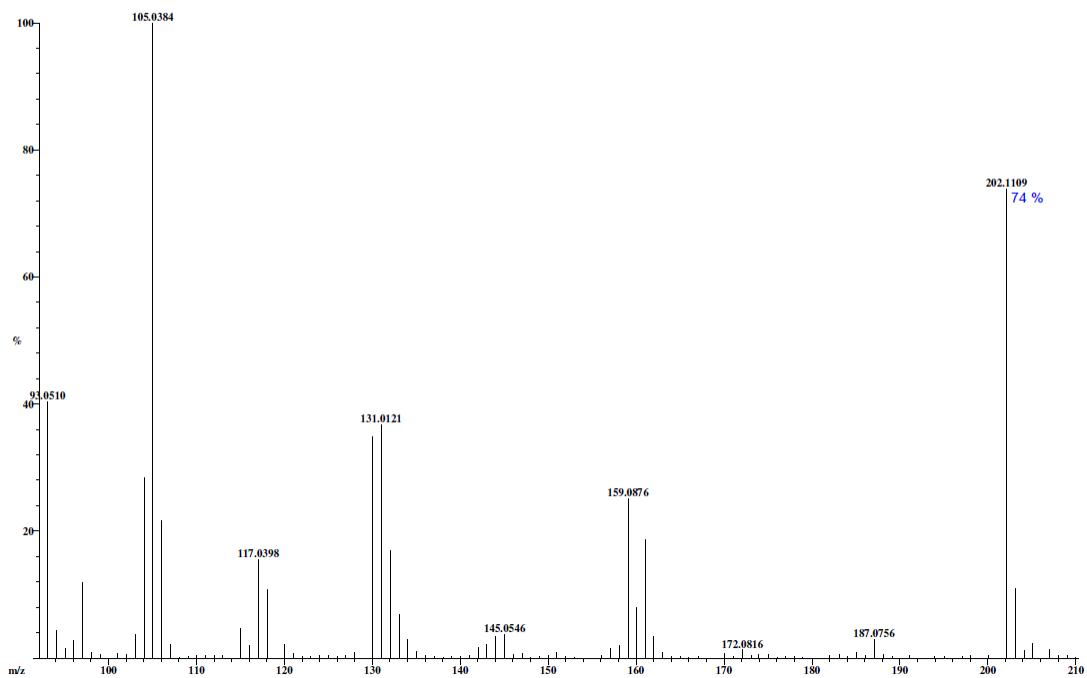
Date Run: 10-05-2016 (Time Run: 10:22:20)
Instrument: JEOL JMSGCmateII

Inlet: Direct Probe

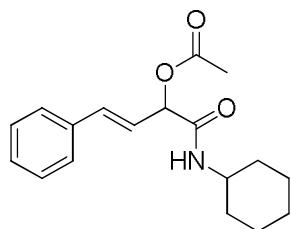
Run By: Vincent Jactel
Ionization mode: EI+

Scan: 128

TIC: 3086184



(E)-1-(cyclohexylamino)-1-oxo-4-phenylbut-3-en-2-yl acetate 2a



C₁₈H₂₃NO₃

M=301.167 g.mol⁻¹

This compound was synthesized according to the general procedure I, using *trans*-cinnamaldehyde (0.38 ml, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and cyclohexyl isocyanide (0.37 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 80% isolated yield (720 mg, 2.4 mmol).

Aspect: white solid

M.P. = 129-130°C

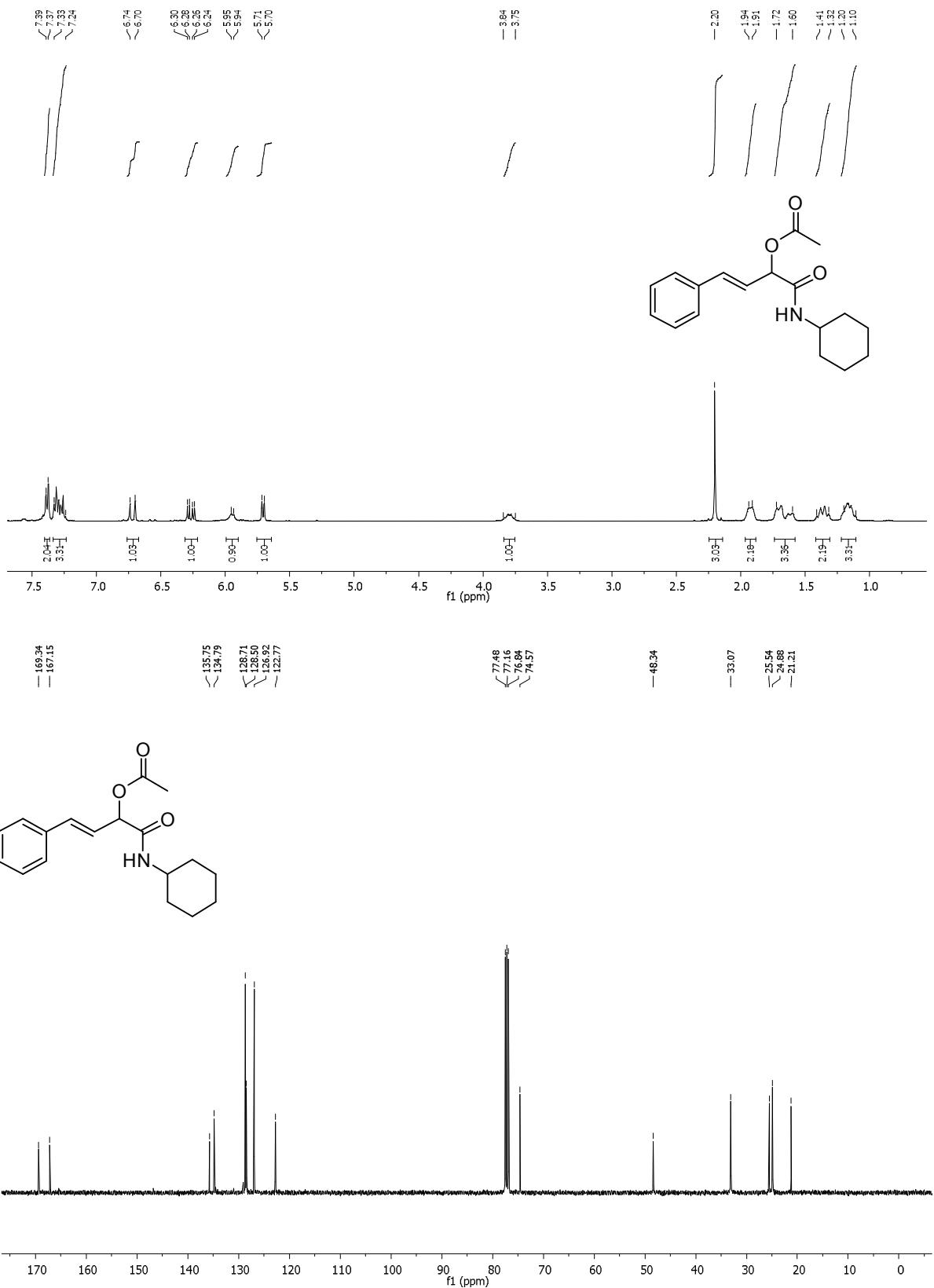
R_f: 0.39 (70:30 diethyl ether / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.33-7.24 (m, 3H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 16.0, 6.9 Hz, 1H), 5.95 (d, *J* = 7.5 Hz, 1H), 5.71 (d, *J* = 6.9 Hz, 1H), 3.84-3.75 (m, 1H), 2.20 (s, 3H), 1.94-1.91 (m, 2H), 1.72-1.60 (m, 3H), 1.41-1.32 (m, 2H), 1.20-1.10 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.3, 167.1, 135.7, 134.7, 128.7, 128.5, 126.9, 122.7, 74.5, 48.3, 33.0, 25.5, 24.8, 21.2.

HRMS: calculated for C₁₈H₂₃NO₃ : 301.1678, found 301.1677.

I.R. (thin film): 3282, 2929, 2853, 1741, 1653, 1540, 1449, 1370, 1227, 1030 cm⁻¹.



File: EE732

Date Run: 11-06-2014 (Time Run: 11:28:15)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

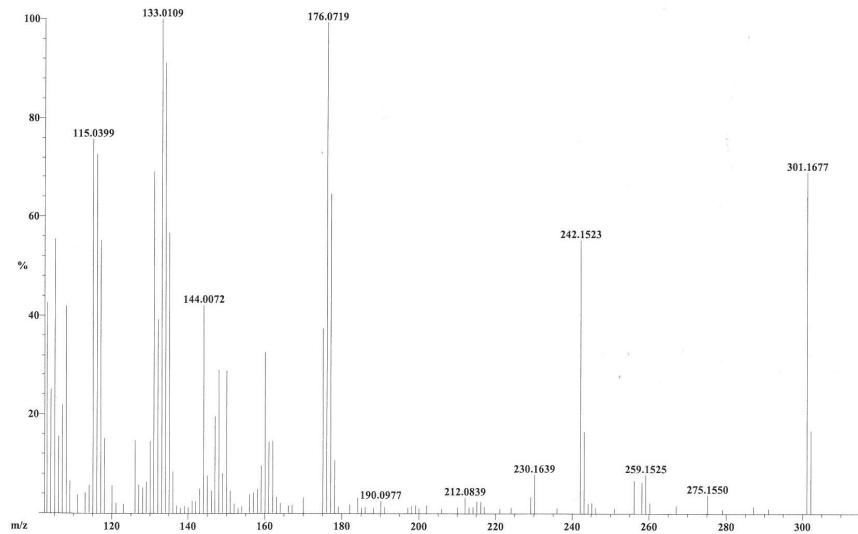
Ionization mode: EI+

Scan: 136

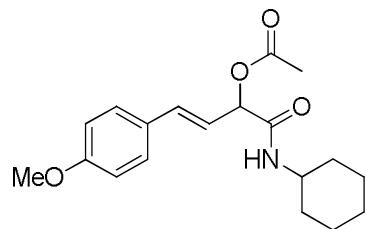
R.T.: 2.78

Base: m/z 133; 78.3%FS TIC: 13472192

#Ions: 184



(E)-1-(cyclohexylamino)-4-(4-methoxyphenyl)-1-oxobut-3-en-2-yl acetate 2b



C₁₉H₂₅NO₄

M=331.178 g.mol⁻¹

This compound was synthesized according to the general procedure **I**, using *trans*-*p*-methoxycinnamaldehyde (486 mg, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and cyclohexyl isocyanide (0.37 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 75% isolated yield (750 mg, 2.2 mmol).

Aspect: white solid

M.P. = 134-135°C

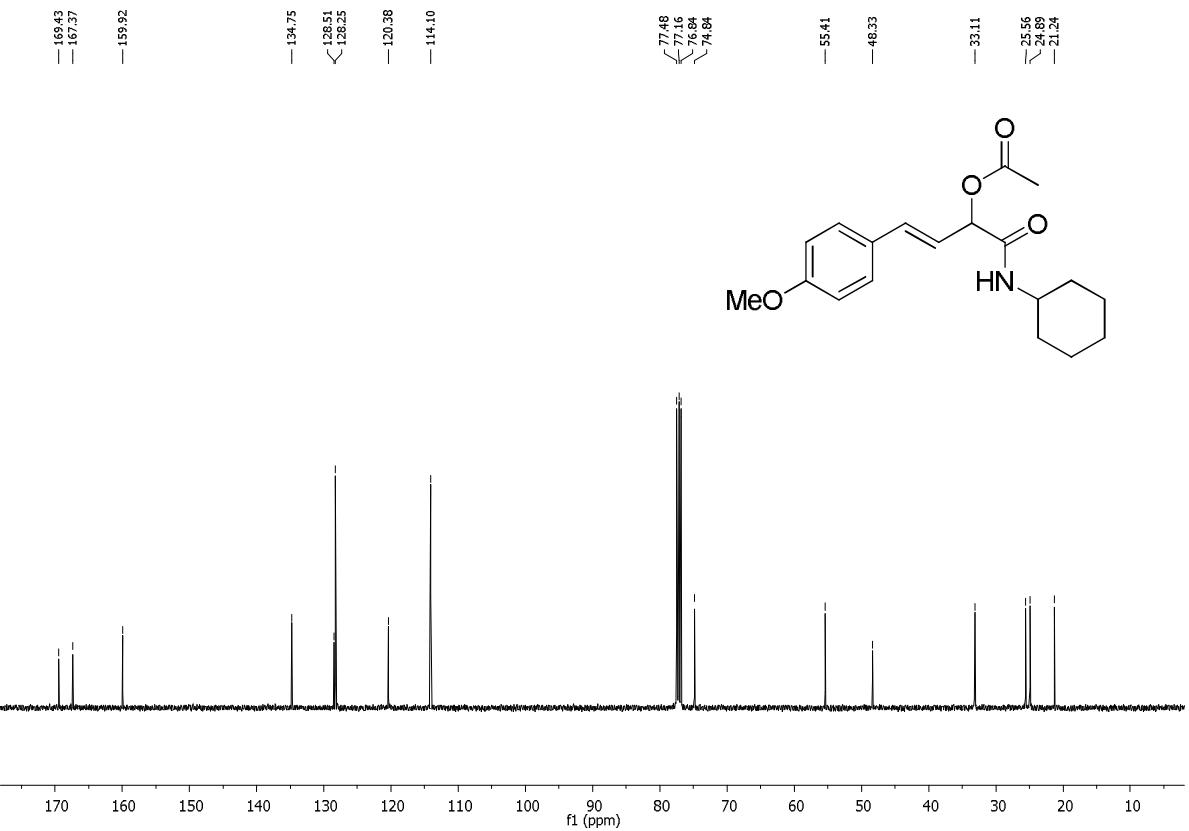
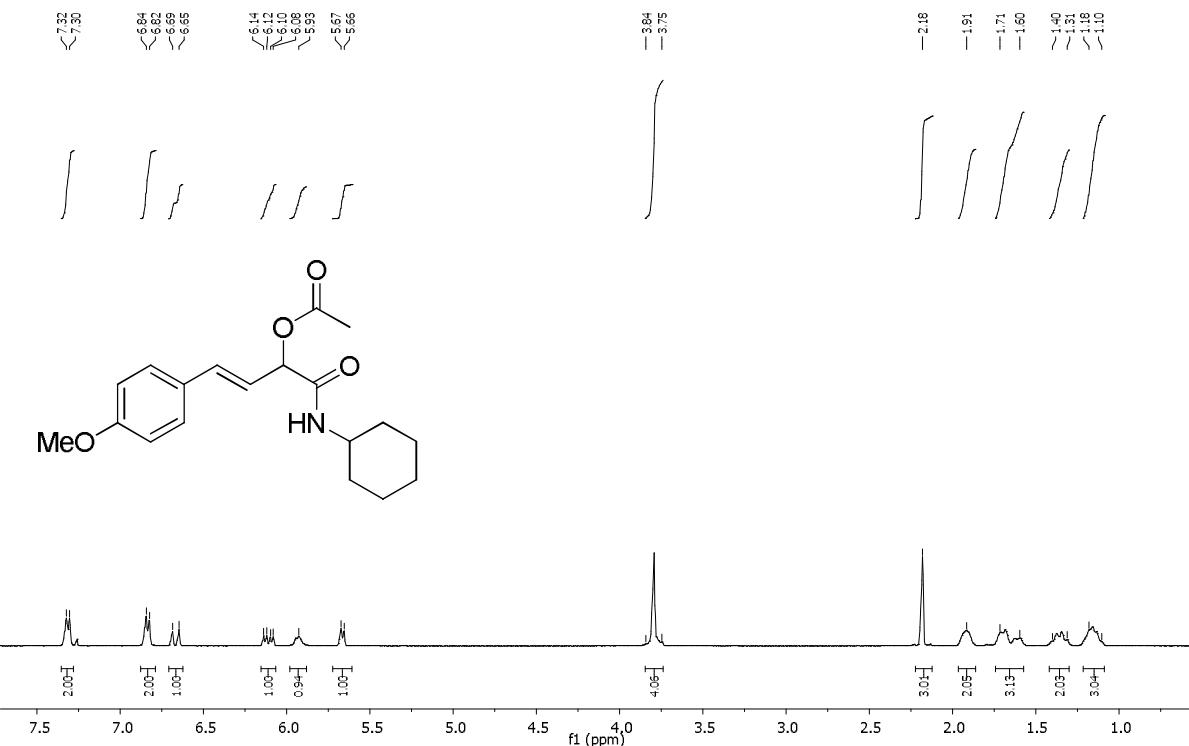
R_f: 0.37 (90:10 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.31 (d, *J* = 7.5 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 2H), 6.67 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.93 (br s, 1H, NH), 5.66 (d, *J* = 7.0 Hz, 1H), 3.84-3.75 (m, 4H), 2.18 (s, 3H), 1.97-1.86 (m, 2H), 1.71-1.60 (m, 3H), 1.40-1.31 (m, 2H), 1.18-1.10 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.4, 167.3, 159.9, 134.7, 128.5, 128.2, 120.3, 114.1, 74.8, 55.4, 48.3, 33.1, 25.5, 24.8, 21.2.

HRMS: calculated for C₁₉H₂₅NO₄: 331.1784, found: 331.1784.

I.R. (thin film): 3278, 2930, 2853, 1741, 1651, 1510, 1449, 1370, 1226, 1174, 1028, 965cm⁻¹.



File: EE1182

Date Run: 11-06-2014 (Time Run: 15:57:42)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

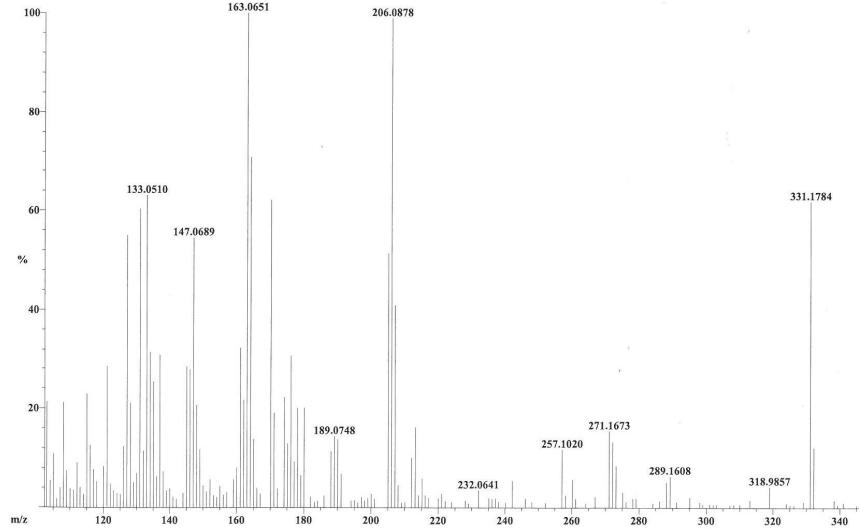
Ionization mode: EI+

Scan: 156

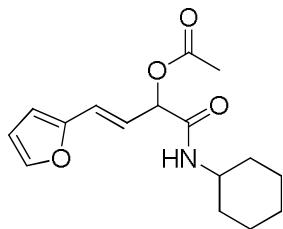
R.T.: 3.2

Base: m/z 163; 68.2%FS TIC: 12968800

#Ions: 294



(E)-1-(cyclohexylamino)-4-(furan-2-yl)-1-oxobut-3-en-2-yl acetate 2c



C₁₆H₂₁NO₄

M=291.147 g.mol⁻¹

This compound was synthesized according to the general procedure **I**, using *trans*-3-(2-furyl)acrolein (366 mg, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and cyclohexyl isocyanide (0.37 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 80% isolated yield (700 mg, 2.4 mmol).

Aspect: beige solid

M.P. = 138-139°C

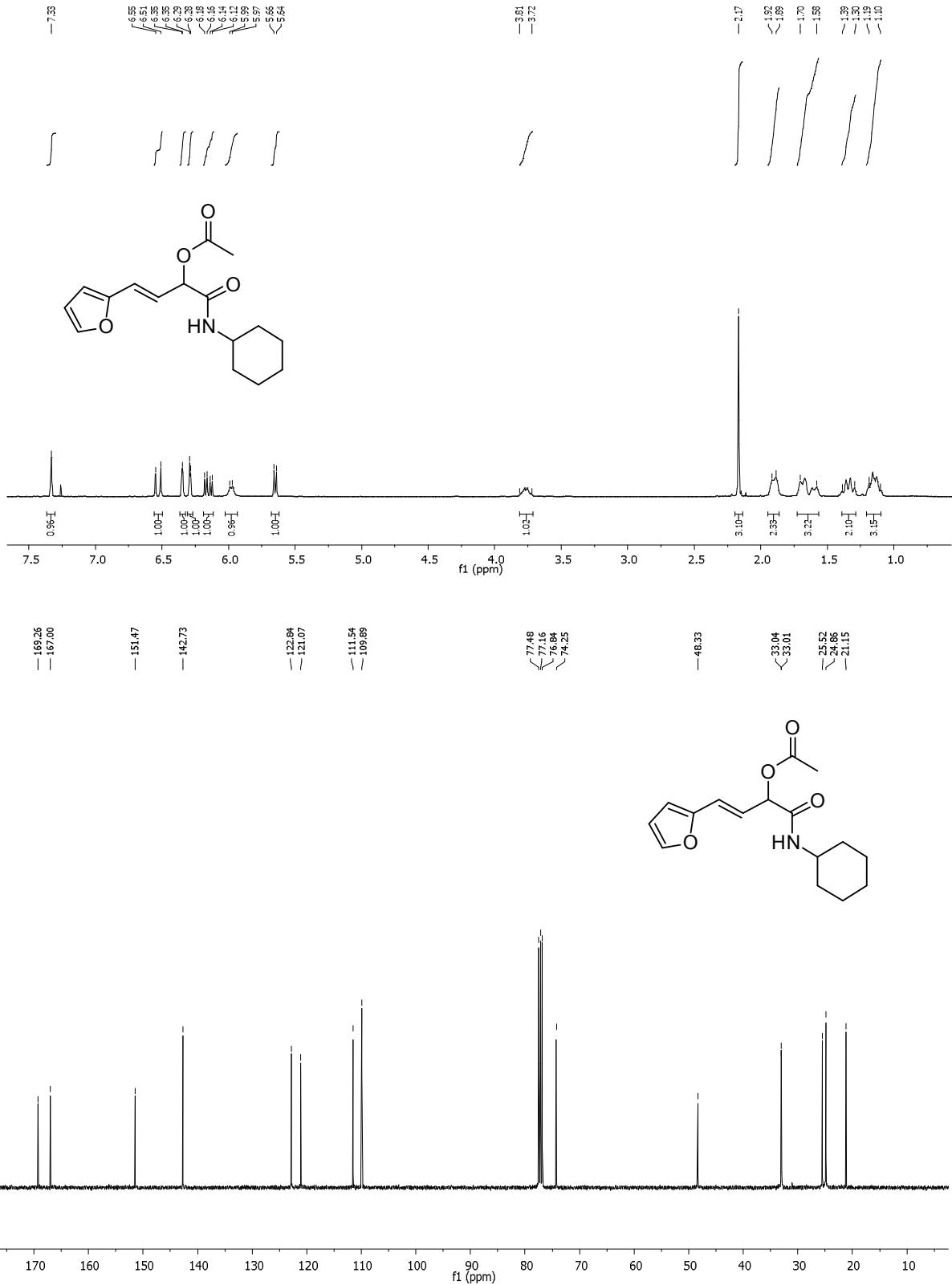
R_f: 0.34 (70:30 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.33 (s, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.37-6.32 (m, 1H), 6.29 (d, *J* = 3.1 Hz, 1H), 6.15 (dd, *J* = 15.8, 7.0 Hz, 1H), 5.98 (d, *J* = 7.6 Hz, 1H), 5.65 (d, *J* = 7.0 Hz, 1H), 3.81-3.72 (m, 1H), 2.17 (s, 3H), 1.92-1.89 (m, 2H), 1.70-1.58 (m, 3H), 1.39-1.30 (m, 2H), 1.19-1.10 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.2, 167.0, 151.4, 142.7, 122.8, 121.0, 111.5, 109.8, 74.2, 48.3, 33.0, 33.0, 25.5, 24.8, 21.1.

HRMS: calculated for C₁₆H₂₁NO₄: 291.1471, found: 291.1475.

I.R. (thin film): 3282, 2930, 2854, 1741, 1651, 1537, 1449, 1370, 1222, 1151, 1089, 1013 cm⁻¹.



File: EE108

Date Run: 11-06-2014 (Time Run: 11:37:09)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

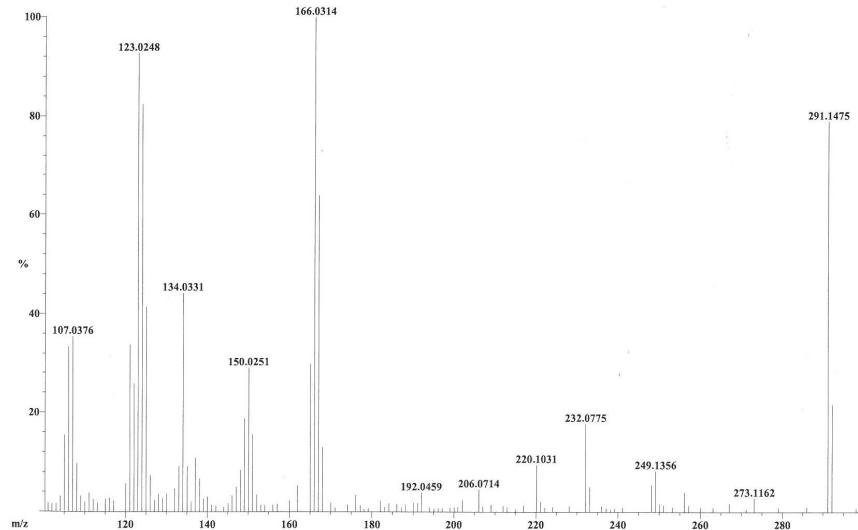
Ionization mode: EI+

Scan: 166

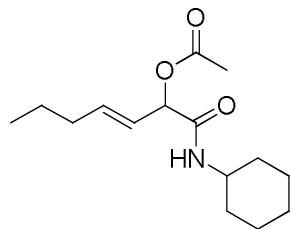
R.T.: 3.4

Base: m/z 166; 76.7%FS TIC: 9240928

#Ions: 283



(E)-1-(cyclohexylamino)-1-oxohept-3-en-2-yl acetate 2d



C₁₅H₂₅NO₃

M=267.183 g.mol⁻¹

This compound was synthesized according to the general procedure **I**, using *trans*-2-hexenal (348 µl, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and cyclohexyl isocyanide (0.37 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 70% isolated yield (561 mg, 2.1 mmol).

Aspect: Colorless oil

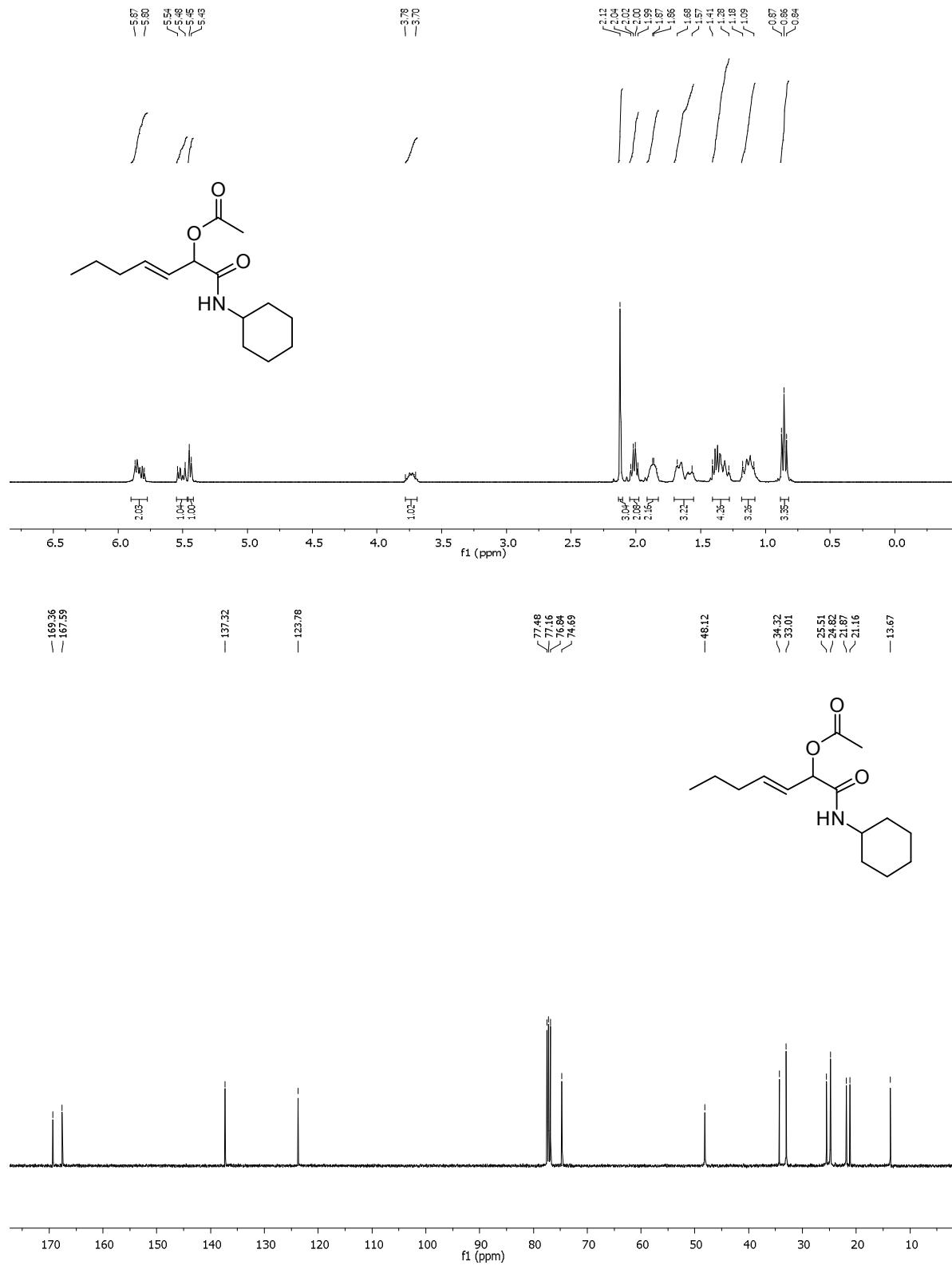
R_f: 0.29 (50:50 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 5.87-5.80 (m, 2H), 5.54-5.48 (m, 1H), 5.44 (d, *J* = 7.3 Hz, 1H), 3.78-3.70 (m, 1H), 2.12 (s, 3H), 2.01 (q, *J* = 7.08 Hz, 2H), 1.87 (m, 2H), 1.68-1.57 (m, 3H), 1.41-1.28 (m, 4H), 1.18 – 1.09 (m, 3H), 0.86 (t, *J* = 7.37 Hz, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.3, 167.5, 137.3, 123.7, 74.6, 48.1, 34.3, 33.0, 25.5, 24.8, 21.8, 21.1, 13.6.

HRMS: calculated for C₁₉H₂₅NO₄: 267.1834, found: 267.1838.

I.R. (thin film): 3441, 2959, 2934, 2857, 1754, 1689, 1512, 1451, 1371, 1220, 1044, 1022, 966 cm⁻¹.

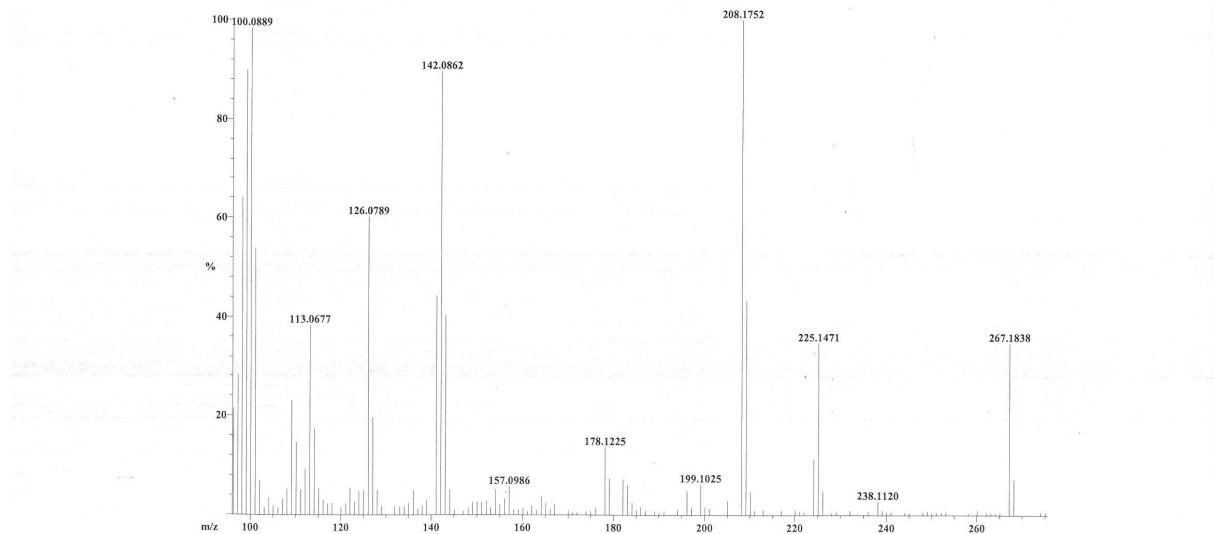


File: EE1193
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Instrument: JEOL GCmate
Inlet: Direct Probe
Date Run: 02-10-2015 (Time Run: 16:03:34)
Ionization mode: EI+

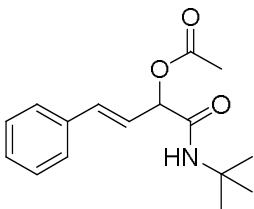
Scan: 45
Base: m/z 208; 69%FS TIC: 8927216

R.T.: .92

#Ions: 246



(E)-1-(tert-butylamino)-1-oxo-4-phenylbut-3-en-2-yl acetate 2e



C₁₆H₂₁NO₃

M=275.152 g.mol⁻¹

This compound was synthesized according to the general procedure **I**, using *trans*-cinnamaldehyde (0.38 ml, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and *tert*-butyl isocyanide (0.34 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 75% isolated yield (620 mg, 2.2 mmol).

Aspect: white solid

M.P. = 116-118°C

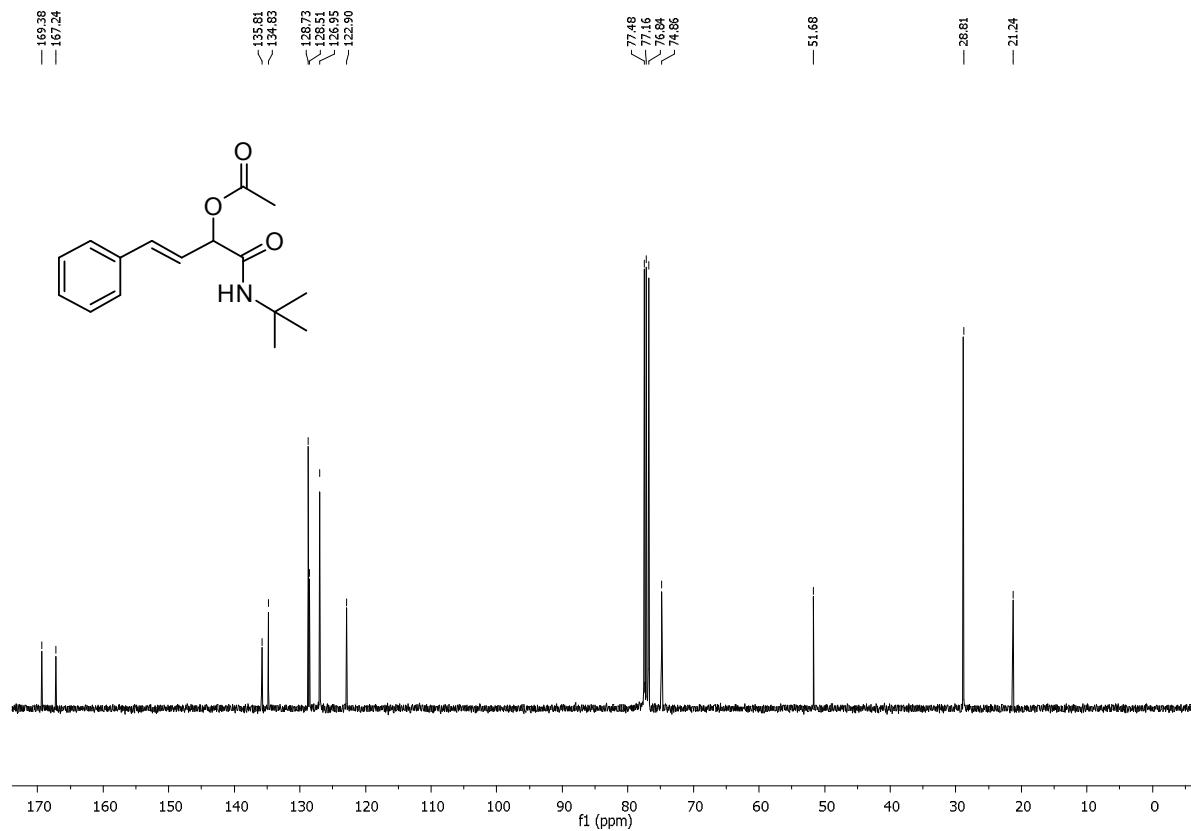
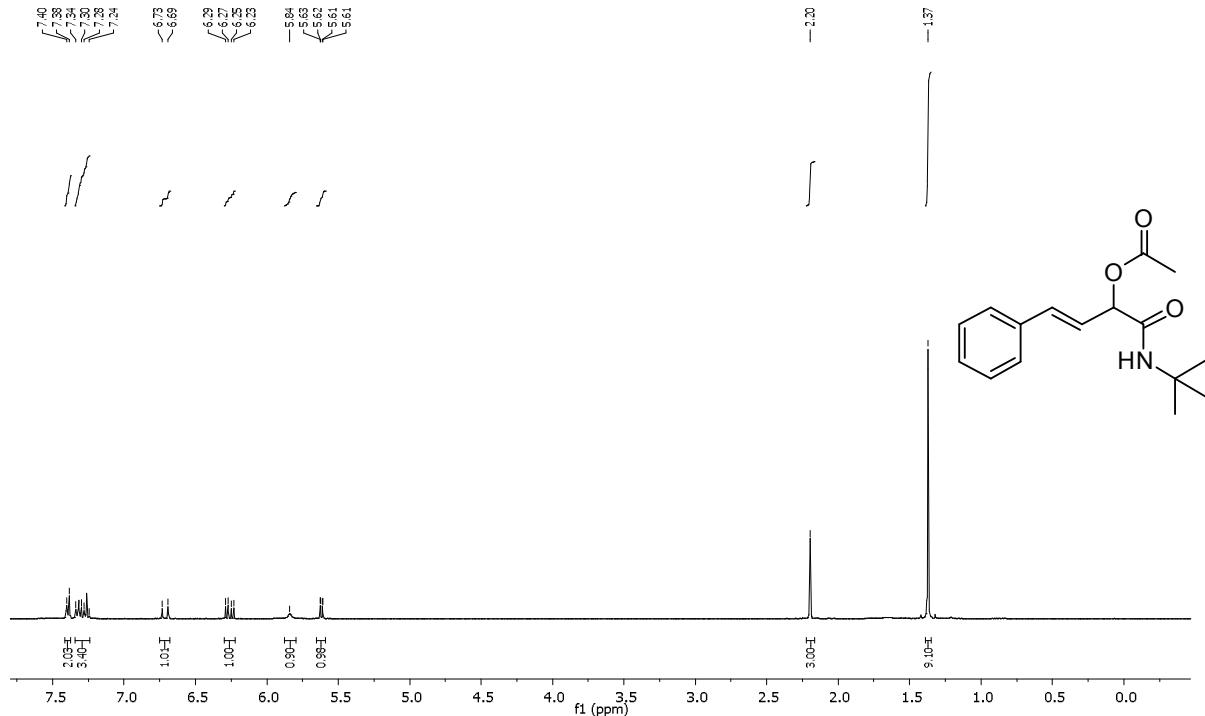
R_f: 0.30 (60:40 diethyl ether / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.39 (d, *J* = 7.6 Hz, 2H), 7.35 – 7.25 (m, 3H), 6.71 (d, *J* = 16.0 Hz, 1H), 6.26 (dd, *J* = 16.0, 7.0 Hz, 1H), 5.84 (s, 1H), 5.62 (dd, *J* = 7.0, 1.2 Hz, 1H), 2.20 (s, 3H), 1.37 (s, 9H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.3, 167.2, 135.8, 134.8, 128.7, 128.5, 126.9, 122.9, 74.8, 51.6, 28.8, 21.2.

HRMS: calculated for C₁₆H₂₁NO₃: 275.1521, found: 275.1519.

I.R. (thin film): 3307, 2968, 1740, 1664, 1523, 1364, 1218, 1027 cm⁻¹.



File: EE106

Date Run: 11-06-2014 (Time Run: 15:47:41)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

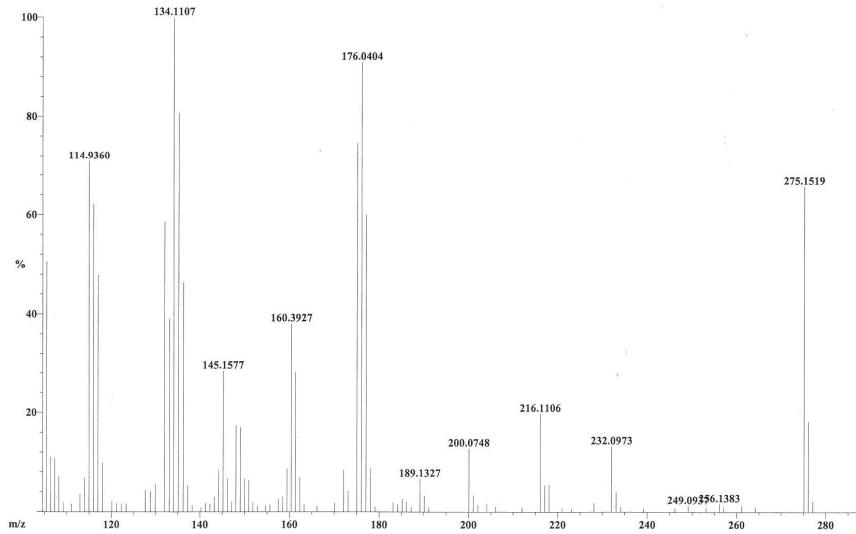
Ionization mode: EI+

Scan: 13

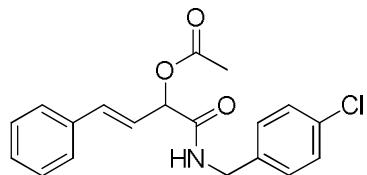
R.T.: .25

Base: m/z 134; 81.4%FS TIC: 11863024

#Ions: 177



(E)-1-((4-chlorobenzyl)amino)-1-oxo-4-phenylbut-3-en-2-yl acetate 2f



C₁₉H₁₈ClNO₃

M=343.097 g.mol⁻¹

This compound was synthesized according to the general procedure I, using *trans*-cinnamaldehyde (0.38 ml, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and 4-chlorobenzyl isocyanide (0.45 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 74% isolated yield (764 mg, 2.2 mmol).

Aspect: white solid

M.P. = 103-104°C

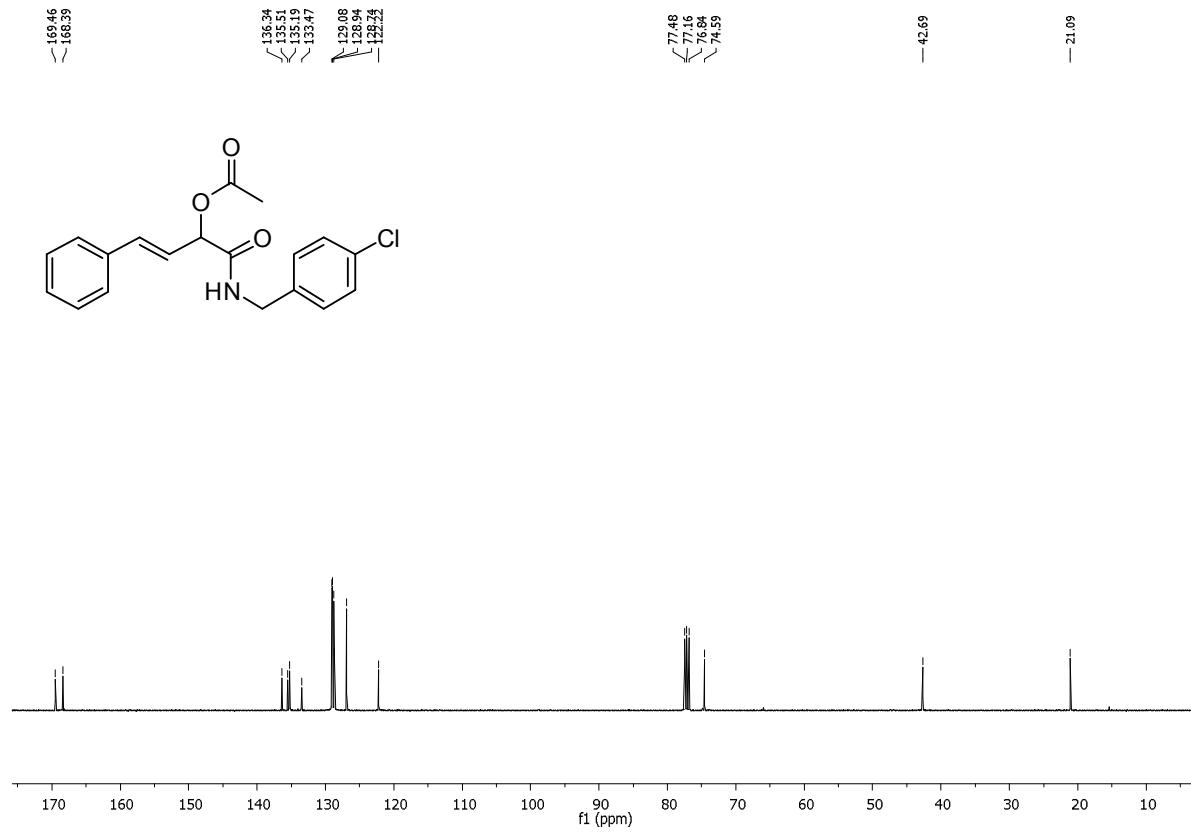
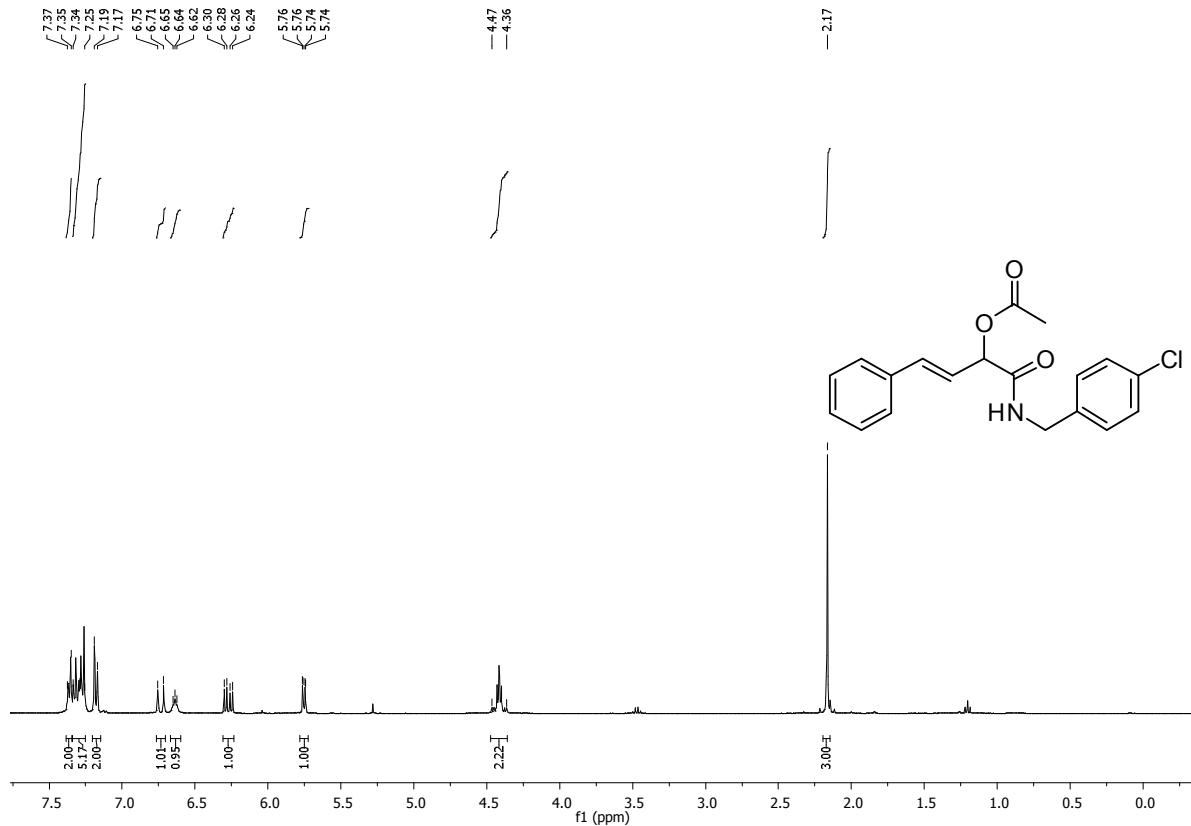
R_f: 0.36 (90:10 diethyl ether / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.37-7.35 (m, 2H), 7.34-7.25 (m, 5H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.64 (t, *J* = 5.6 Hz, 1H), 6.27 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.75 (dd, *J* = 7.0, 1.0 Hz, 1H), 4.47-4.36 (m, 2H), 2.17 (s, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.4, 168.3, 136.3, 135.3, 135.1, 133.4, 129.0, 128.9, 128.7, 128.6, 126.8, 122.2, 74.5, 42.6, 21.0.

HRMS: calculated for C₂₀H₂₀ClNO₄: 343.0975, found: 343.0957.

I.R. (thin film): 3450, 3030, 2934, 1769, 1752, 1696, 1514, 1494, 1371, 1215, 1094, 1017, 965 cm⁻¹.



File: EE2041

Date Run: 02-10-2015 (Time Run: 15:58:16)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

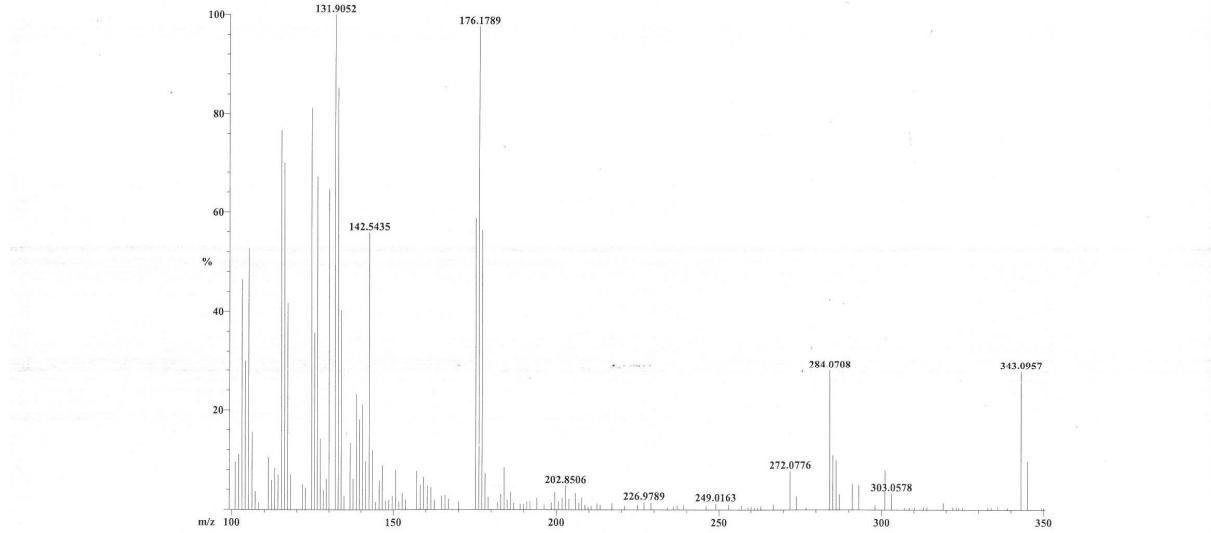
Ionization mode: EI+

Scan: 13

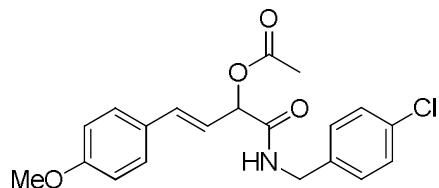
R.T.: .25

Base: m/z 132; 74.3%FS TIC: 12855648

#Ions: 286



(E)-1-((4-chlorobenzyl)amino)-4-(4-methoxyphenyl)-1-oxobut-3-en-2-yl acetate 2g



C₂₀H₂₀ClNO₄

M=373.108 g.mol⁻¹

This compound was synthesized according to the general procedure **I**, using *trans*-*p*-methoxycinnamaldehyde (486 mg, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and 4-chlorobenzyl isocyanide (0.45 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 76% isolated yield (850 mg, 2.3 mmol).

Aspect: cream solid

M.P. = 102-103°C

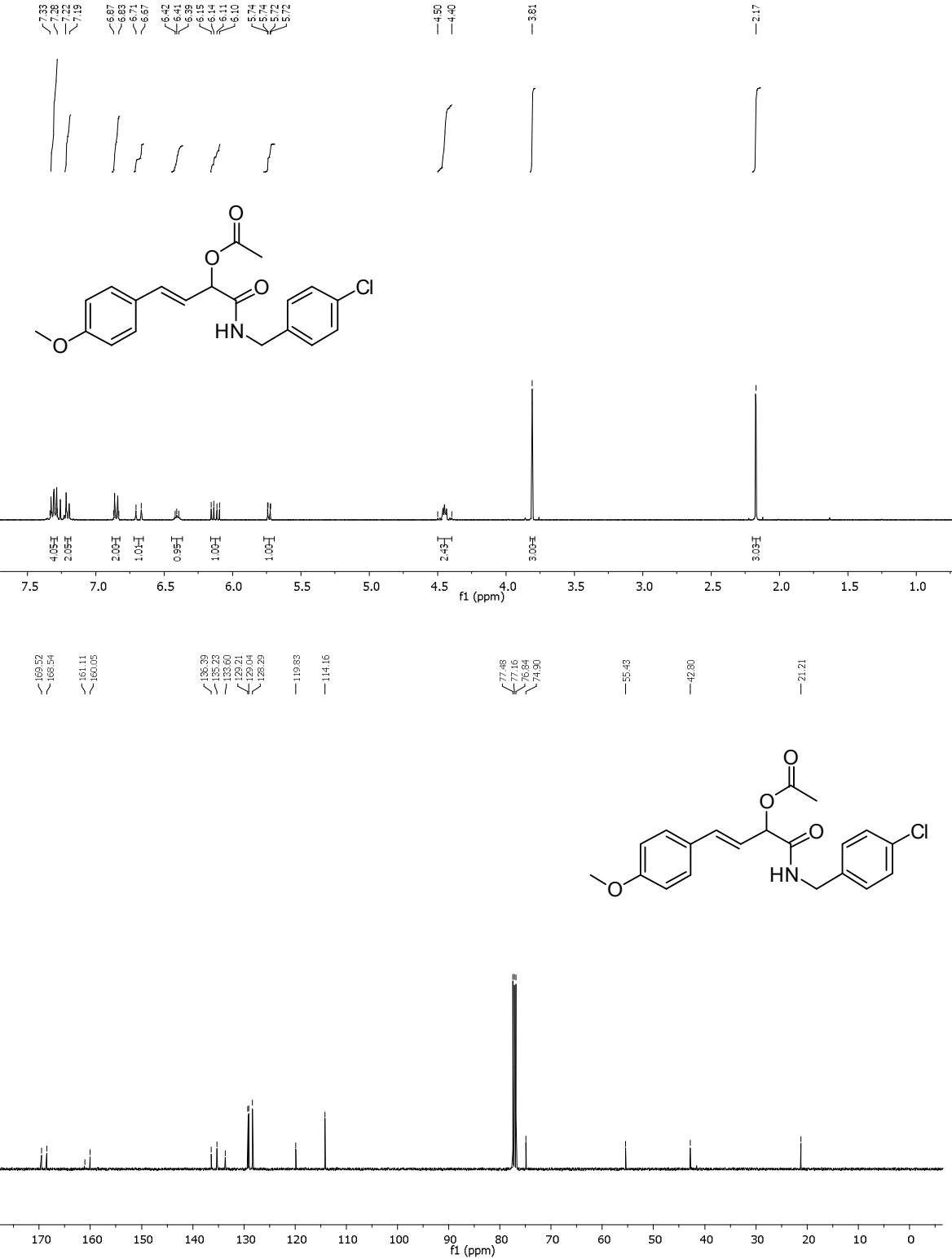
R_f: 0.36 (90:10 diethyl ether / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.33-7.28 (m, 4H), 7.22-7.19 (m, 2H), 6.87-6.83 (m, 2H), 6.69 (d, *J* = 15.8 Hz, 1H), 6.41 (t, *J* = 5.7 Hz, 1H), 6.13 (dd, *J* = 15.9, 7.3 Hz, 1H), 5.73 (dd, *J* = 7.3, 1.1 Hz, 1H), 4.45 (m, 2H), 3.81 (s, 3H), 2.17 (s, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.5, 168.5, 161.1, 160.0, 136.3, 135.2, 133.6, 129.2, , 129.0, 128.2, 119.8, 114.1, 74.9, 55.4, 42.8, 21.2.

HRMS: calculated for C₂₀H₂₀ClNO₄: 373.1081, found: 373.1075.

I.R. (thin film): 3449, 2936, 2838, 1751, 1699, 1607, 1513, 1494, 1371, 1254, 1215, 1094, 1039, 1017, 966 cm⁻¹.



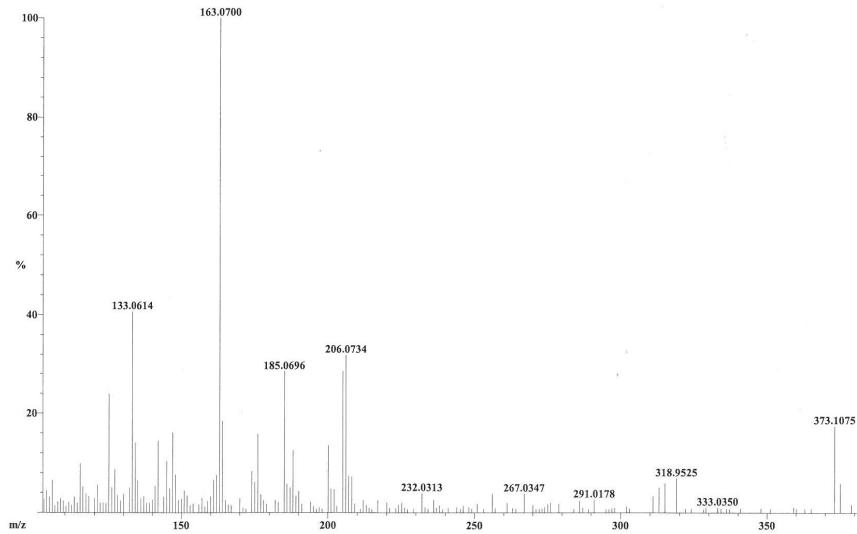
File: EE120
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 11-06-2014 (Time Run: 16:16:27)
Ionization mode: EI+

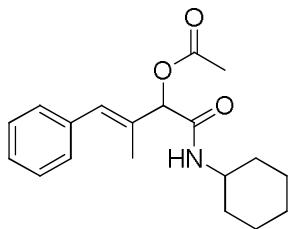
Scan: 159
Base: m/z 163; 42.8%FS TIC: 3801952

R.T.: 3.25

#Ions: 268



(E)-1-(cyclohexylamino)-3-methyl-1-oxo-4-phenylbut-3-en-2-yl acetate 2h



C₁₉H₂₅NO₃

M=315.183 g.mol⁻¹

This compound was synthesized according to the general procedure **I**, using alpha-Methyl-*trans*-cinnamaldehyde (438 mg, 3.0 mmol), acetic acid (0.17 ml, 3.0 mmol), and cyclohexyl isocyanide (0.37 ml, 3.0 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 100/0) gave the desired product in 79% isolated yield (750 mg, 2.4 mmol).

Aspect: white solid

M.P. = 103-104°C

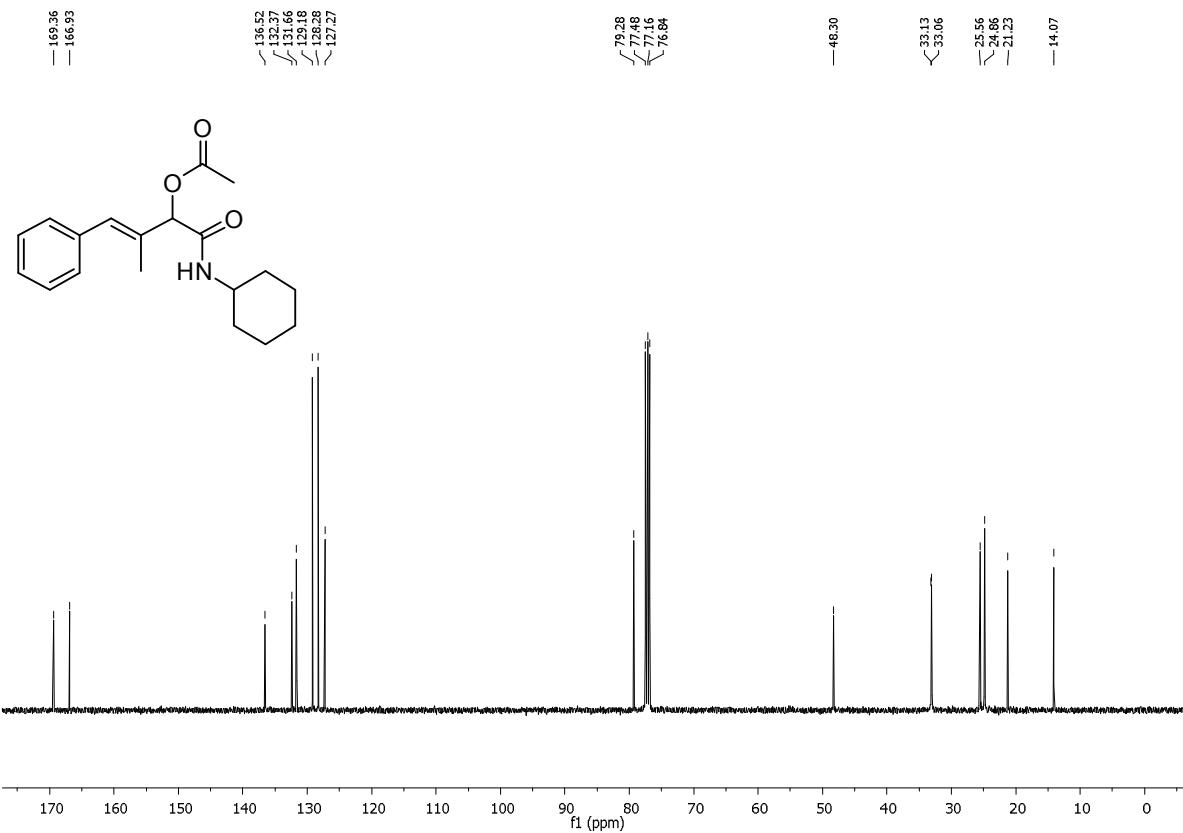
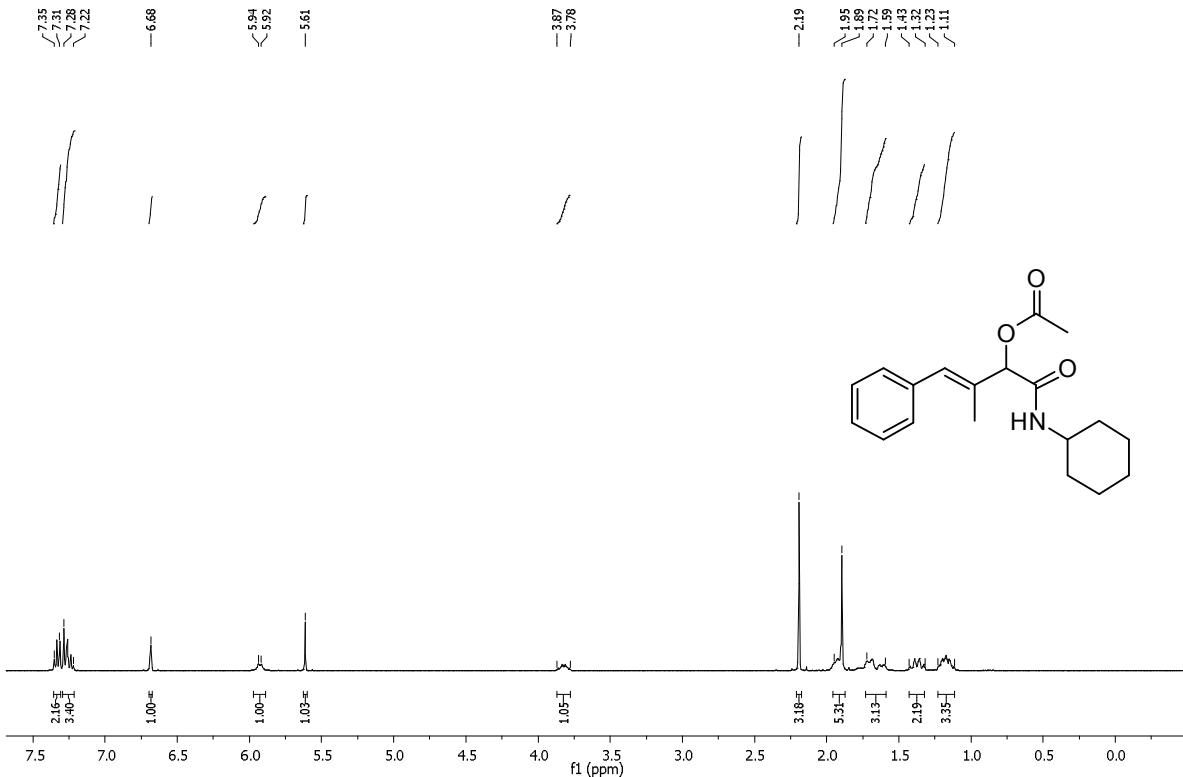
R_f: 0.38 (70:30 diethyl ether / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.35-7.31 (m, 2H), 7.28 – 7.22 (m, 3H), 6.68 (s, 1H), 5.93 (d, J = 7.8 Hz, 1H), 5.61 (s, 1H), 3.87-3.78 (m, 1H), 2.19 (s, 3H), 1.95-1.89 (m, 5H), 1.72-1.59 (m, 3H), 1.43 – 1.32 (m, 2H), 1.23 – 1.11 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.3, 166.9, 136.5, 132.3, 131.6, 129.1, 128.2, 127.2, 79.2, 48.3, 33.1, 33.0, 25.5, 24.8, 21.2, 14.0.

HRMS: calculated for C₁₉H₂₅NO₃ : 315.1834, found 315.1827.

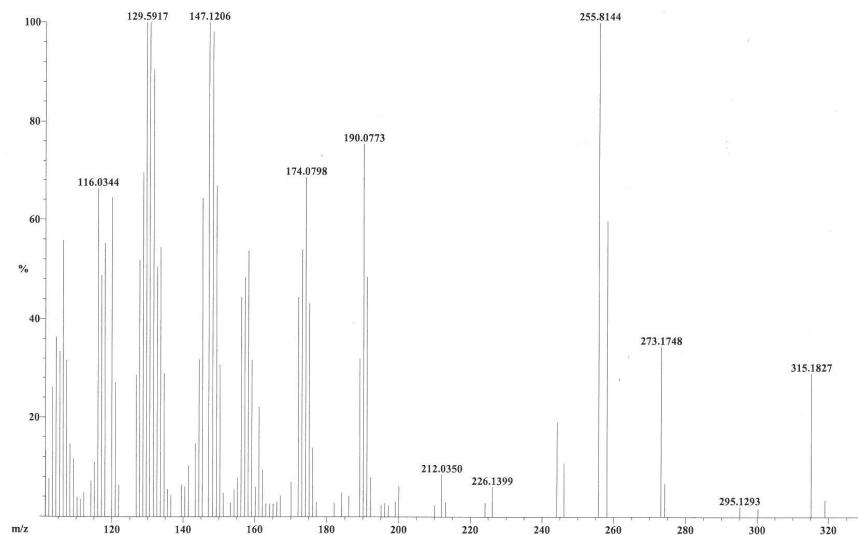
I.R. (thin film): 3303, 2934, 2819, 1745, 1652, 1540, 1448, 1371, 1228, 1022 cm⁻¹.



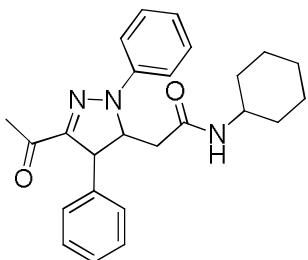
File: EE107
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 11-06-2014 (Time Run: 11:03:31)
Ionization mode: EI+

Scan: 154 R.T.: 3.15
Base: m/z 256; 100%FS TIC: 27250752 #Ions: 136



2-(3-acetyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide 3a



C₂₅H₂₉N₃O₂

M=403.226 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **1a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (43 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (60/40 to 80/20) gave the desired product in 72% isolated yield (77 mg, 0.2 mmol).

Aspect: ocher solid

M.P. = 150-160°C

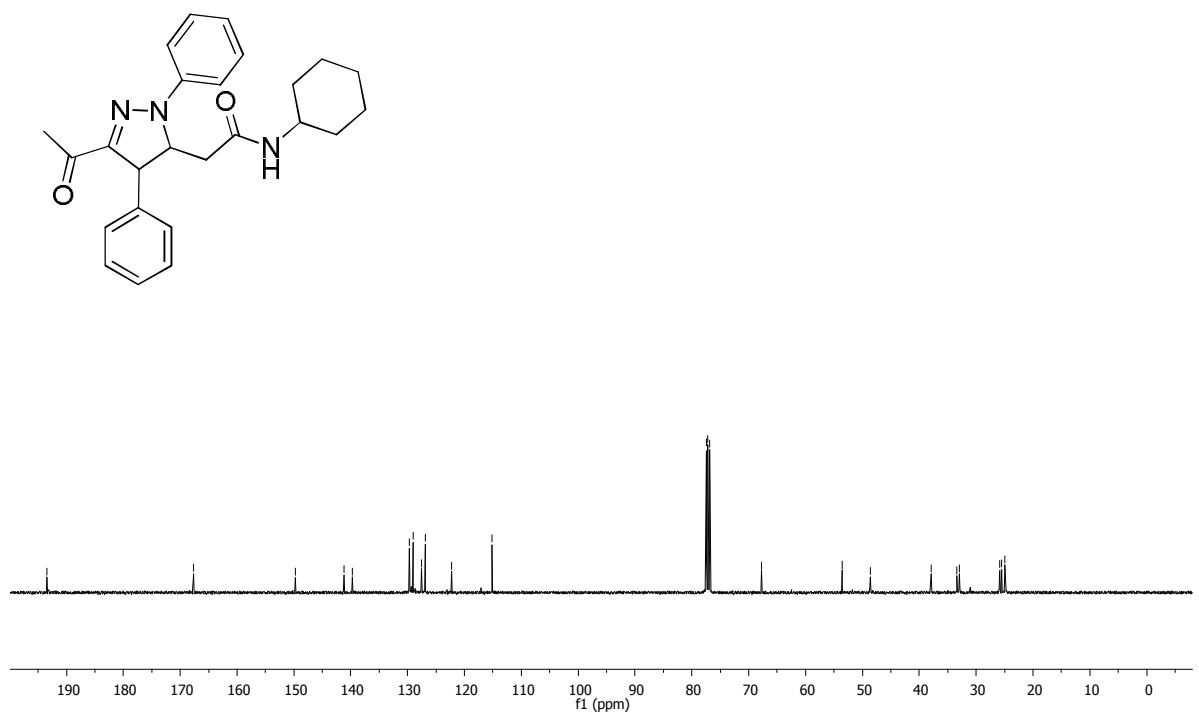
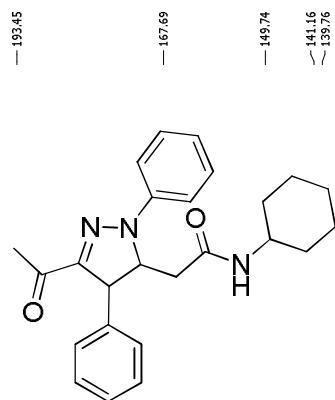
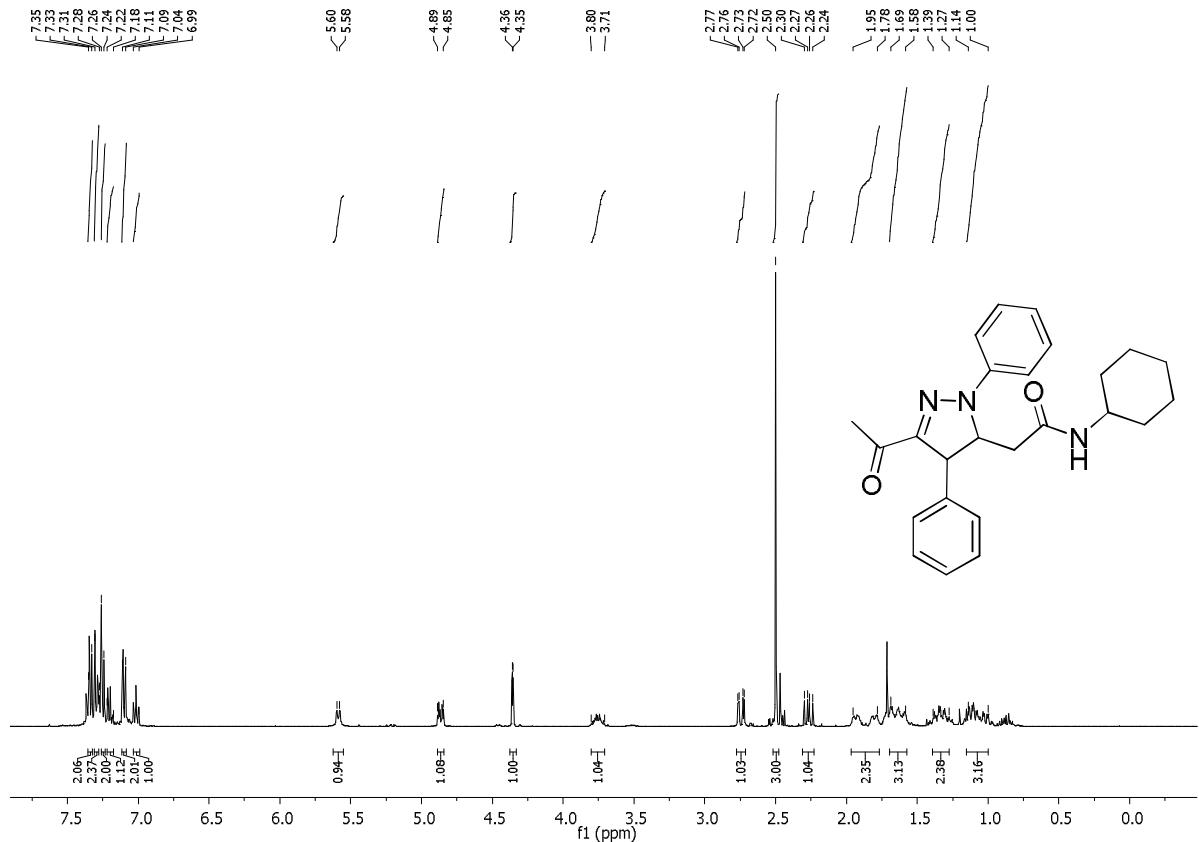
R_f: 0.2 (60:40 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.35-7.32 (m, 2H), 7.31-7.28 (m, 2H), 7.26-7.23 (m, 2H), 7.22-7.18 (m, 1H), 7.12-7.08 (m, 2H), 7.04-6.99 (m, 1H), 5.59 (d, *J* = 8.0 Hz, 1H), 4.89-4.84 (m, 1H), 4.36 (d, *J* = 2.6 Hz, 1H), 3.80-3.71 (m, 1H), 2.74 (dd, *J* = 14.5, 3.5 Hz, 1H), 2.50 (s, 3H), 2.27 (dd, *J* = 14.5, 9.9 Hz, 1H), 1.95-1.78 (m, 2H), 1.69-1.58 (m, 3H), 1.39-1.27 (m, 2H), 1.14-1.00 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.4, 167.6, 149.7, 141.1, 139.7, 129.6, 129.0, 127.5, 126.9, 122.2, 115.1, 67.7, 53.5, 48.6, 37.8, 33.3, 33.0, 25.8, 25.5, 24.9.

HRMS: calculated for C₂₅H₂₉N₃O₂: 403.2260, found: 403.2264.

I.R. (thin film): 3305, 2928, 1637, 1597, 1526, 1496, 1453, 1269, 1212, 1139 cm⁻¹.



File: EE86

Date Run: 11-06-2014 (Time Run: 16:47:06)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

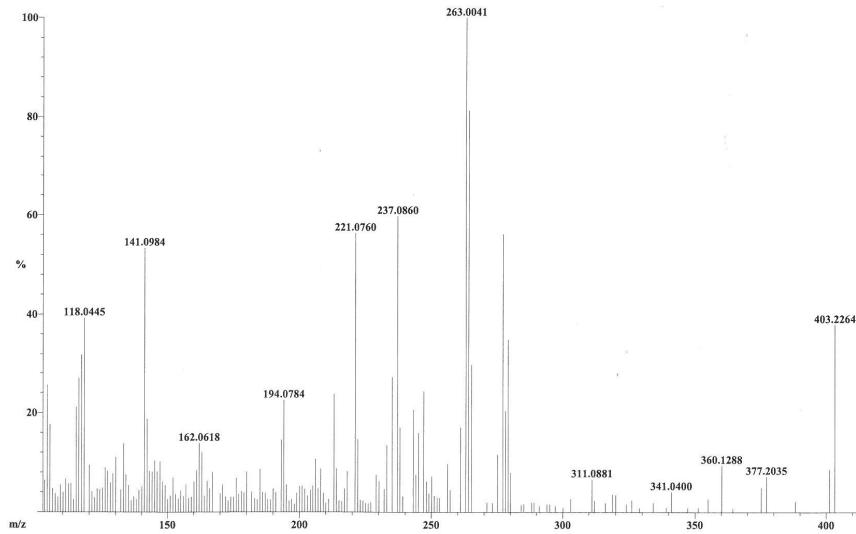
Ionization mode: EI+

Scan: 81

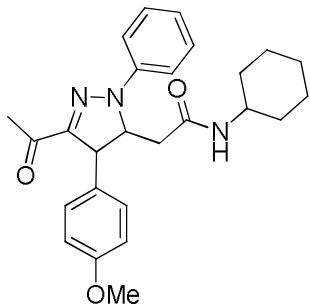
R.T.: 1.65

Base: m/z 263; 100%FS TIC: 18327280

#Ions: 268



2-(3-acetyl-4-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide 3b



C₂₆H₃₁N₃O₃

M=433.236 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **6a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (49 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (50/50 to 80/20) gave the desired product in 54% isolated yield (70 mg, 0.2 mmol).

Aspect: brown yellow oil

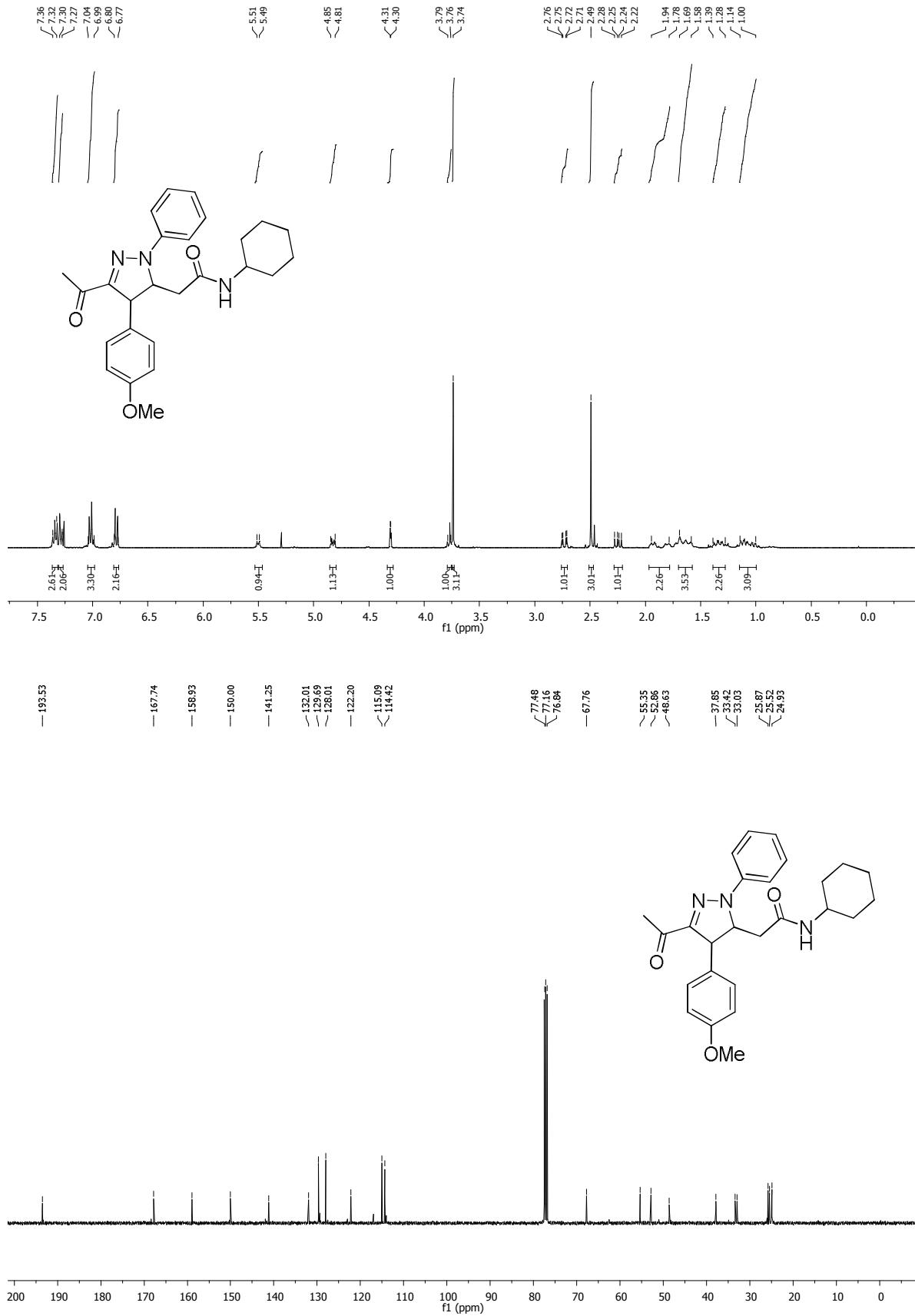
R_f: 0.34 (80:20 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.36-7.32 (m, 2H), 7.30-7.27 (m, 2H), 7.04-6.99 (m, 3H), 6.80-6.77 (m, 2H), 5.50 (d, *J* = 8.0 Hz, 1H), 4.85-4.81 (m, 1H), 4.31 (d, *J* = 2.6 Hz, 1H), 3.77-3.79-3.75 (m, 1H), 3.74 (s, 3H), 2.73 (dd, *J* = 14.5, 3.5 Hz, 1H), 2.49 (s, 3H), 2.25 (dd, *J* = 14.5, 9.8 Hz, 1H), 1.94-1.78 (m, 2H), 1.69-1.58 (m, 3H), 1.39-1.28 (m, 2H), 1.14-1.00 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.5, 167.7, 158.9, 150.0, 141.2, 132.0, 129.6, 128.0, 122.2, 155.0, 114.4, 67.7, 55.3, 52.8, 48.6, 37.8, 33.4, 33.0, 25.8, 25.5, 24.9.

HRMS: calculated for C₂₆H₃₁N₃O₃: 433.2365, found: 433.2355.

I.R. (thin film): 3302, 2928, 2847, 1636, 1597, 1497, 1245, 1138, 1032, 824, 732, 688 cm⁻¹.



File: EE1242

Date Run: 11-07-2014 (Time Run: 09:58:00)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

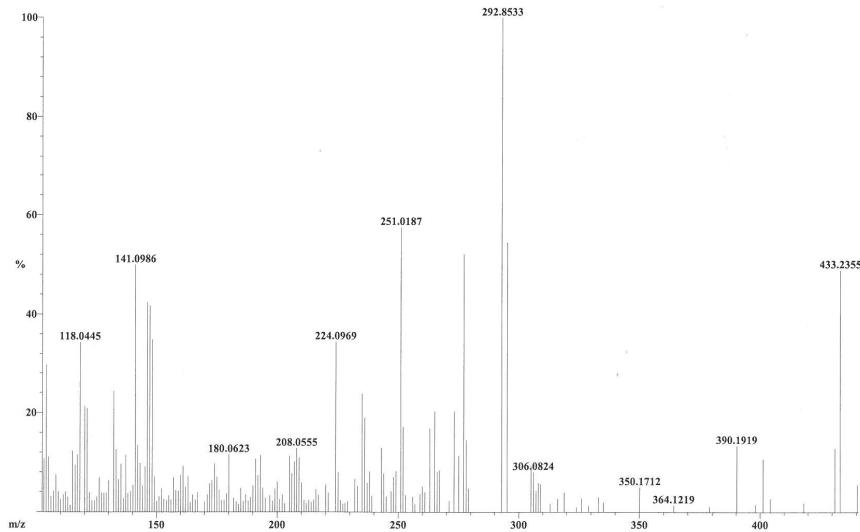
Ionization mode: EI+

Scan: 286

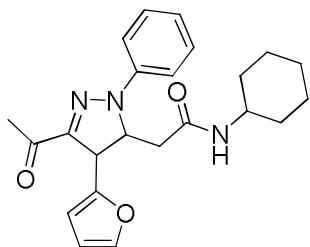
R.T.: 5.87

Base: m/z 293; 100%FS TIC: 17245344

#Ions: 226



**2-(3-acetyl-4-(furan-2-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide
3c**



C₂₃H₂₇N₃O₃

M=393.205 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **4a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (56 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (50/50 to 80/20) gave the desired product in 51% isolated yield (69 mg, 0.2 mmol).

Aspect: brown yellow oil

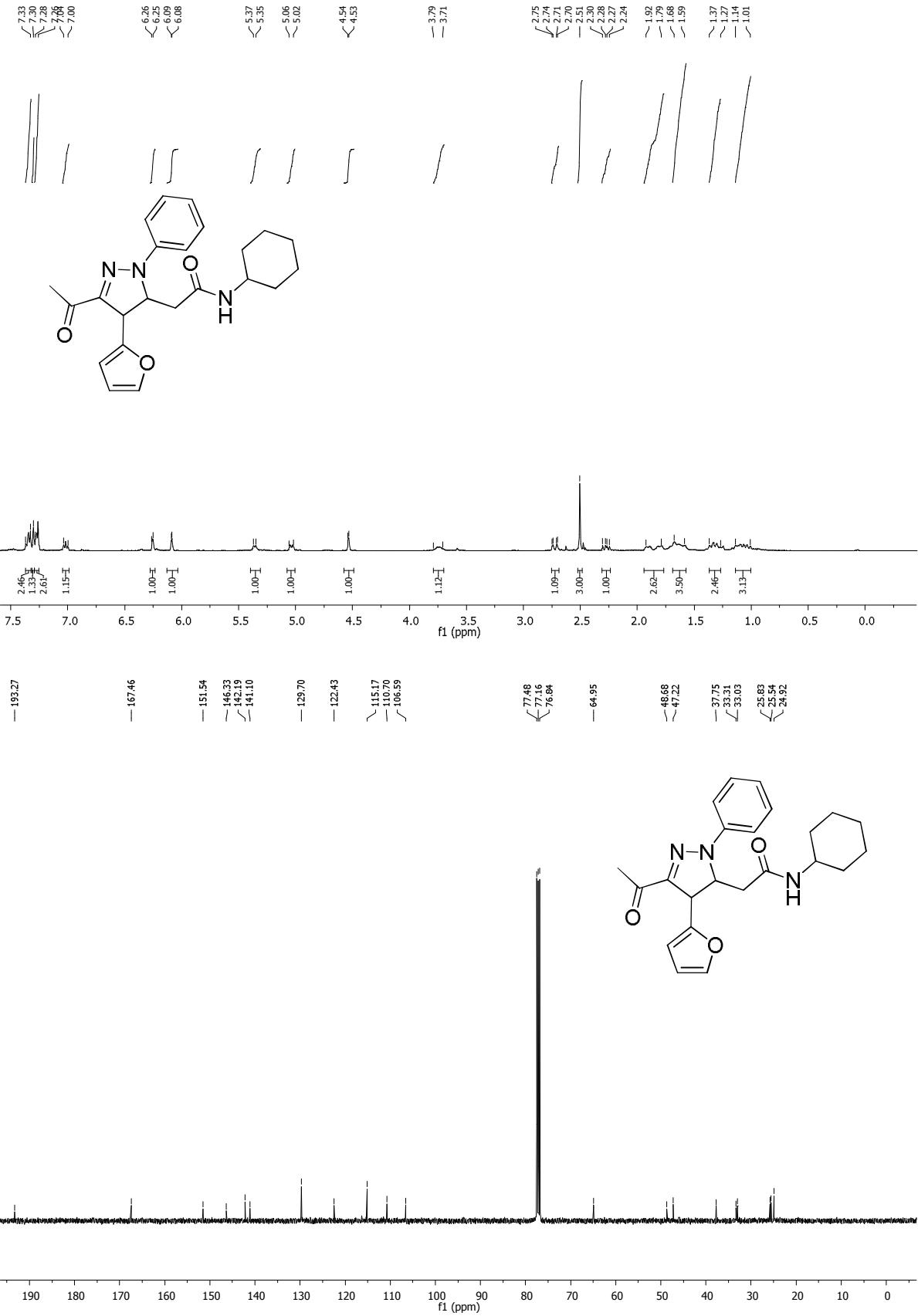
R_f: 0.26 (70:30 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.37-7.33 (m, 2H), 7.31-7.29 (m, 1H), 7.28-7.26 (m, 2H), 7.04-7.00 (m, 1H), 6.26-6.25 (m, 1H), 6.09 (d, *J* = 3.0 Hz, 1H), 5.36 (d, *J* = 7.6 Hz, 1H), 5.06-5.02 (m, 1H), 4.54 (d, *J* = 2.8 Hz, 1H), 3.79-3.71 (m, 1H), 2.73 (dd, *J* = 14.6, 3.4 Hz, 1H), 2.51 (s, 3H), 2.27 (dd, *J* = 14.6, 9.4 Hz, 1H), 1.92-1.79 (m, 2H), 1.68-1.59 (m, 3H), 1.37-1.27 (m, 2H), 1.14-1.01 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.2, 167.4, 151.5, 146.3, 142.1, 141.1, 129.6, 122.4, 115.1, 110.7, 106.5, 64.9, 48.6, 47.2, 37.7, 33.3, 33.0, 31.0, 25.8, 25.5, 24.9.

HRMS: calculated for C₂₃H₂₇N₃O₃ 393.2052, found 393.2057.

I.R. (thin film): 3304, 2929, 2843, 1638, 1598, 1532, 1497, 1355, 1270, 1149 cm⁻¹.



File: EE114

Date Run: 11-06-2014 (Time Run: 16:58:51)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

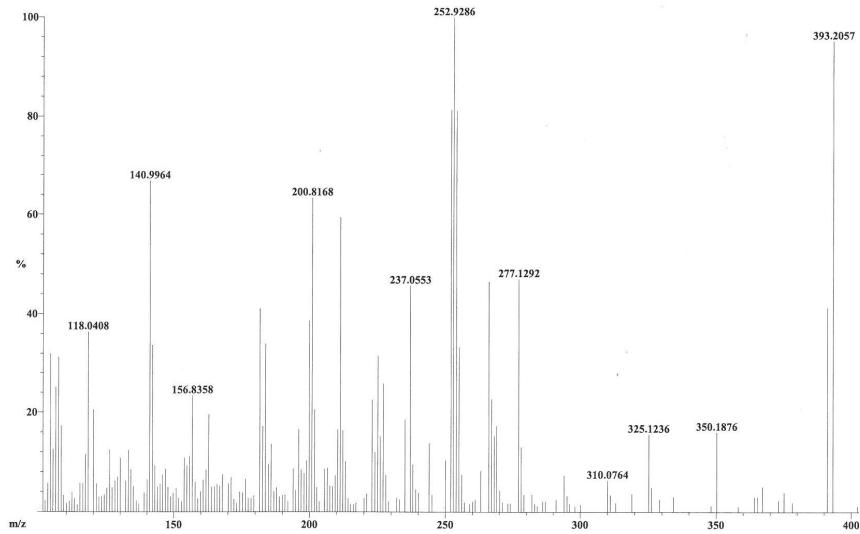
Ionization mode: EI+

Scan: 205

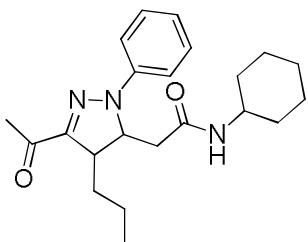
R.T.: 4.2

Base: m/z 253; 100%FS TIC: 22909584

#Ions: 238



2-(3-acetyl-1-phenyl-4-propyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide 3d



C₂₂H₃₁N₃O₂

M=369.241 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **7a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (60 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 80/20) gave the desired product in 35% isolated yield (48 mg, 0.1 mmol).

Aspect: brown yellow oil

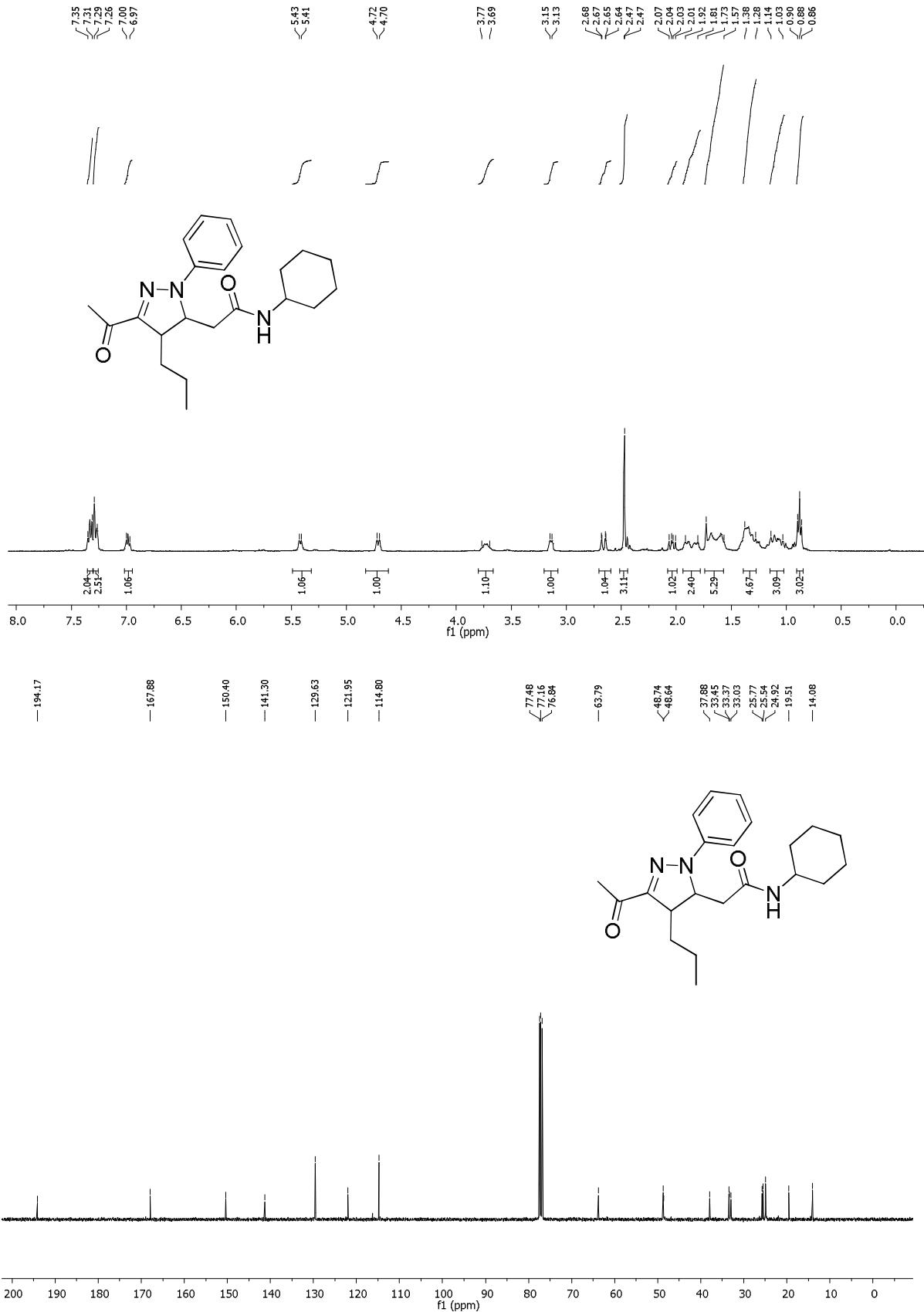
R_f: 0.38 (50:50 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.35-7.31 (m, 2H), 7.29-7.26 (m, 2H), 7.00-6.97 (m, 1H), 5.42 (d, *J* = 7.8 Hz, 1H), 4.71 (d, *J* = 9.9 Hz, 1H), 3.77-3.69 (m, 1H), 3.14 (d, *J* = 7.6 Hz, 1H), 2.66 (dd, *J* = 14.3, 2.5 Hz, 1H), 2.47 (s, 3H), 2.04 (dd, *J* = 14.3, 10.0 Hz, 1H), 1.92-1.81 (m, 2H), 1.74-1.56 (m, 5H), 1.38-1.28 (m, 4H), 1.14-1.03 (m, 3H), 0.88 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 194.1, 167.8, 150.4, 141.3, 129.6, 121.9, 114.8, 63.7, 48.7, 48.6, 37.8, 33.4, 33.3, 33.0, 25.7, 25.5, 24.9, 19.5, 14.0.

HRMS: calculated for C₂₂H₃₁N₃O₂: 369.2416, found: 369.2412.

I.R. (thin film): 3259, 2928, 2853, 1650, 1601, 1548, 1493, 1356, 1230, 1166, 996 cm⁻¹.



File: EE1252

Date Run: 11-07-2014 (Time Run: 10:26:46)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

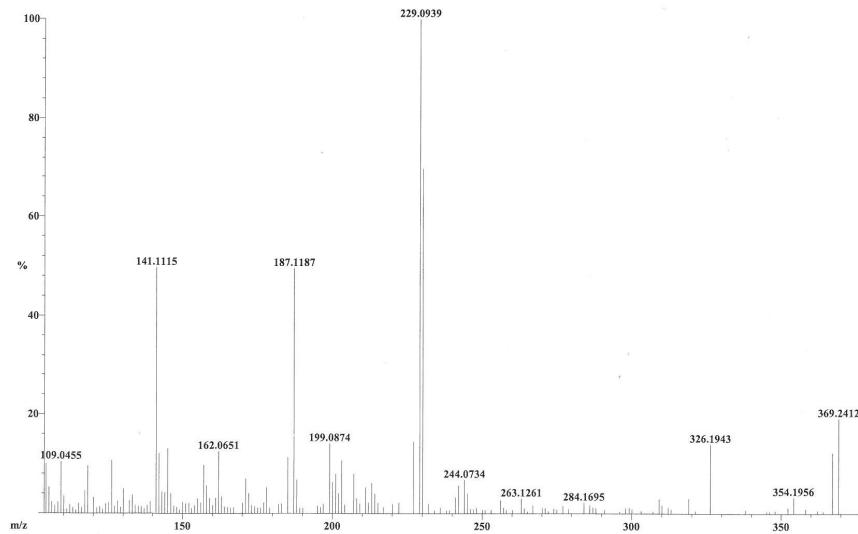
Ionization mode: EI+

Scan: 120

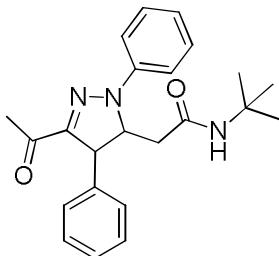
R.T.: 2.45

Base: m/z 229; 86.1%FS TIC: 7352384

#Ions: 289



2-(3-acetyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-(tert-butyl)acetamide 3e



C₂₃H₂₇N₃O₂

M=377.210 g·mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **3a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (59 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (60/40 to 80/20) gave the desired product in 71% isolated yield (98 mg, 0.2 mmol).

Aspect: ochre solid

M.P. = 180-190°C

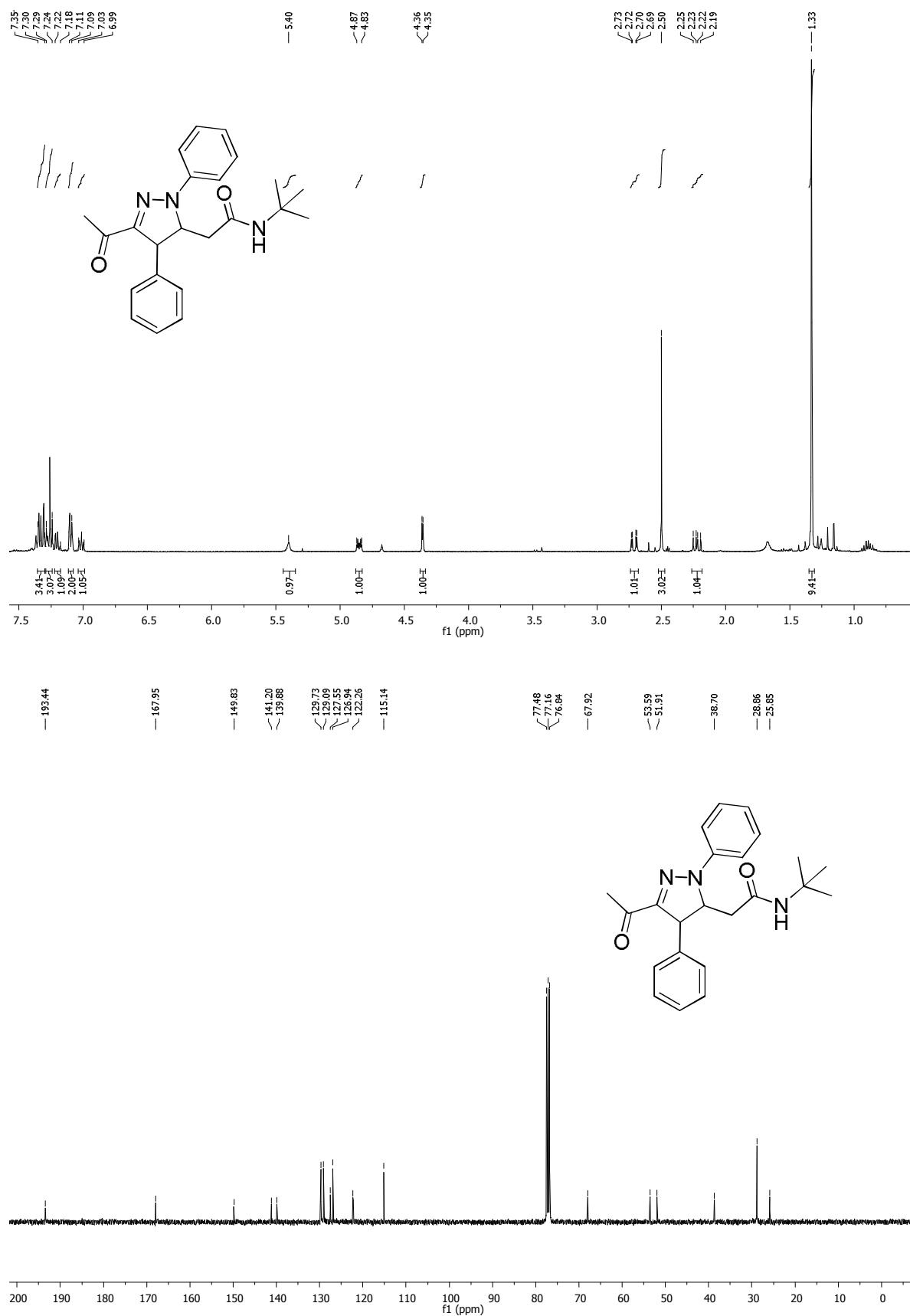
R_f: 0.34 (60:40 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.35-7.30 (m, 3H), 7.29-7.24 (m, 3H), 7.22-7.18 (m, 1H), 7.11-7.08 (m, 2H), 7.03-6.99 (m, 1H), 5.40 (s, 1H), 4.87-4.83 (m, 1H), 4.36 (d, *J* = 2.7 Hz, 1H), 2.71 (dd, *J* = 14.4, 3.3 Hz, 1H), 2.50 (s, 3H), 2.22 (dd, *J* = 14.4, 9.7 Hz, 1H), 1.33 (s, 9H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.4, 167.9, 149.8, 141.2, 139.8, 129.7, 129.0, 127.5, 126.9, 122.2, 115.1, 67.9, 53.5, 51.9, 38.7, 28.8, 25.8.

HRMS: calculated for C₂₃H₂₇N₃O₂: 377.2103, found: 377.2106.

I.R. (thin film): 3324, 2964, 1643, 1597, 1497, 1454, 1355, 1268, 1213, 1139 cm⁻¹.



File: EE97

Date Run: 11-06-2014 (Time Run: 16:25:25)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

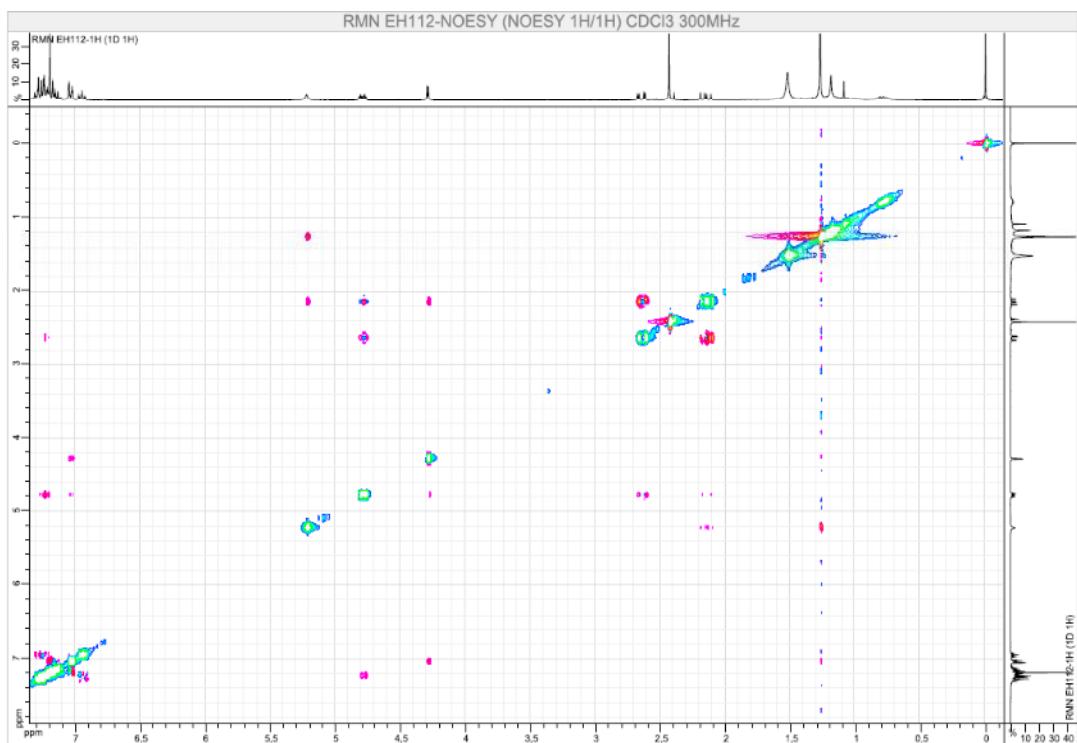
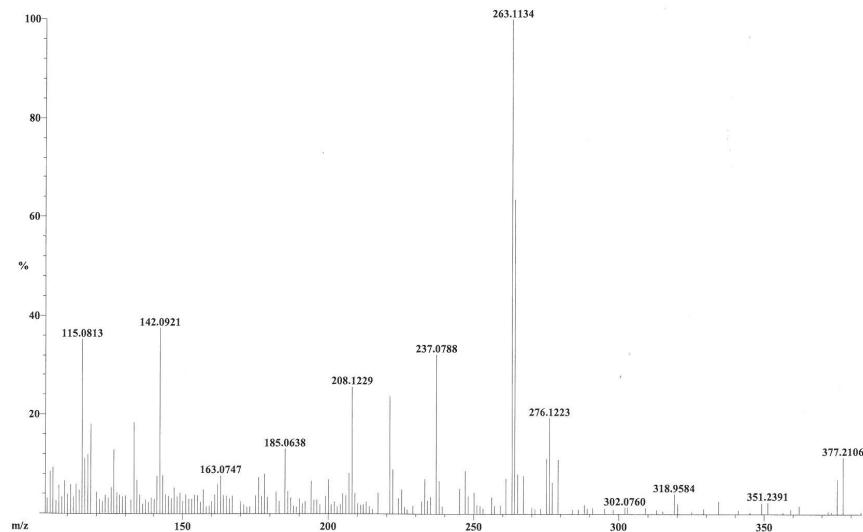
Ionization mode: EI+

Scan: 146

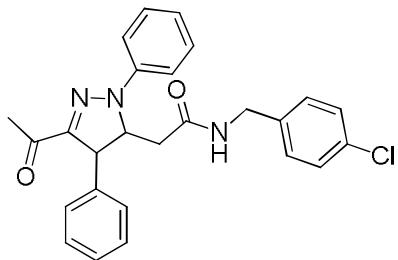
R.T.: 2.98

Base: m/z 263; 80.5%FS TIC: 9594752

#Ions: 304



2-(3-acetyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-(4-chlorobenzyl)acetamide 3f



$$M=445.155 \text{ g.mol}^{-1}$$

This compound was synthesized according to the general procedure **II**, using Passerini adduct **8a** (100 mg, 0.2 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (47 mg, 0.2 mmol). Purification by flash chromatography with a gradient Et₂O/EP (60/40 to 80/20) gave the desired product in 50% isolated yield (65 mg, 0.1 mmol).

Aspect: Green yellow solid

M.P. = 134-135°C

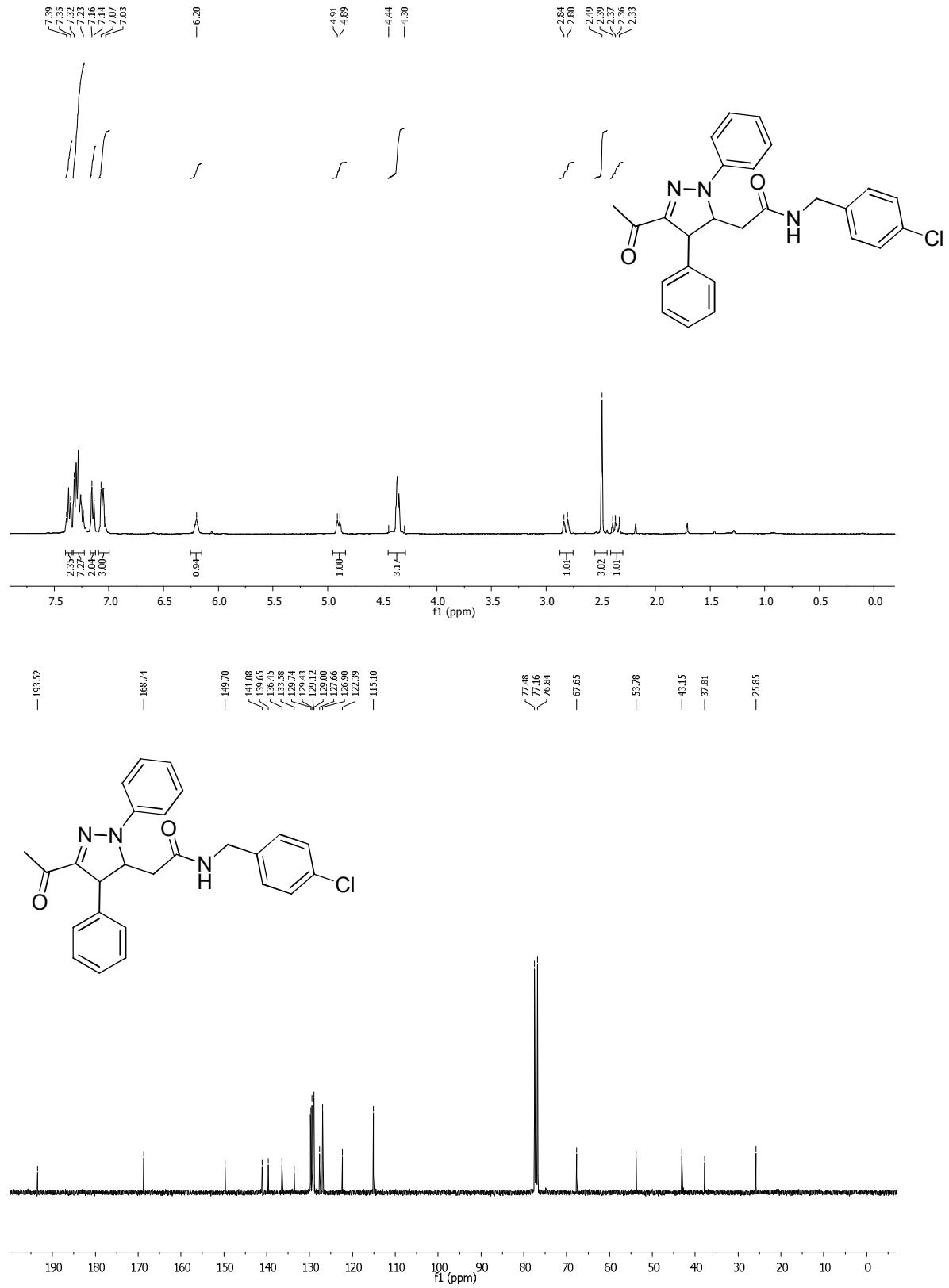
R_f: 0.21 (70:30 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.39-7.35 (m, 2H), 7.32-7.23 (m, 7H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.07-7.03 (m, 3H), 6.20 (br s, 1H), 4.91-4.89 (m, 1H), 4.44-4.30 (m, 3H), 2.82 (d, *J* = 14.5 Hz, 1H), 2.49 (s, 3H), 2.36 (dd, *J* = 14.5, 9.9 Hz, 1H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.5, 168.7, 149.7, 141.1, 139.6, 136.4, 133.5, 129.7, 129.4, 129.1, 129.0, 127.6, 126.9, 122.3, 115.1, 67.6, 53.7, 43.1, 37.8, 25.8.

HRMS: calculated for C₂₆H₂₄ClN₃O₂: 445.1557, found: 445.1558.

I.R. (thin film): 3448, 3067, 3033, 2931, 1685, 1669, 1600, 1500, 1458, 1356, 1270, 1212, 1139, 1095, 1017, 909 cm⁻¹.

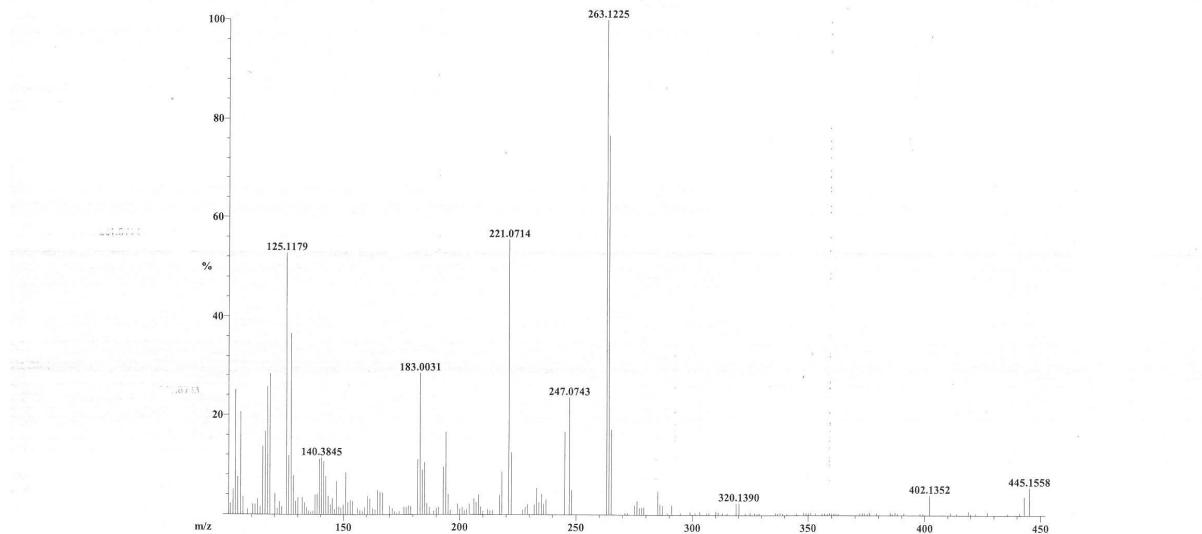


File: EE2001
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

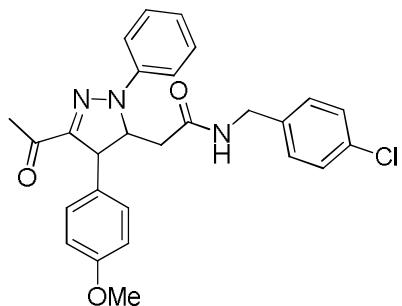
Date Run: 02-10-2015 (Time Run: 16:10:41)

Ionization mode: EI+

Scan: 340 R.T.: 6.98
Base: m/z 263; 94.2%FS TIC: 9744368 #Ions: 284



2-(3-acetyl-4-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-(4-chlorobenzyl)acetamide 3g



$$M=475.166 \text{ g.mol}^{-1}$$

This compound was synthesized according to the general procedure **II**, using Passerini adduct **5a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (43 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (60/40 to 80/20) gave the desired product in 70% isolated yield (89 mg, 0.2 mmol).

Aspect: Green yellow oil

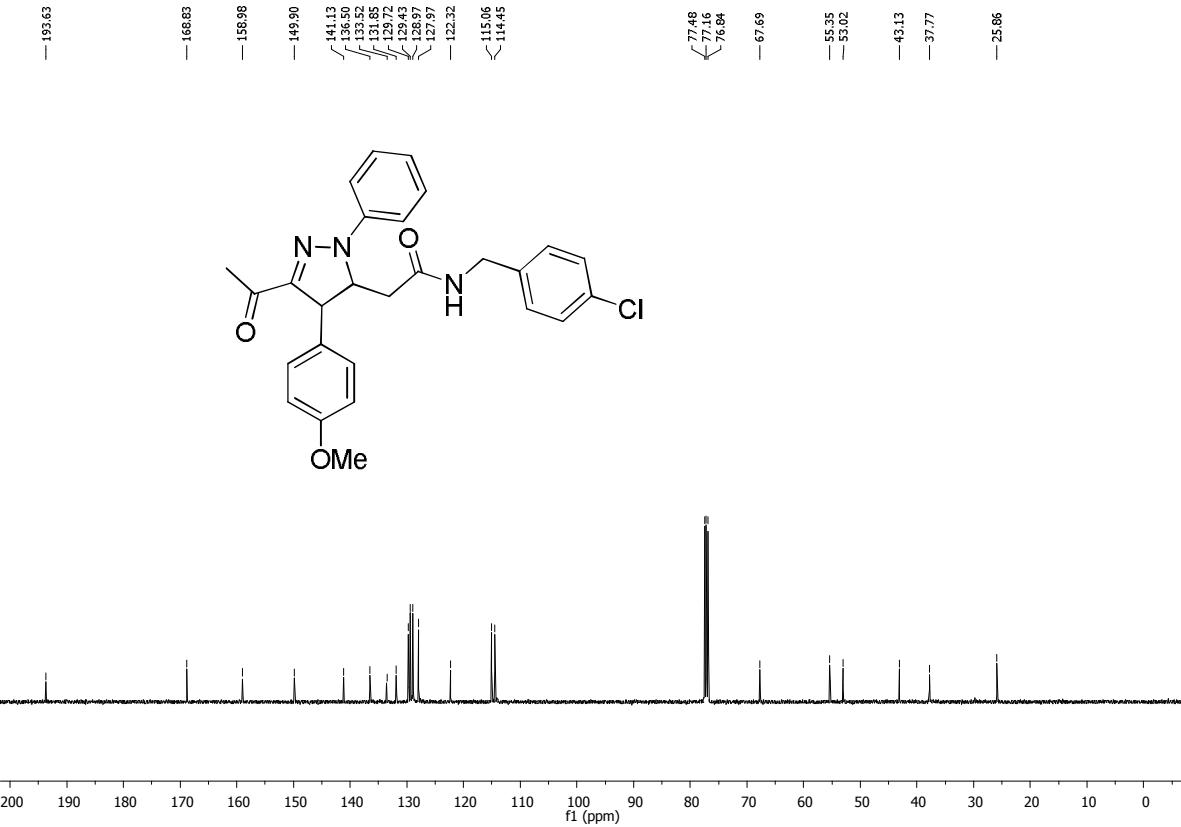
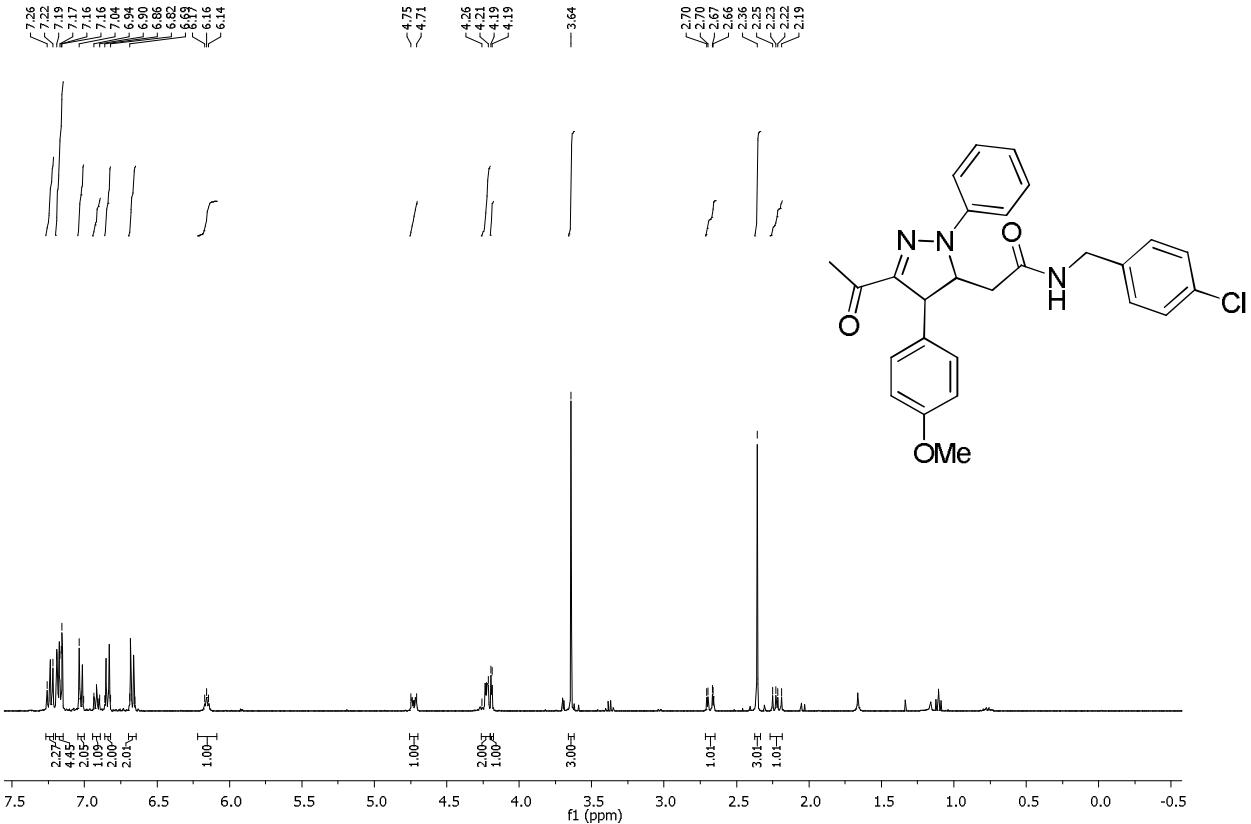
R_f: 0.25 (80:20 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.27-7.22 (m, 2H), 7.20-7.15 (m, 4H), 7.05-7.00 (m, 2H), 6.94-6.90 (m, 1H), 6.86-6.82 (m, 2H), 6.69-6.65 (m, 2H), 6.16 (t, *J* = 5.8 Hz, 1H), 4.73 (dt, *J* = 9.8, 3.16 Hz, 1H), 4.26-4.21 (m, 2H), 4.19 (d, *J* = 2.6 Hz, 1H), 3.64 (s, 3H), 2.68 (dd, *J* = 14.5, 3.4 Hz, 1H), 2.36 (s, 3H), 2.22 (dd, *J* = 14.5, 9.8 Hz, 1H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.6, 168.8, 158.9, 149.9, 141.1, 136.5, 133.5, 131.8, 129.7, 129.4, 128.9, 127.9, 122.3, 115.0, 114.4, 67.6, 55.3, 53.0, 43.1, 37.7, 25.8.

HRMS: calculated for C₂₇H₂₆ClN₃O₃ 475.1663, found 475.1662.

I.R. (thin film): 3448, 2933, 2837, 1685, 1685, 1670, 1600, 1512, 1501, 1356, 1304, 1262, 1250, 1212, 1179, 1138, 1040, 1017, 964 cm⁻¹.



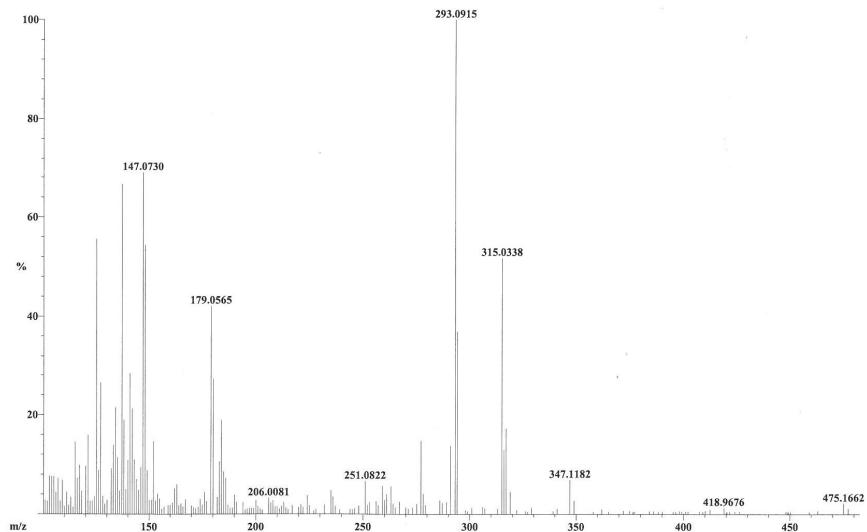
File: EE123
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 11-06-2014 (Time Run: 17:09:21)
Ionization mode: EI+

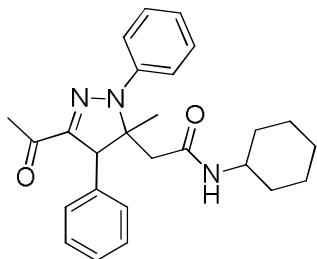
Scan: 232
Base: m/z 293; 76%FS TIC: 10172336

R.T.: 4.77

#Ions: 305



**2-(3-acetyl-5-methyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide
3h**



C₂₆H₃₁N₃O₂

M=417.241 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **2a** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (51 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (40/60 to 80/20) gave the desired product in 53% isolated yield (70 mg, 0.2 mmol).

Aspect: brown yellow oil

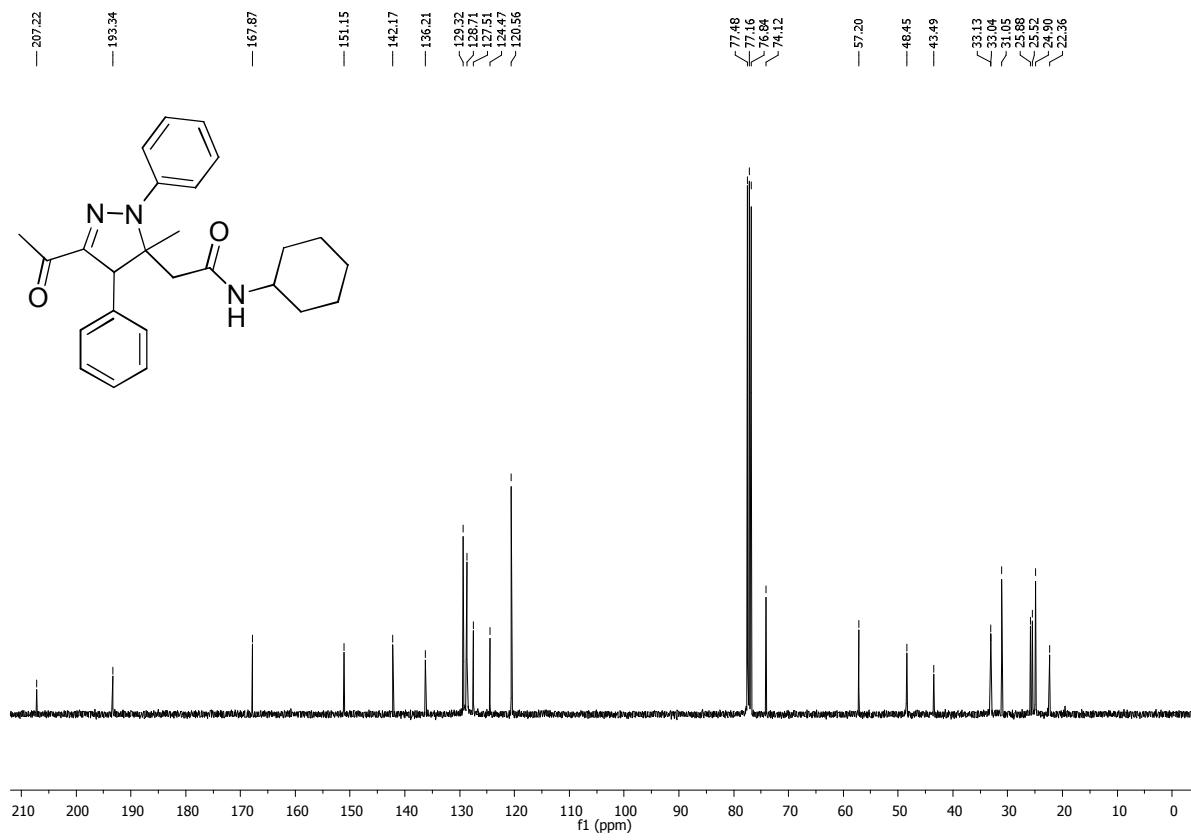
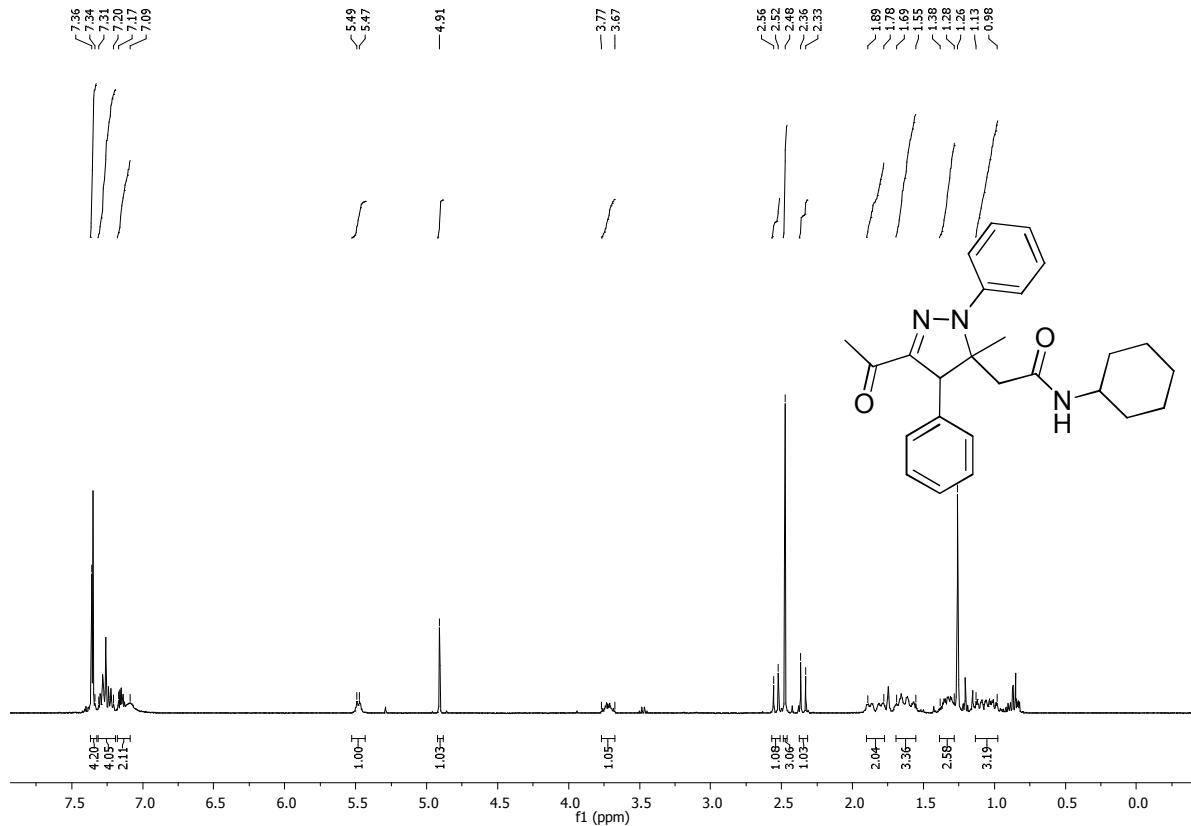
R_f: 0.27 (60:40 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.37-7.34 (m, 4H), 7.31-7.20 (m, 4H), 7.17-7.09 (m, 2H), 5.48 (d, *J* = 7.8 Hz, 1H), 4.91 (s, 1H), 3.77-3.67 (m, 1H), 2.54 (d, *J* = 14.0 Hz, 1H), 2.48 (s, 3H), 2.35 (d, *J* = 14.0 Hz, 1H), 1.89-1.78 (m, 2H), 1.69-1.55 (m, 3H), 1.38-1.28 (m, 2H), 1.26 (s, 3H), 1.13-0.98 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 207.7, 193.3, 167.8, 151.1, 142.1, 136.2, 129.3, 128.7, 127.5, 124.4, 120.5, 74.1, 57.2, 48.4, 43.4, 33.1, 33.0, 25.8, 25.5, 24.9, 22.3.

HRMS: calculated for C₂₆H₃₁N₃O₂: 417.2416, found: 417.2430.

I.R. (thin film): 3305, 2930, 2854, 1638, 1596, 1537, 1491, 1452, 1292, 1220, 1107, 731, 397cm⁻¹.



File: EE96

Date Run: 11-06-2014 (Time Run: 16:39:54)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

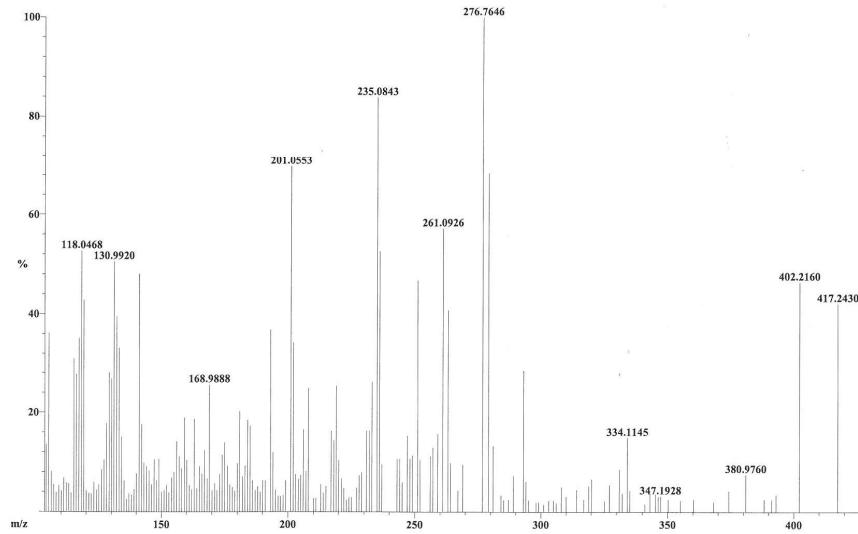
Ionization mode: EI+

Scan: 126

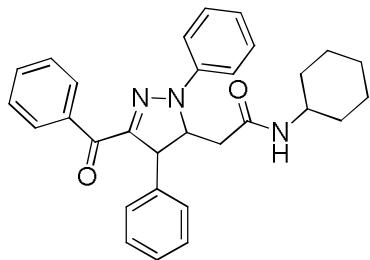
R.T.: 2.58

Base: m/z 277; 100%FS TIC: 26742816

#Ions: 226



2-(3-benzoyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide 3i



C₃₀H₃₁N₃O₂

M=465.241 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **1a** (100 mg, 0.3 mmol) and (*E*)-1-phenyl-2-(2-phenylhydrazone)ethanone (74 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (60/40 to 80/20) gave the desired product in 70% isolated yield (108 mg, 0.2 mmol).

Aspect: yellow oil

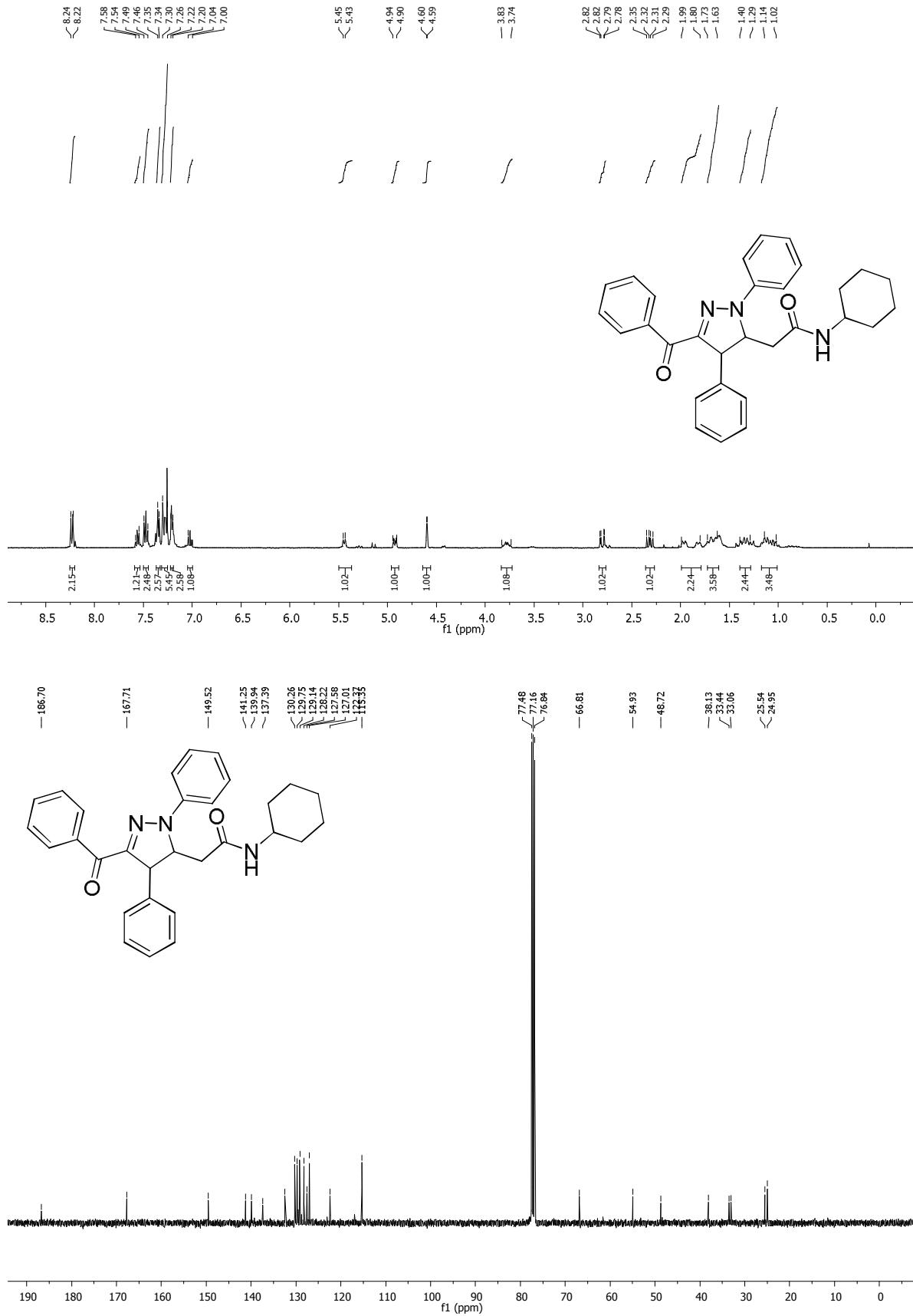
R_f: 0.30 (60:40 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.24-8.22 (m, 2H), 7.58-7.54 (m, 1H), 7.49-7.46 (m, 2H), 7.35-7.34 (m, 2H), 7.30-7.26 (m, 5H), 7.22-7.20 (m, 2H), 7.04-7.00 (m, 1H), 5.44 (d, *J* = 8.0 Hz, 1H), 4.94-4.90 (m, 1H), 4.60 (d, *J* = 2.6 Hz, 1H), 3.83-3.74 (m, 1H), 2.80 (dd, *J* = 14.6, 3.4 Hz, 1H), 2.32 (dd, *J* = 14.6, 9.9 Hz, 1H), 1.99-1.80 (m, 2H), 1.73-1.63 (m, 3H), 1.40-1.29 (m, 2H), 1.14-1.02 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 186.7, 167.7, 149.5, 141.2, 139.9, 137.3, 132.4, 130.2, 129.7, 129.1, 128.2, 127.5, 127.0, 122.3, 115.3, 66.8, 54.9, 48.7, 38.1, 33.4, 33.0, 25.5, 24.9.

HRMS: calculated for C₃₀H₃₁N₃O₂ 465.2416, found 465.2413.

I.R. (thin film): 3439, 3362, 2934, 2857, 1678, 1633, 1599, 1532, 1500, 1457, 1330, 1273, 1223, 1160, 1148, 909 cm⁻¹.



File: EE128
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

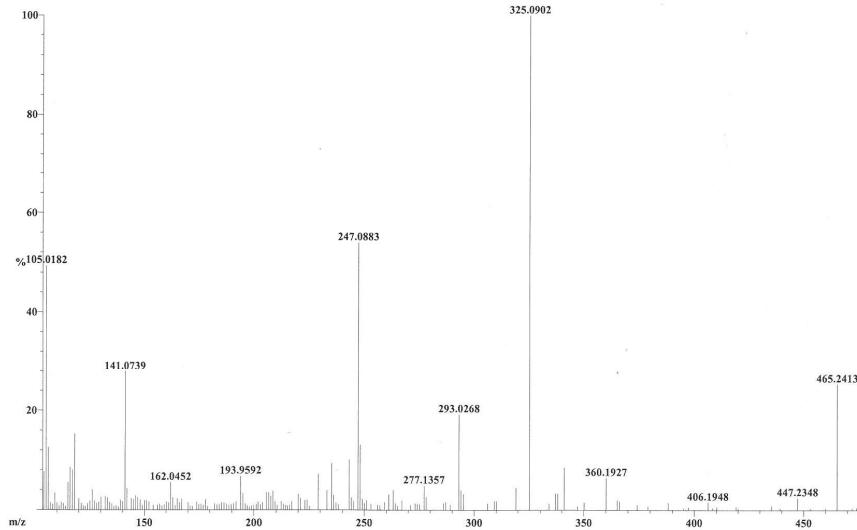
Date Run: 11-07-2014 (Time Run: 10:12:09)

Ionization mode: EI+

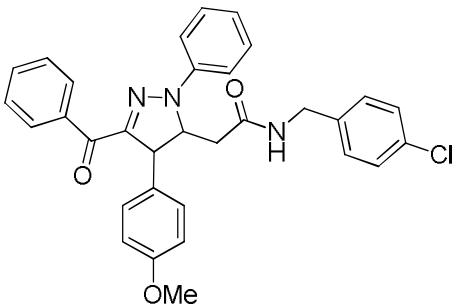
Scan: 305
Base: m/z 325; 100%FS TIC: 7279872

R.T.: 6.27

#Ions: 285



2-(3-benzoyl-4-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-(4-chlorobenzyl)acetamide 3j



M=537.181 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **5a** (100 mg, 0.3 mmol) and (*E*)-1-phenyl-2-(2-phenylhydrazone)ethanone (60 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (60/40 to 80/20) gave the desired product in 50% isolated yield (72 mg, 0.1 mmol).

Aspect: yellow oil

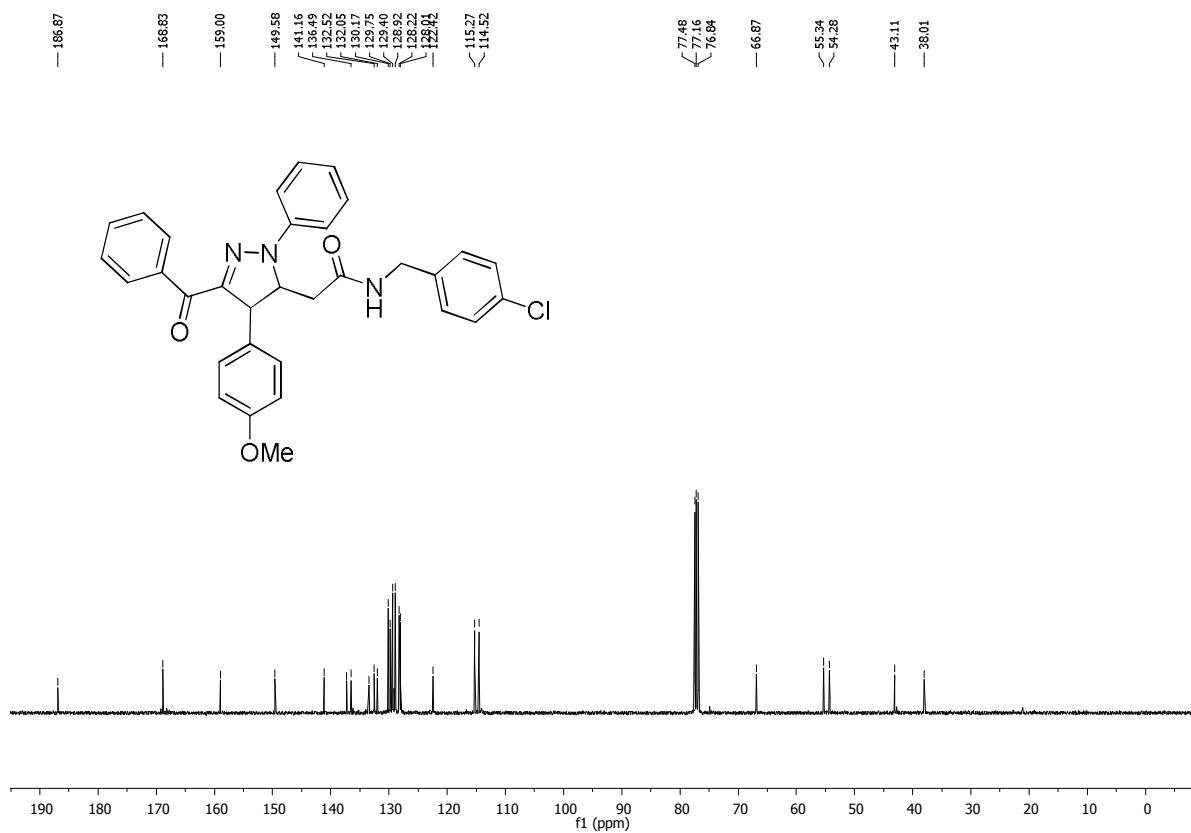
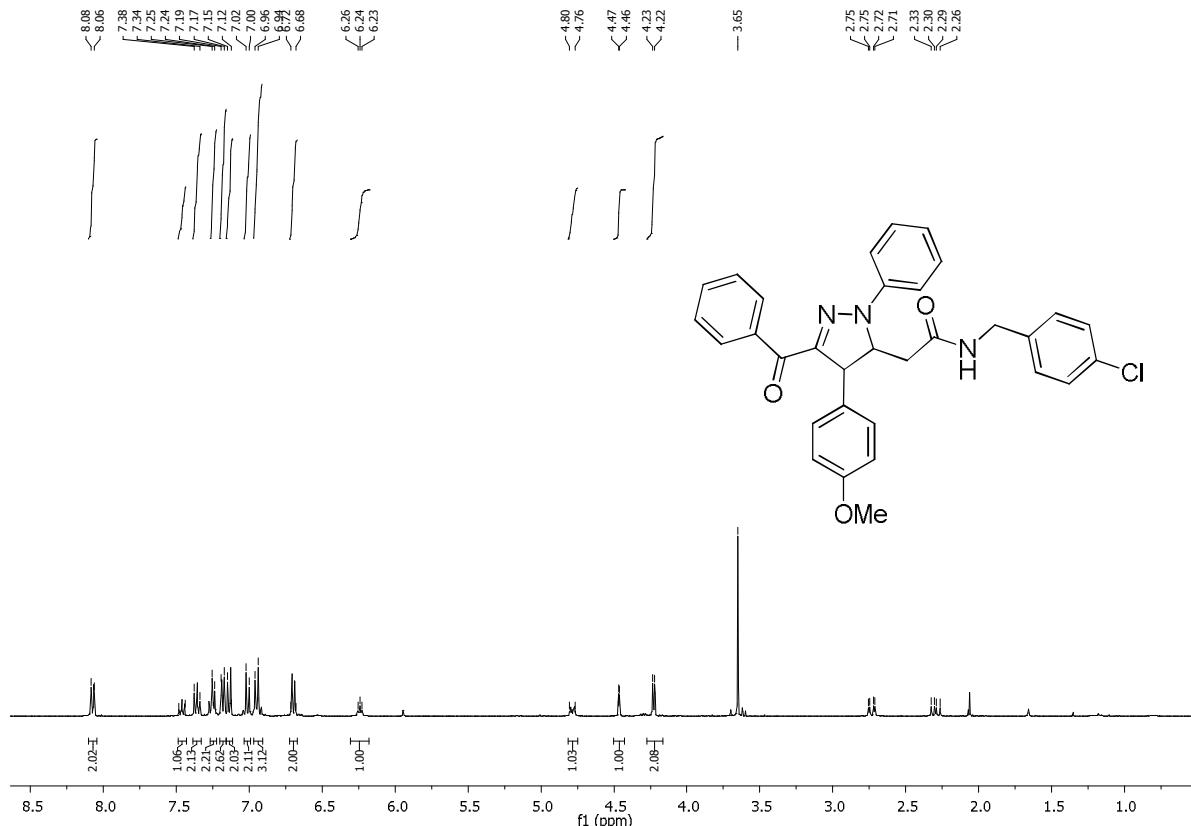
R_f: 0.28 (80:20 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.08-8.06 (m, 2H), 7.48-7.44 (m, 1H), 7.38-7.34 (m, 2H), 7.25-7.24 (m, 2H), 7.19-7.17 (m, 2H), 7.15-7.12 (m, 2H), 7.02-7.00 (m, 2H), 6.96-6.94 (m, 3H), 6.72-6.68 (m, 2H), 6.24 (t, *J* = 5.8 Hz, 1H), 4.80-4.76 (m, 1H), 4.47 (d, *J* = 2.7 Hz, 1H), 4.23 (d, *J* = 5.8 Hz, 2H), 3.65 (s, 3H), 2.73 (dd, *J* = 14.5, 3.4 Hz, 1H), 2.30 (dd, *J* = 14.5, 9.8 Hz, 1H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 186.8, 168.8, 159.0, 149.5, 141.1, 136.4, 132.5, 132.0, 130.1, 129.7, 129.4, 128.9, 128.2, 128.0, 122.4, 115.2, 114.5, 66.8, 55.3, 54.2, 43.1, 38.0.

HRMS: calculated for C₃₂H₂₈ClN₃O₃ 537.1819, found 537.1808.

I.R. (thin film): 3448, 3362, 3068, 2954, 2935, 2836, 1684, 1632, 1599, 1512, 1500, 1337, 1322, 1266, 1249, 1224, 1179, 1147, 1095, 1039, 1017, 909 cm⁻¹.



File: EE130

Date Run: 11-07-2014 (Time Run: 10:35:07)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

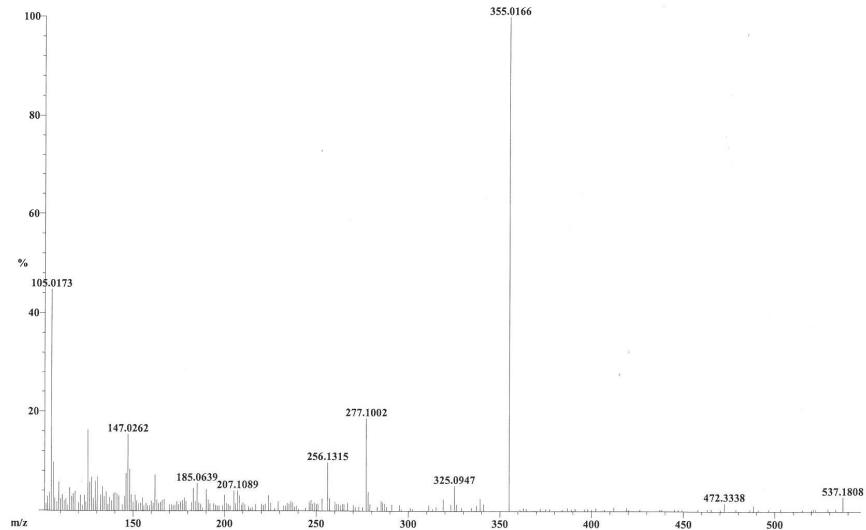
Ionization mode: EI+

Scan: 8

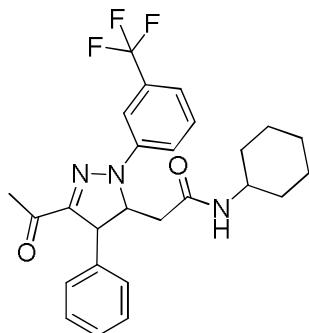
R.T.: .15

Base: m/z 355; 90.5%FS TIC: 5766352

#Ions: 284



2-(3-acetyl-4-phenyl-1-(3-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide 3k



C₂₆H₂₈F₃N₃O₂

M=471.213 g.mol⁻¹

This compound was synthesized according to the general procedure **II**, using Passerini adduct **1a** (100 mg, 0.3 mmol) and (*E*)-1-(2-(3-(trifluoromethyl)phenyl)hydrazono)propan-2-one (84 mg, 0.3 mmol). Purification by flash chromatography with a gradient Et₂O/EP (50/50 to 80/20) gave the desired product in 60% isolated yield (94 mg, 0.2 mmol).

Aspect: brown yellow oil

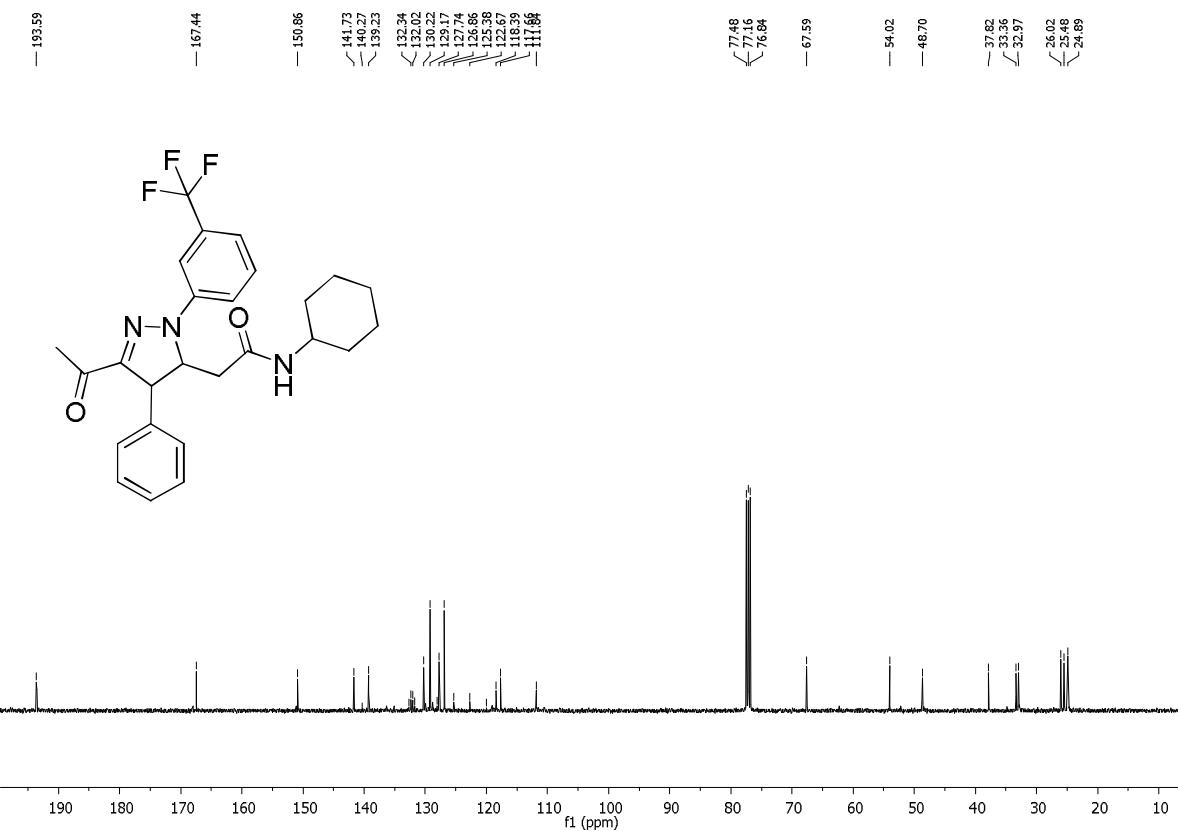
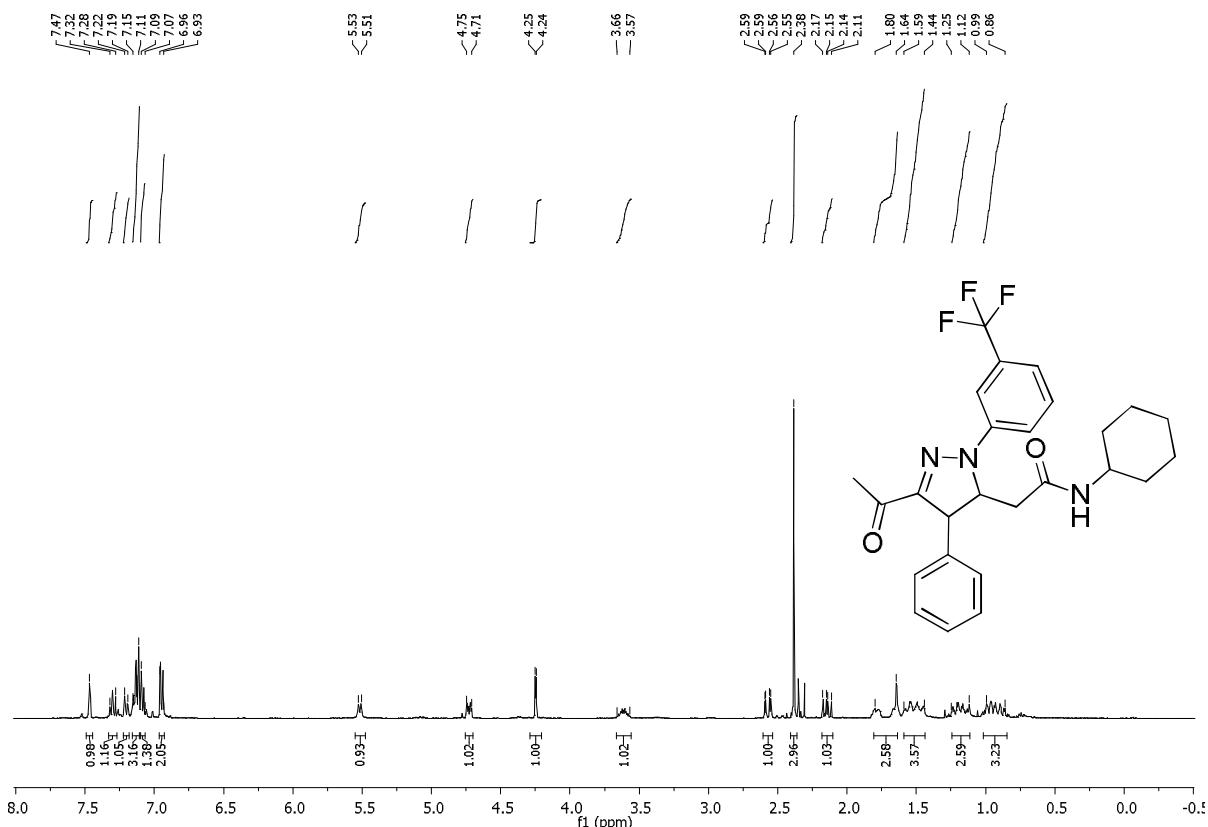
R_f: 0.26 (60:40 diethyl ether/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.47 (br s, 1H), 7.32-7.28 (m, 1H), 7.22-7.18 (m, 1H), 7.15-7.11 (m, 3H), 7.09-7.07 (m, 1H), 6.96-6.93 (m, 2H), 5.52 (d, *J* = 8.0 Hz, 1H), 4.75-4.71 (m, 1H), 4.25 (d, *J* = 2.5 Hz, 1H), 3.66-3.57 (m, 1H), 2.57 (dd, *J* = 14.6, 3.6 Hz, 1H), 2.38 (s, 3H), 2.14 (dd, *J* = 14.6, 9.8 Hz, 1H), 1.80-1.64 (m, 2H), 1.59-1.44 (m, 3H), 1.25-1.12 (m, 2H), 0.99-0.86 (m, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.5, 167.4, 150.8, 141.7, 139.2, 132.6, 132.3, 132.0, 131.6, 130.2, 129.1, 128.0, 127.7, 126.8, 125.3, 122.6, 119.9, 118.3, 117.6, 111.8, 67.5, 54.0, 48.7, 37.8, 33.3, 32.9, 26.0, 25.4, 24.8.

HRMS: calculated for C₂₆H₂₈F₃N₃O₂: 471.2134, found: 471.2134.

I.R. (thin film): 3297, 2929, 2837, 1638, 1536, 1492, 1454, 1321, 1123, 790, 697 cm⁻¹.



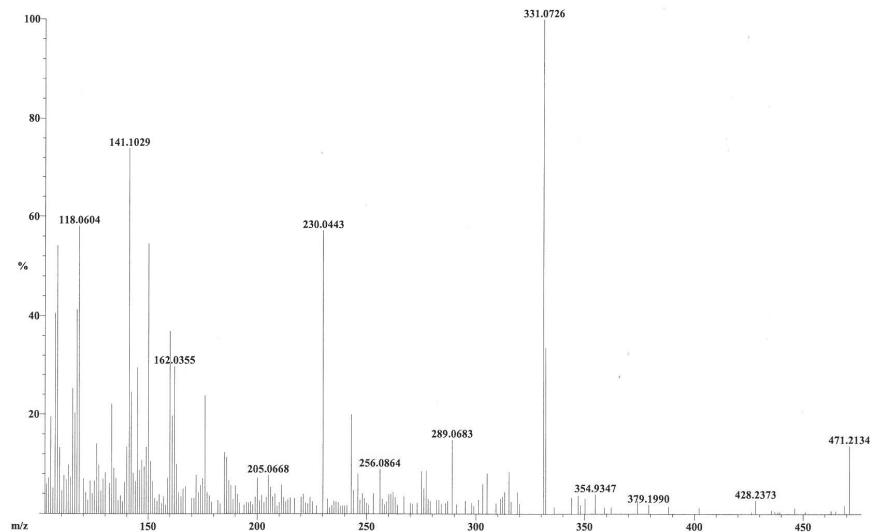
File: EE116
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 11-06-2014 (Time Run: 17:04:03)
Ionization mode: EI+

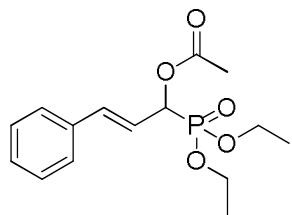
Scan: 64
Base: m/z 331; 77.1%FS TIC: 13450336

R.T.: 1.3

#Ions: 299



(E)-1-(diethoxyphosphoryl)-3-phenylallyl acetate 5



C₁₅H₂₁N₂O₅P

M=312.112 g.mol⁻¹

Potassium carbonate (900 mg, 6.5 mmol) was added to a stirred mixture of diethylphosphite (0.38 ml, 3 mmol) and cinnamaldehyde (0.38 ml, 3 mmol), at room temperature and stirred for 10 min. Acetic anhydride (0.84 ml, 9 mmol) was added to this mixture which was then stirred for 4h at room temperature. The mixture was washed with ethyl acetate (4×50 ml), dried with MgSO₄, and the solvent evaporated to give crude product. Purification by flash chromatography with a gradient AcOEt/EP (40/60 to 70/30) gave the desired product in 80% isolated yield (750 mg, 2.4 mmol).

Aspect: white oil

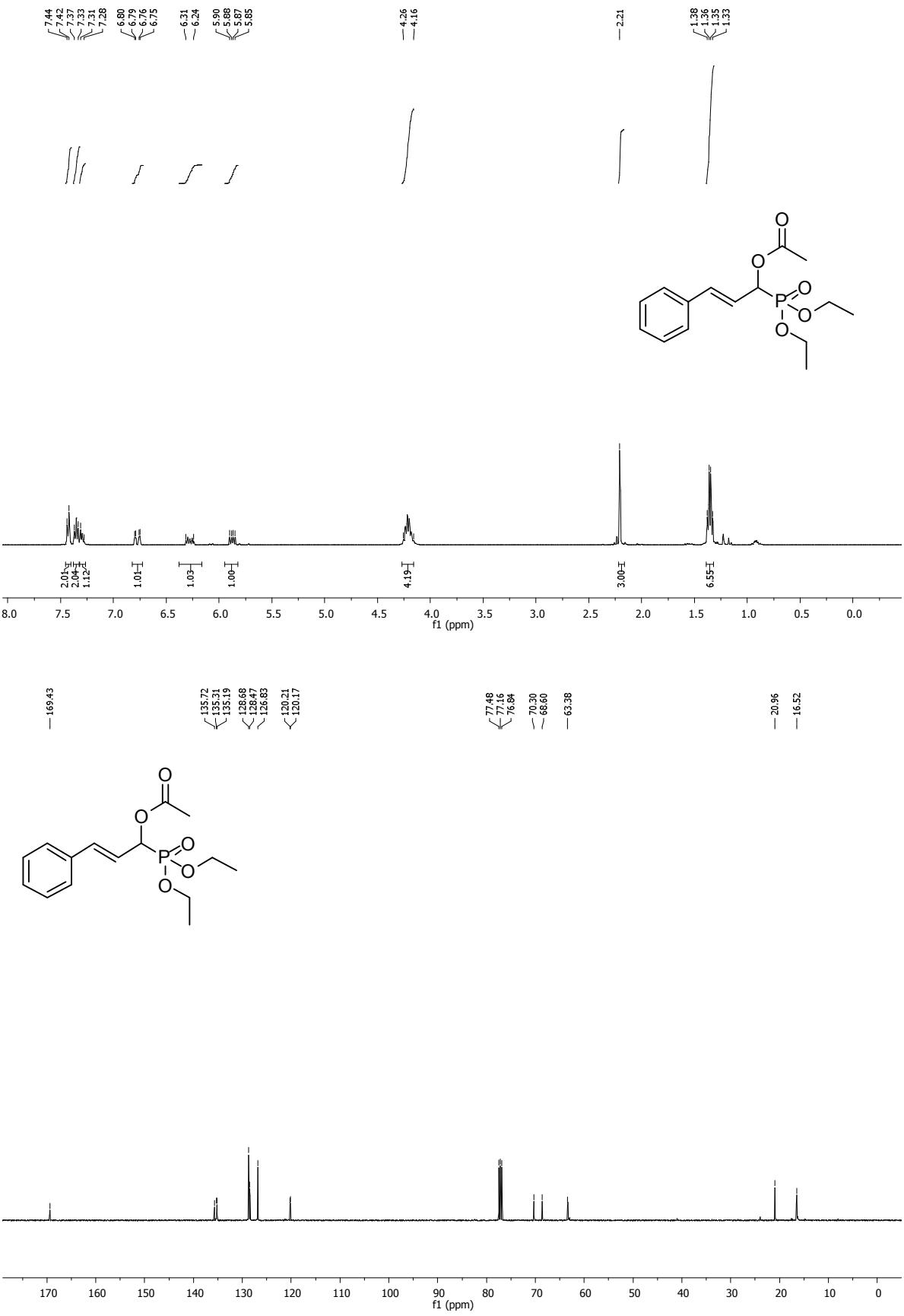
R_f: 2.30 (70:30 ethyl acetate/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.43 (d, *J* = 7.5 Hz, 2H), 7.38-7.32 (m, 2H), 7.23-7.27 (m, 1H), 6.77 (dd, *J* = 15.9, 3.7 Hz, 1H), 6.33-6.21 (m, 1H), 5.87 (dd, *J* = 14.0, 7.4 Hz, 1H), 4.27-4.16 (m, 4H), 2.21 (s, 3H), 1.35 (q, *J* = 6.5 Hz, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 169.4, 135.7, 135.3, 135.1, 128.6, 128.4, 126.8, 120.2, 120.1, 70.3, 68.6, 63.3, 20.9, 16.5.

HRMS: calculated for C₁₅H₂₁N₂O₅P: 312.1127, found: 312.1132.

I.R. (thin film): 3085, 3063, 3029, 2983, 2932, 2910, 1759, 1648, 1496, 1449, 1393, 1370, 1259, 1229, 1165, 1029, 968 cm⁻¹.



File: EE152

Date Run: 01-23-2015 (Time Run: 10:10:35)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

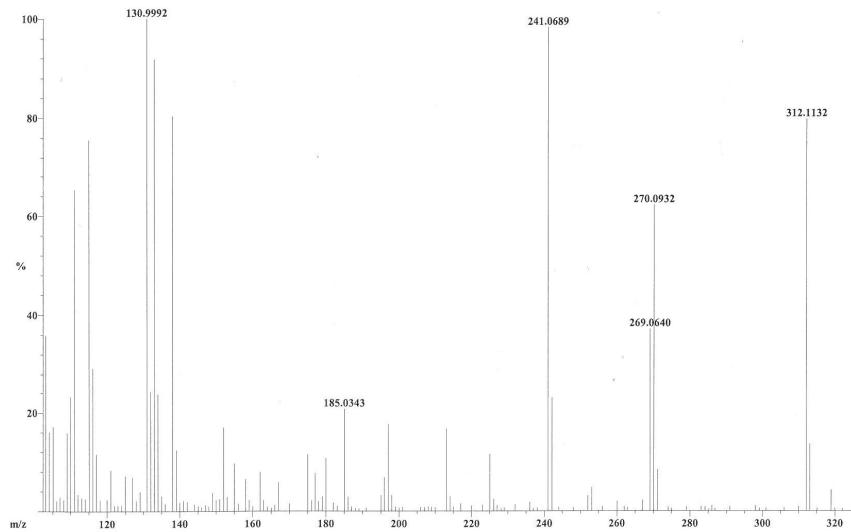
Ionization mode: EI+

Scan: 210

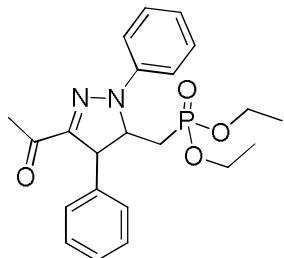
R.T.: 4.3

Base: m/z 131; 54.5%FS TIC: 7518192

#Ions: 230



diethyl ((3-acetyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)methyl)phosphonate 6a



C₂₂H₂₇N₂O₄P

M=414.170 g.mol⁻¹

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (58 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (40/60 to 70/30) gave the desired product in 87% isolated yield (117 mg, 0.3 mmol).

Aspect: yellow oil

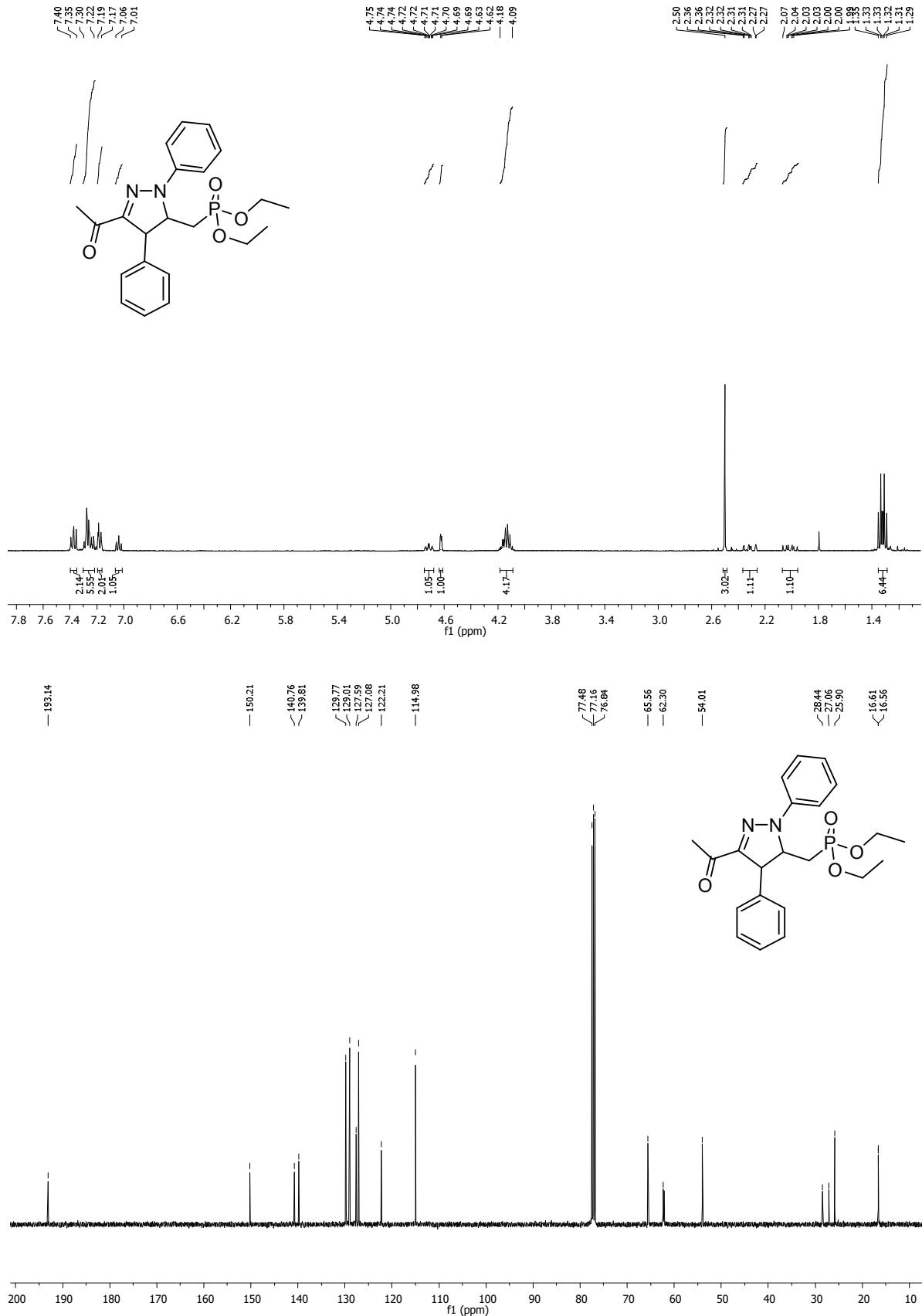
R_f: 0.25 (60:40 ethyl acetate/ petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.40-7.35 (m, 2H), 7.30-7.22 (m, 5H), 7.20-7.16 (m, 2H), 7.06-7.01 (m, 1H), 4.72 (ddt, *J* = 11.0, 8.5, 2.4 Hz, 1H), 4.62 (d, *J* = 2.4 Hz, 1H), 4.18-4.09 (m, 4H), 2.50 (s, 3H), 2.31 (ddd, *J* = 21.0, 15.3, 1.8 Hz, 1H), 2.01 (ddd, *J* = 16.6, 15.3, 11.0 Hz, 1H), 1.32 (dt, *J* = 10.6, 7.1 Hz, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.1, 150.2, 140.7, 139.8, 129.7, 129.0, 127.5, 127.0, 122.2, 114.9, 65.5, 62.3, 54.0, 28.4, 27.0, 25.9, 16.6.

HRMS: calculated for C₂₂H₂₇N₂O₄P: 414.1708, found: 414.1706.

I.R. (thin film): 3067, 3034, 2983, 2909, 2932, 1670, 1600, 1536, 1501, 1457, 1356, 1275, 1260, 1215, 1160, 1056, 1027, 964 cm⁻¹.



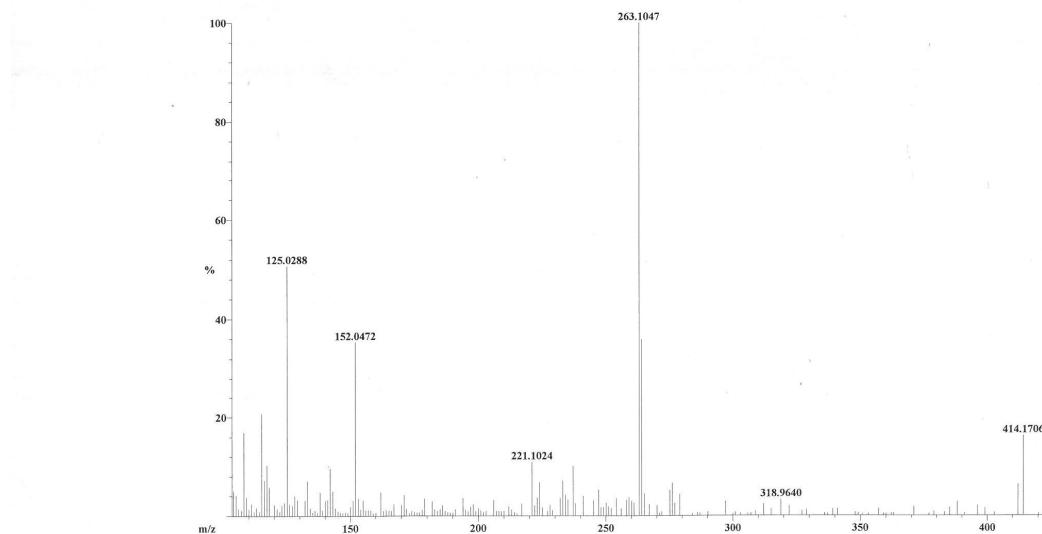
File: EE164 165
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 01-23-2015 (Time Run: 10:50:30)
Ionization mode: EI+

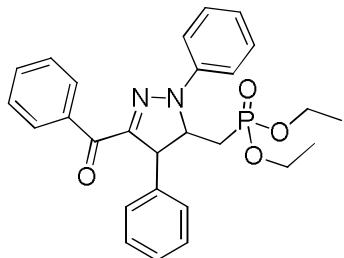
Scan: 238
Base: m/z 263; 72.8%FS TIC: 5397520

R.T.: 4.88

#Ions: 278



diethyl ((3-benzoyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)methyl)phosphonate 6b



C₂₇H₂₉N₂O₄P

M=476.186 g·mol⁻¹

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (79 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (40/60 to 70/30) gave the desired product in 70% isolated yield (107 mg, 0.2 mmol).

Aspect: yellow oil

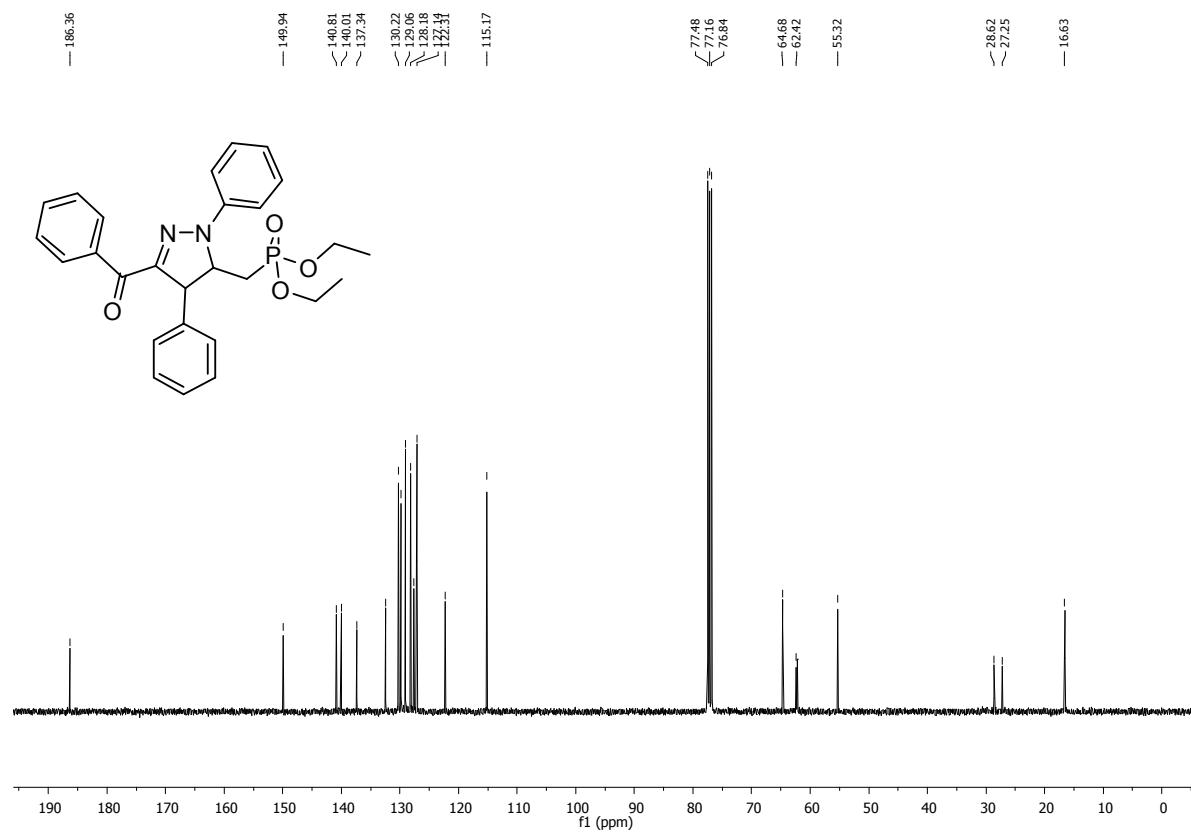
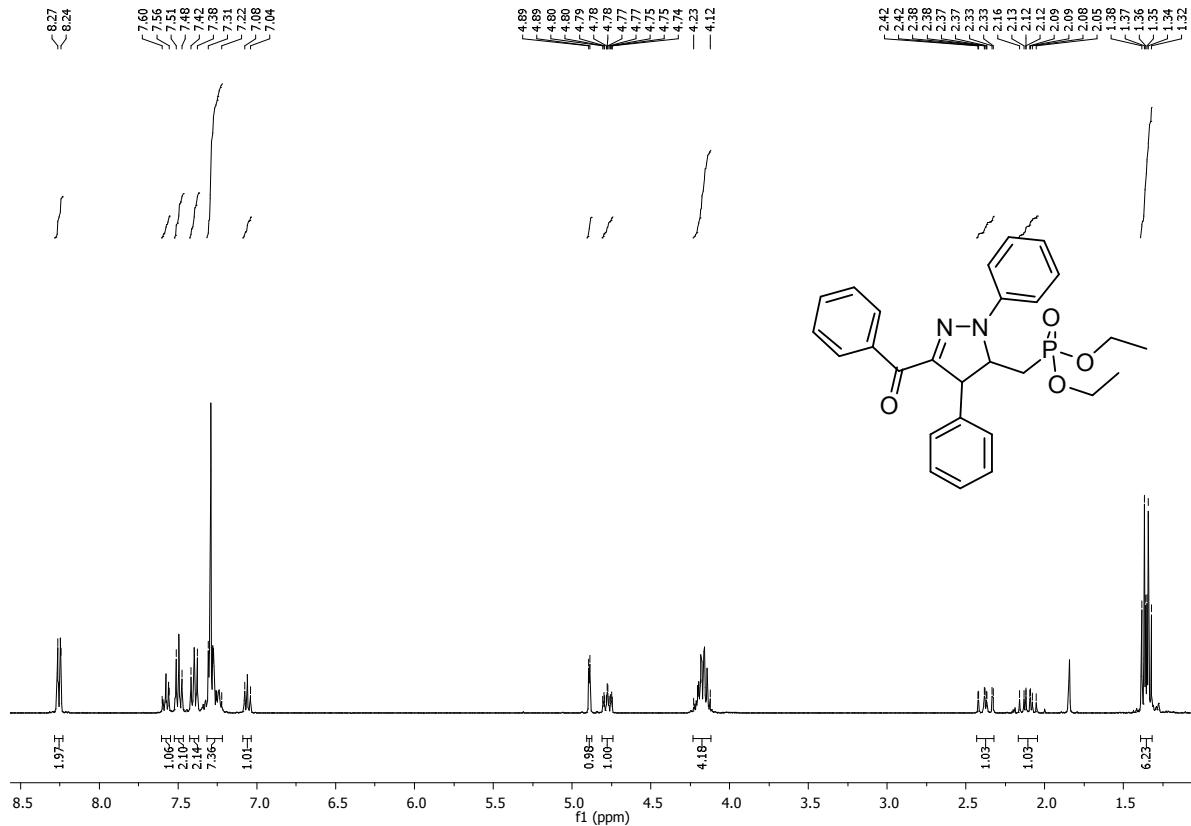
R_f: 0.29 (60:40 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.28-8.23 (m, 2H), 7.60-7.55 (m, 1H), 7.52-7.48 (m, 2H), 7.42-7.37 (m, 2H), 7.32-7.22 (m, 7H), 7.08-7.04 (m, 1H), 4.89 (d, *J* = 2.4 Hz, 1H), 4.77 (ddt, *J* = 10.8, 8.7, 2.0 Hz, 1H), 4.23-4.12 (m, 4H), 2.38 (ddd, *J* = 20.9, 15.3, 1.7 Hz, 1H), 2.11 (ddd, *J* = 16.4, 15.5, 11.0 Hz, 1H), 1.35 (dt, *J* = 10.5, 7.1 Hz, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 186.3, 149.9, 140.8, 140.0, 137.3, 132.4, 130.2, 129.8, 129.0, 128.1, 127.6, 127.1, 122.3, 115.1, 64.6, 62.4, 55.3, 28.6, 27.2, 16.6.

HRMS: calculated for C₂₇H₂₉N₂O₄P: 476.1865, found: 476.1861.

I.R. (thin film): 3067, 3033, 2983, 2909, 2834, 1634, 1599, 1536, 1500, 1457, 1448, 1326, 1276, 1222, 1160, 1144, 1027, 964 cm⁻¹.



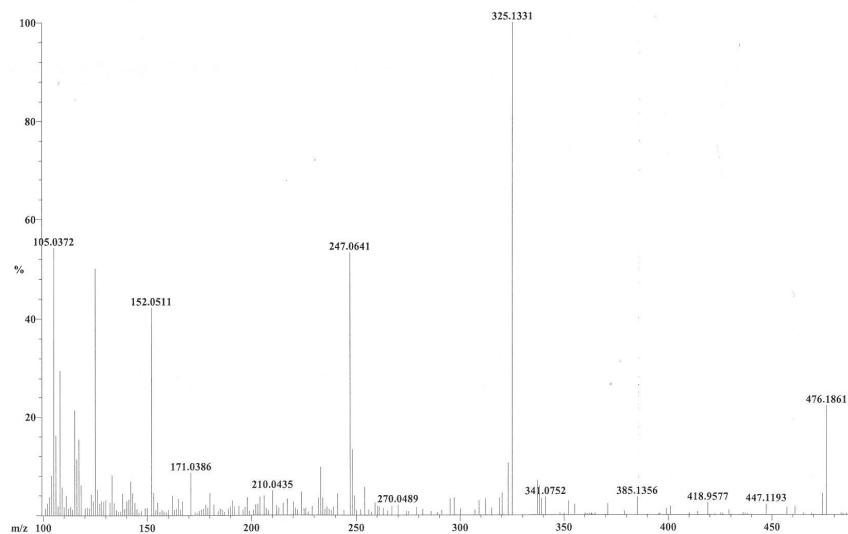
File: EE158
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 01-23-2015 (Time Run: 10:33:53)
Ionization mode: EI+

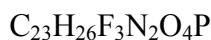
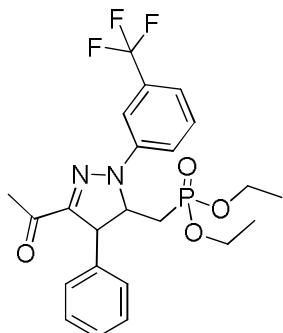
Scan: 175
Base: m/z 325; 100%FS TIC: 9311280

R.T.: 3.58

#Ions: 278



diethyl ((3-acetyl-4-phenyl-1-(3-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)methyl)phosphonate 6c



M=482.158 g.mol⁻¹

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (81 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (30/70 to 70/30) gave the desired product in 51% isolated yield (101 mg, 0.2 mmol).

Aspect: yellow oil

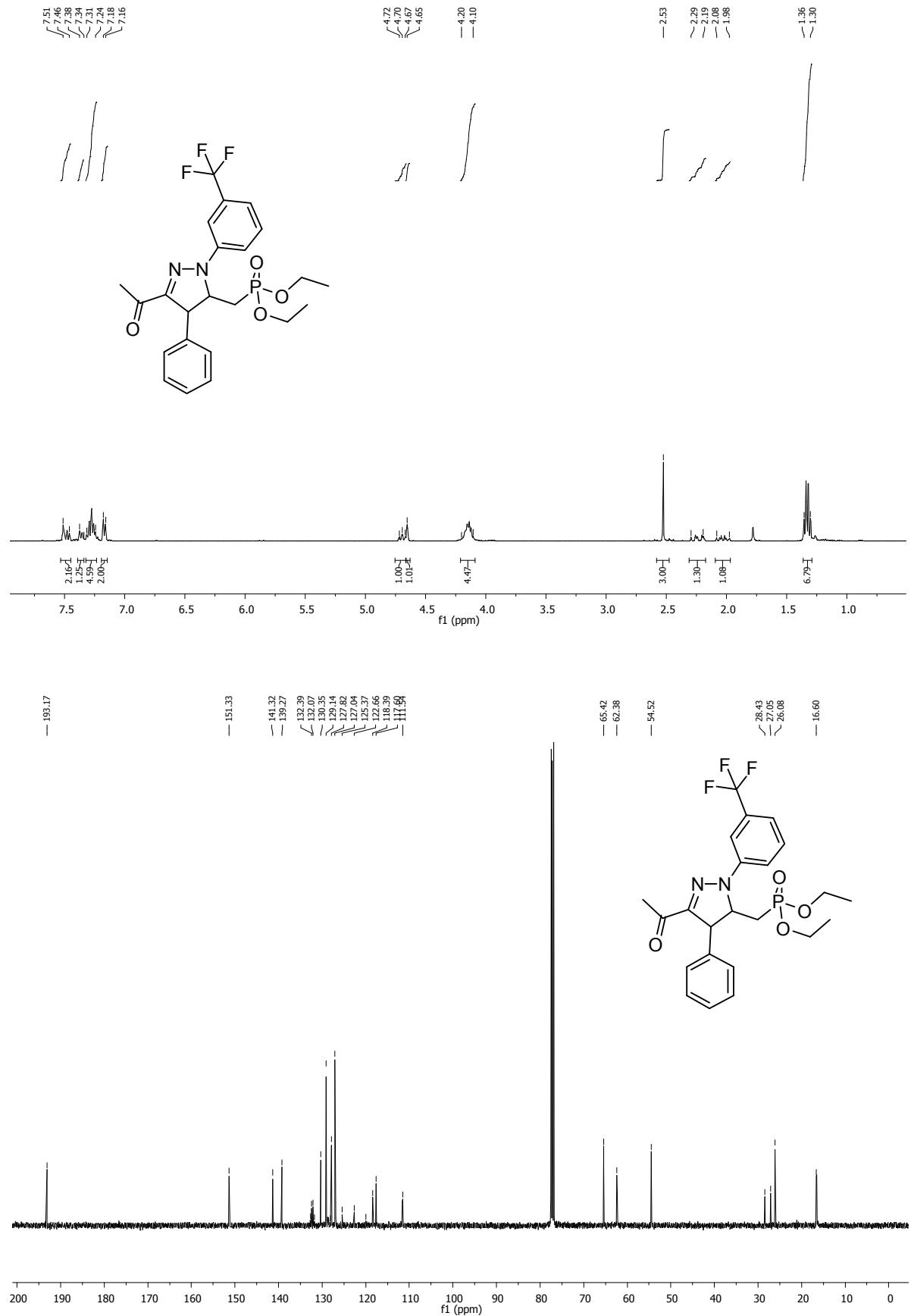
R_f: 0.25 (60:40 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.53-7.45 (m, 2H), 7.39-7.34 (m, 1H), 7.32-7.24 (m, 4H), 7.20-7.15 (m, 2H), 4.69 (t, *J* = 10.1 Hz, 1H), 4.65 (s, 1H), 4.21-4.09 (m, 4H), 2.53 (s, 3H), 2.31-2.18 (m, 1H), 2.10-1.97 (m, 1H), 1.37-1.29 (m, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 193.1, 151.3, 141.3, 139.2, 132.7, 132.3, 132.0, 131.7, 130.3, 129.1, 128.0, 127.8, 127.0, 125.3, 122.6, 119.9, 118.3, 117.6, 111.5, 65.4, 62.3, 54.5, 28.4, 27.0, 26.0, 16.6.

HRMS: calculated for C₂₃H₂₆F₃N₂O₄P: 482.1582, found: 482.1590.

I.R. (thin film): 3067, 3033, 2983, 2938, 2909, 2834, 1675, 1614, 1594, 1544, 1496, 1458, 1358, 1325, 1258, 1216, 1171, 1135, 1055, 1026, 966 cm⁻¹.



File: EE157

Date Run: 01-23-2015 (Time Run: 10:28:51)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

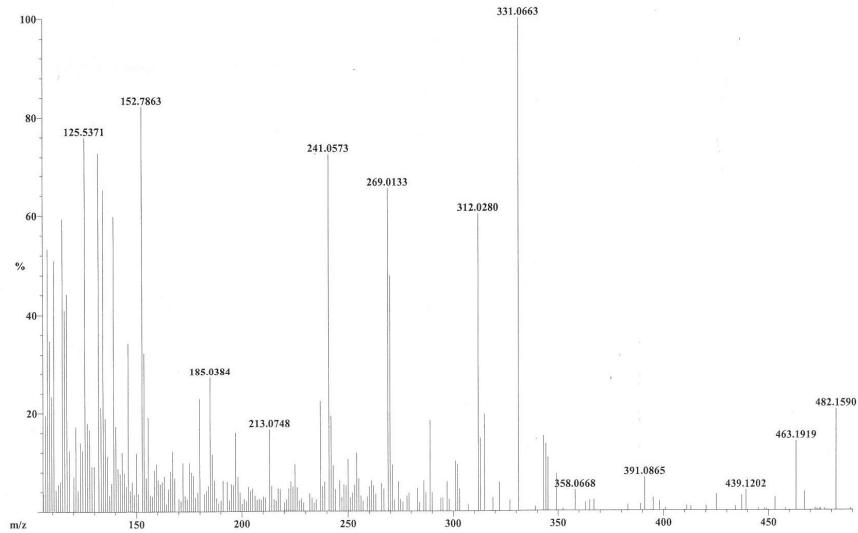
Ionization mode: EI+

Scan: 33

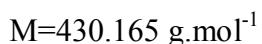
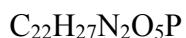
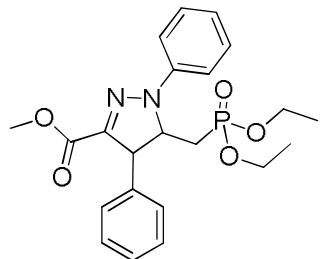
R.T.: .67

Base: m/z 331; 80%FS TIC: 20681856

#Ions: 302



methyl 5-((diethoxyphosphoryl)methyl)-1,4-diphenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate **6d**



This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (63 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (30/70 to 70/30) gave the desired product in 63% isolated yield (87 mg, 0.2 mmol).

Aspect: yellow oil

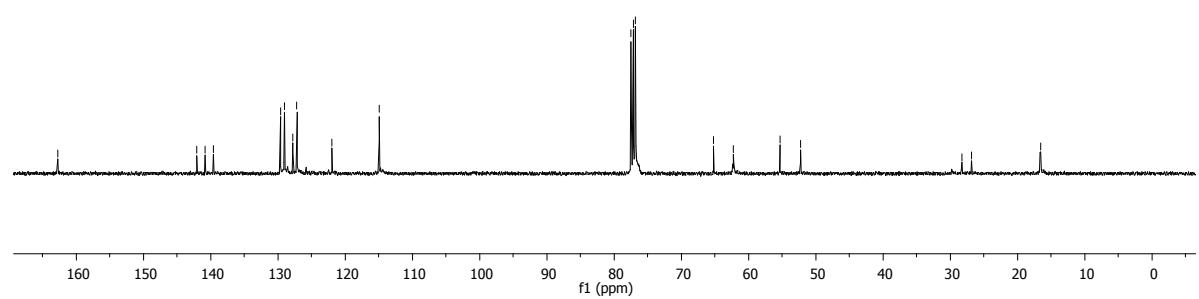
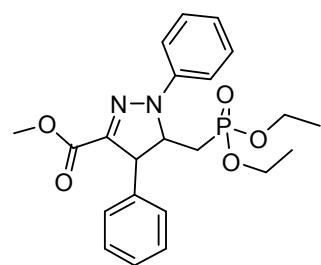
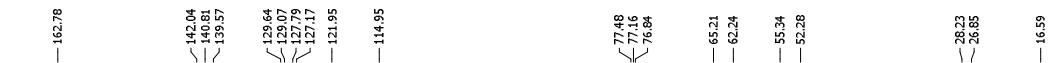
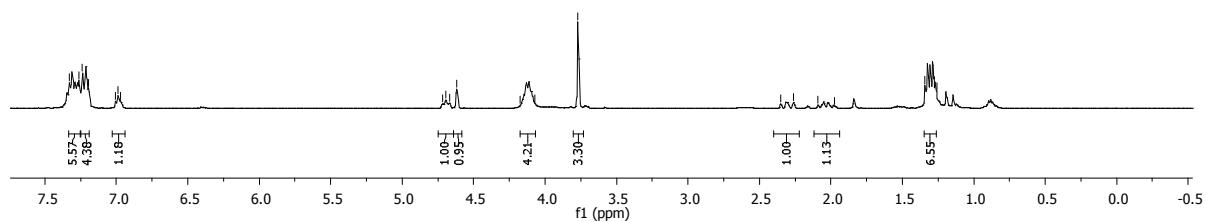
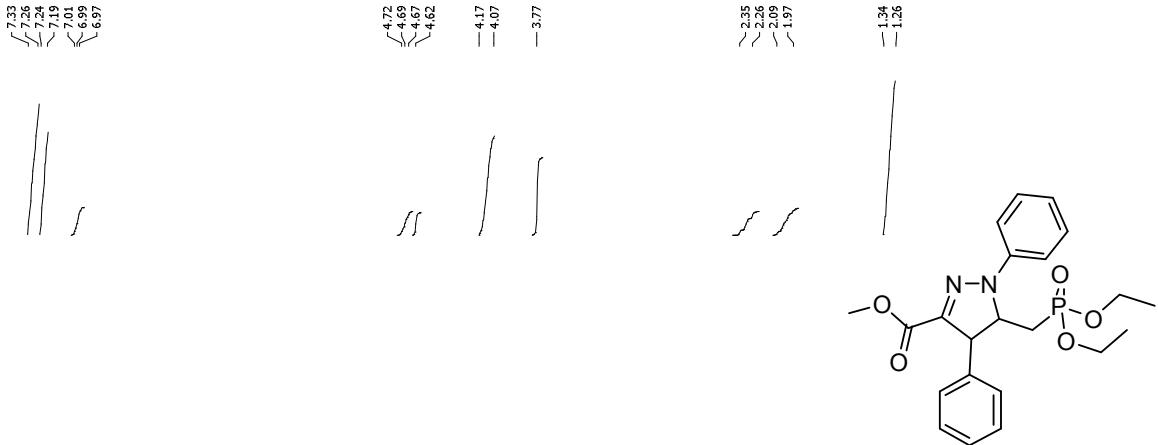
R_f: 0.39 (60:40 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 7.34-7.25 (m, 5H), 7.24-7.18 (m, 4H), 6.99 (t, *J* = 7.2 Hz, 1H), 4.69 (t, *J* = 9.5 Hz, 1H), 4.62 (s, 1H), 4.16-4.07 (m, 4H), 3.77 (s, 3H), 2.39-2.23 (m, 1H), 2.11-1.94 (m, 1H), 1.35-1.26 (m, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 162.7, 142.0, 140.8, 139.5, 129.6, 129.0, 127.7, 127.1, 121.9, 114.9, 65.2, 62.2, 55.3, 52.2, 28.2, 26.8, 16.6.

HRMS: calculated for C₂₂H₂₇N₂O₅P: 430.1658, found: 430.1651.

I.R. (thin film): 3066, 3033, 2983, 2952, 2908, 1732, 1713, 1600, 1551, 1501, 1457, 1444, 1258, 1218, 1161, 1101, 1057, 1028, 964 cm⁻¹.



File: EH196
Sample:

Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 10-27-2015 (Time Run: 16:54:59)

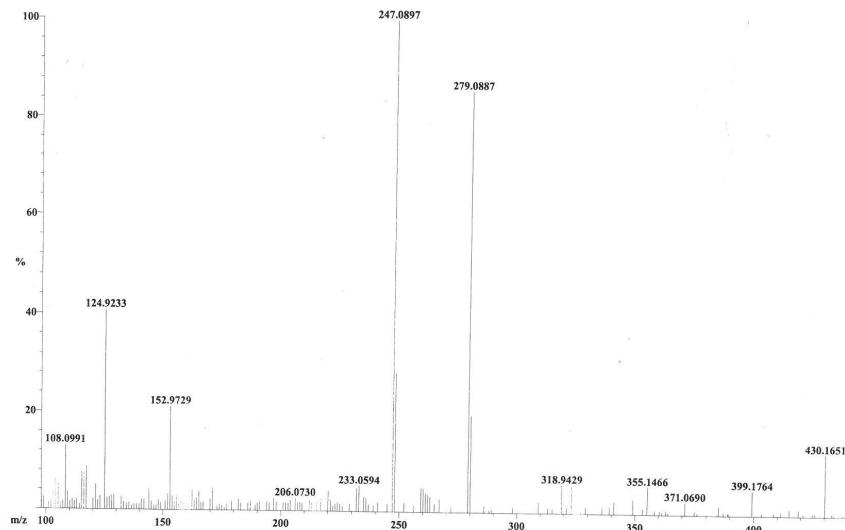
Ionization mode: EI+

Scan: 394

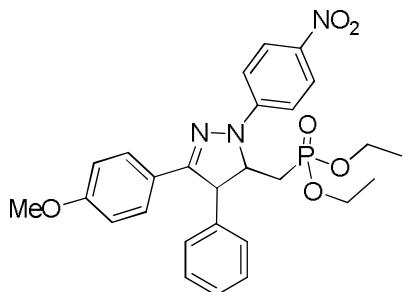
Base: m/z 247; 60.1%FS TIC: 4534416

R.T.: 7.95

#Ions: 272



diethyl ((3-(4-methoxyphenyl)-1-(4-nitrophenyl)-4-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)methyl)phosphonate **6f**



C₂₇H₃₀N₃O₆P

M=523.187 g.mol⁻¹

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (95 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (30/70 to 70/30) gave the desired product in 90% isolated yield (153 mg, 0.3 mmol).

Aspect: yellow oil

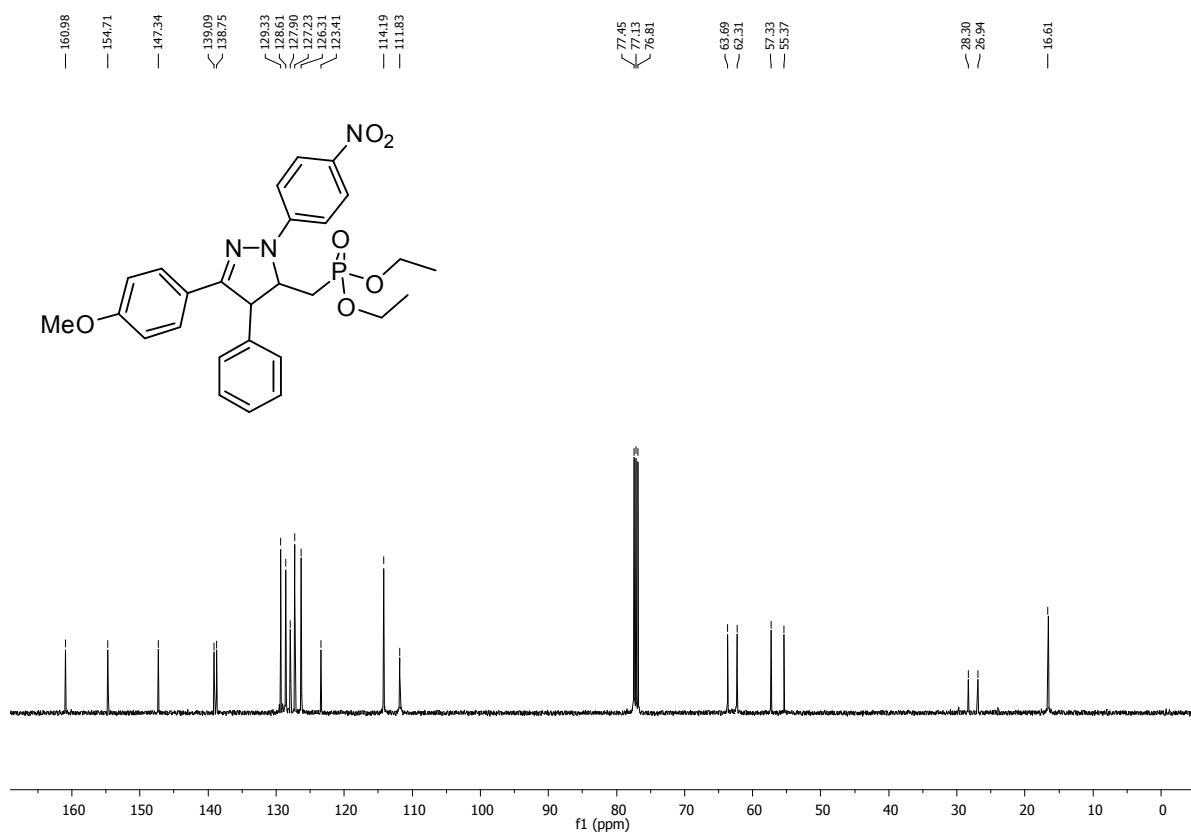
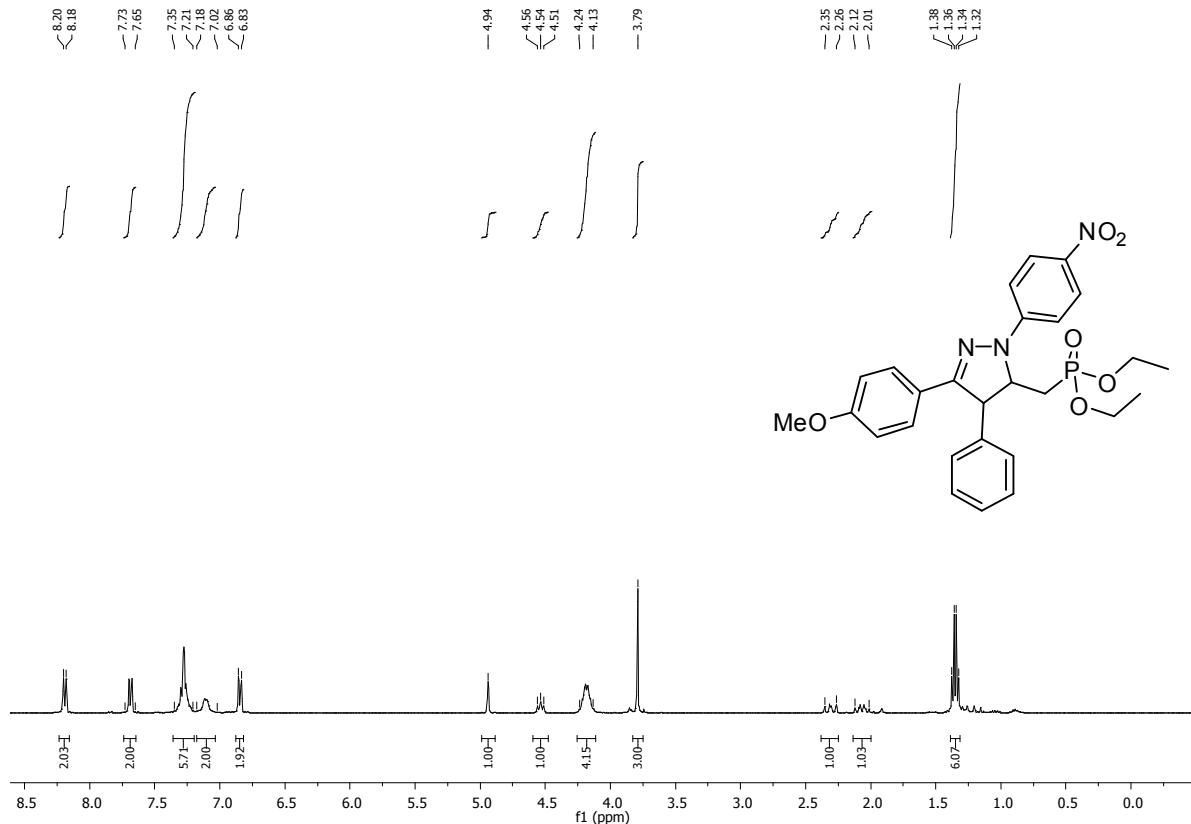
R_f: 0.38 (60:40 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.23-8.16 (m, 2H), 7.73-7.64 (m, 2H), 7.35-7.20 (m, 5H), 7.19-7.02 (m, 2H), 6.88 – 6.81 (m, 2H), 4.94 (s, 1H), 4.54 (t, *J* = 9.3 Hz, 1H), 4.25-4.11 (m, 4H), 3.79 (s, 3H), 2.36-2.26 (m, 1H), 2.12-2.01 (m, 1H), 1.35 (q, *J* = 7.0 Hz, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 160.9, 154.7, 147.3, 139.0, 138.7, 129.3, 128.6, 127.9, 127.2, 126.3, 123.4, 114.1, 111.8, 63.6, 62.3, 57.3, 55.3, 28.3, 26.9, 16.6.

HRMS: calculated for C₂₇H₃₀N₃O₆P: 523.1872, found: 523.1862.

I.R. (thin film): 3067, 3032, 2983, 2961, 2933, 2909, 2838, 1596, 1506, 1424, 1399, 1328, 1252, 1176, 1112, 1098, 1030, 965 cm⁻¹.



File: EE192

Date Run: 02-19-2015 (Time Run: 16:33:49)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

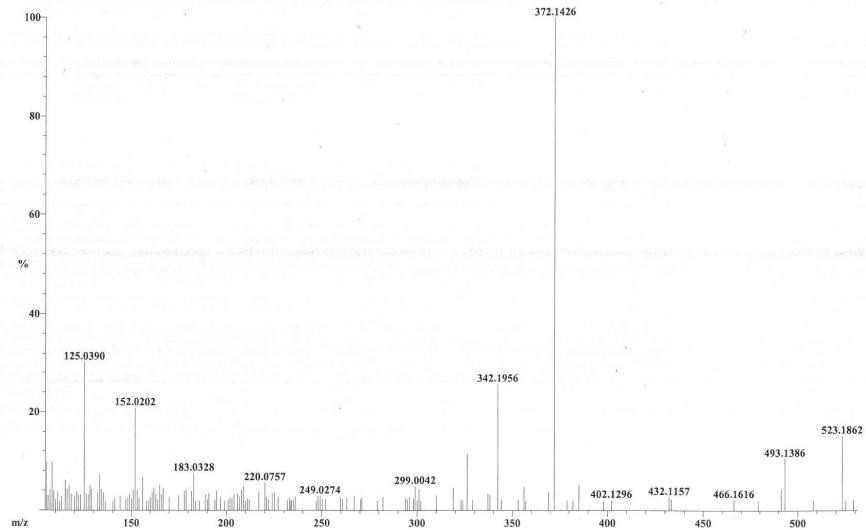
Ionization mode: EI+

Scan: 9

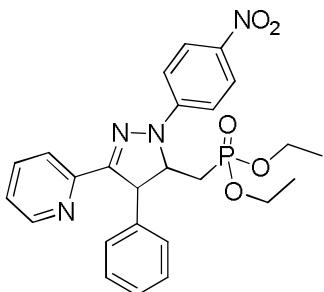
Base: m/z 372; 15.4%FS TIC: 1109040

R.T.: .17

#Ions: 186



diethyl ((1-(4-nitrophenyl)-4-phenyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)methyl)phosphonate **6g**



C₂₅H₂₇N₄O₅P

M=494.171 g.mol⁻¹

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (85 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (50/50 to 70/30) gave the desired product in 60% isolated yield (95 mg, 0.2 mmol).

Aspect: yellow oil

R_f: 0.18 (60:40 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.53 (d, *J* = 4.7 Hz, 1H), 8.25-8.19 (m, 2H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.70-7.64 (m, 1H), 7.29-7.16 (m, 8H), 5.14 (s, 1H), 4.67 (t, *J* = 9.7 Hz, 1H), 4.25-4.10 (m, 4H), 2.30 (dd, *J* = 20.7, 15.3 Hz, 1H), 2.20-2.06 (m, 1H), 1.39-1.31 (m, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 155.9, 150.2, 149.8, 147.0, 139.9, 139.2, 136.2, 129.0, 127.6, 127.4, 126.3, 123.8, 121.8, 112.5, 64.0, 62.3, 56.8, 28.6, 27.3, 16.6.

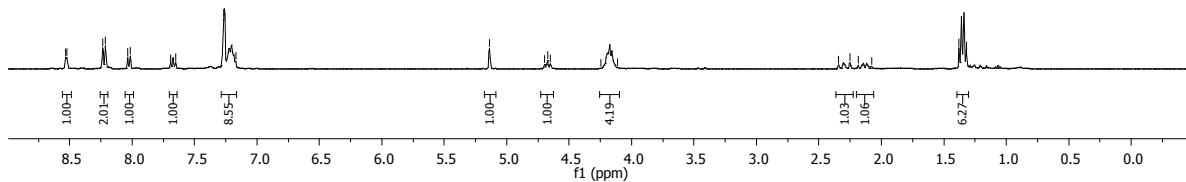
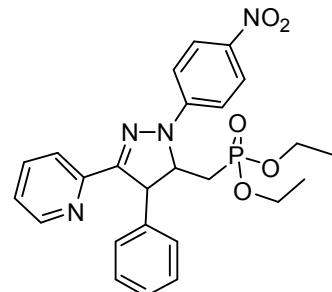
HRMS: calculated for C₂₇H₃₀N₃O₆P: 494.1719, found: 494.1711.

I.R. (thin film): 3066, 2983, 2908, 1598, 1568, 1510, 1471, 1397, 1331, 1318, 1252, 1112, 1055, 1026, 964 cm⁻¹.

<8.53
<8.52
<8.24
<8.21
<8.04
<8.02
>7.69
>7.65

—5.14
—4.70
—4.67
—4.65

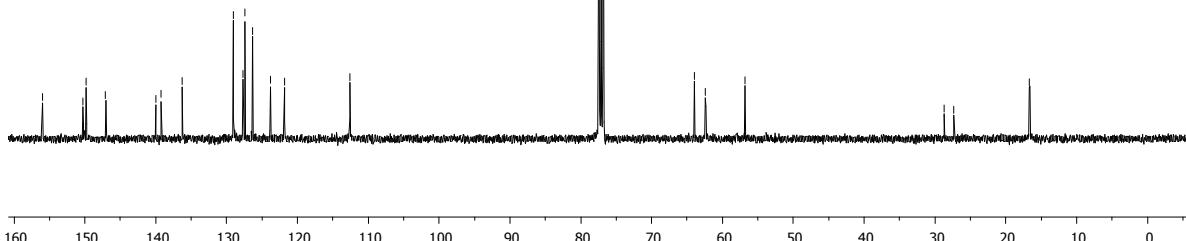
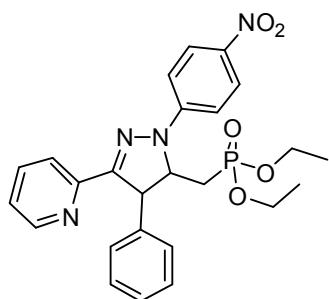
—4.24
—4.11
—2.34
—2.25
—2.19
—2.08



—155.98
150.26
—149.81
~147.98
—139.99
—139.23
—136.26
—129.06
—127.69
—127.42
—126.31
—123.94
—121.85
—112.59

—77.46
—77.16
—76.84

—64.00
—63.38
—56.83
—28.68
—27.31
—16.67



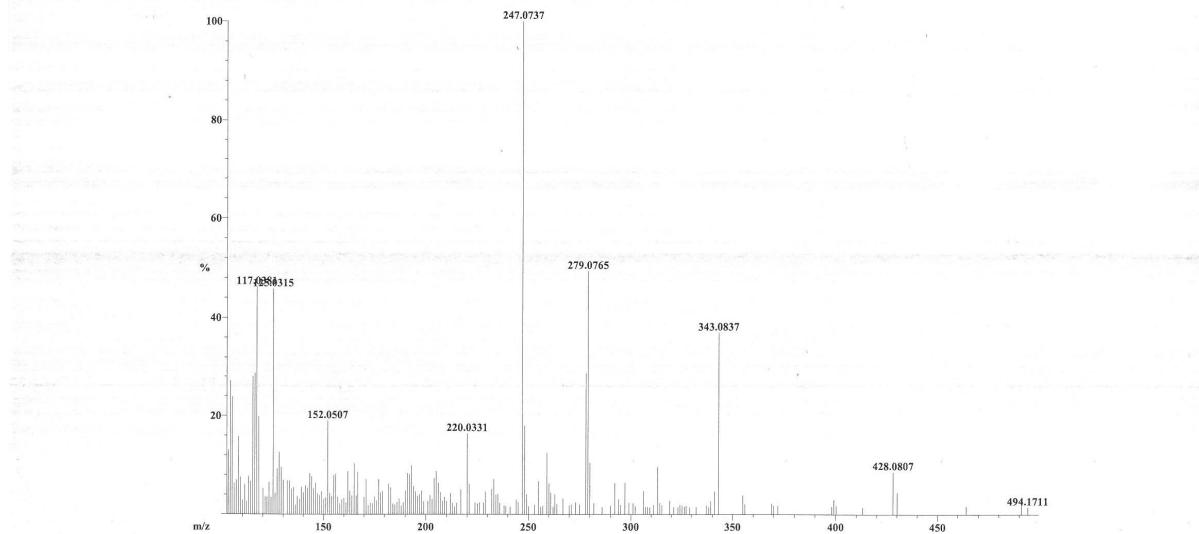
File: EE198
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Date Run: 02-19-2015 (Time Run: 16:47:22)
Ionization mode: EI+

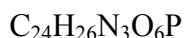
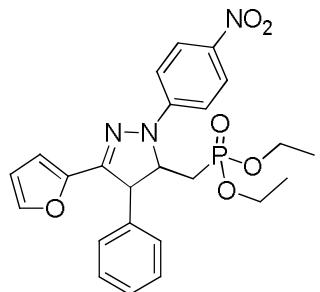
Scan: 3
Base: m/z 247; 20%FS TIC: 2779616

R.T.: .05

#Ions: 224



diethyl ((3-(furan-2-yl)-1-(4-nitrophenyl)-4-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)methyl)phosphonate 7b



$$M=483.155 \text{ g.mol}^{-1}$$

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(2-phenylhydrazone)propan-2-one (81 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (40/60 to 70/30) gave the desired product in 30% isolated yield (47 mg, 0.1 mmol).

Aspect: yellow oil

R_f: 0.30 (60:40 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.15-8.09 (m, 2H), 7.43-7.40 (m, 1H), 7.25-7.20 (m, 3H), 7.20-7.15 (m, 3H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.49 (d, *J* = 3.5 Hz, 1H), 6.35-6.30 (m, 1H), 4.75 (s, 1H), 4.52-4.43 (m, 1H), 4.14-4.03 (m, 4H), 2.24 (dd, *J* = 20.7, 15.2 Hz, 1H), 2.00 (td, *J* = 15.8, 11.2 Hz, 1H), 1.26 (dt, *J* = 14.3, 7.0 Hz, 6H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 147.0, 146.9, 146.7, 144.6, 139.6, 138.7, 129.3, 128.1, 127.2, 126.3, 113.0, 112.2, 112.1, 63.5, 62.4, 57.9, 28.5, 27.1, 16.6.

HRMS: calculated for C₂₄H₂₆N₃O₆P: 483.1559, found: 483.1557.

I.R. (thin film): 3067, 2983, 2930, 2909, 1597, 1508, 1393, 1378, 1330, 1252, 1162, 1112, 1052, 1027, 966 cm⁻¹.

> 6.14

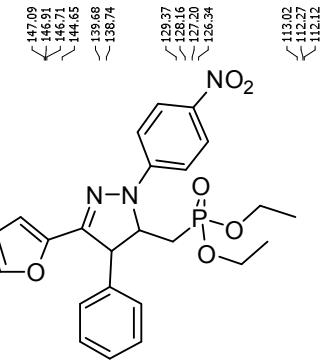
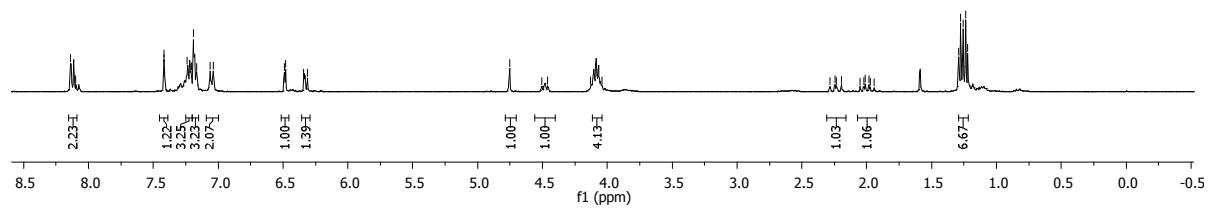
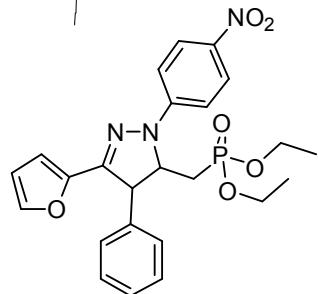
> 6.10

7.42
7.42
7.24
7.21
7.19
7.16
7.06
7.04

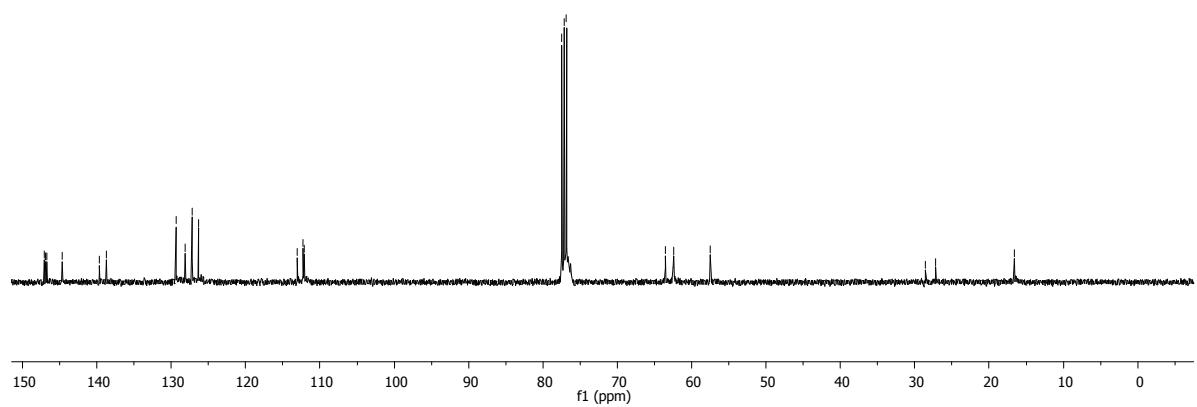
6.49
6.48
6.34
6.31

-4.75
4.51
4.46
4.43
-4.04

2.28
2.25
2.23
2.19
2.05
2.02
2.01
1.98
1.97
1.95
1.29
1.18
1.26
1.24
1.22



147.09
146.91
146.71
144.65
139.68
138.74
129.37
128.16
127.20
126.34
113.02
112.12
77.16
76.94
63.52
62.43
-57.50
-29.53
-27.16
-16.61



File: EE199

Date Run: 02-19-2015 (Time Run: 16:52:22)

Sample:

Instrument: JEOL GCmate

Inlet: Direct Probe

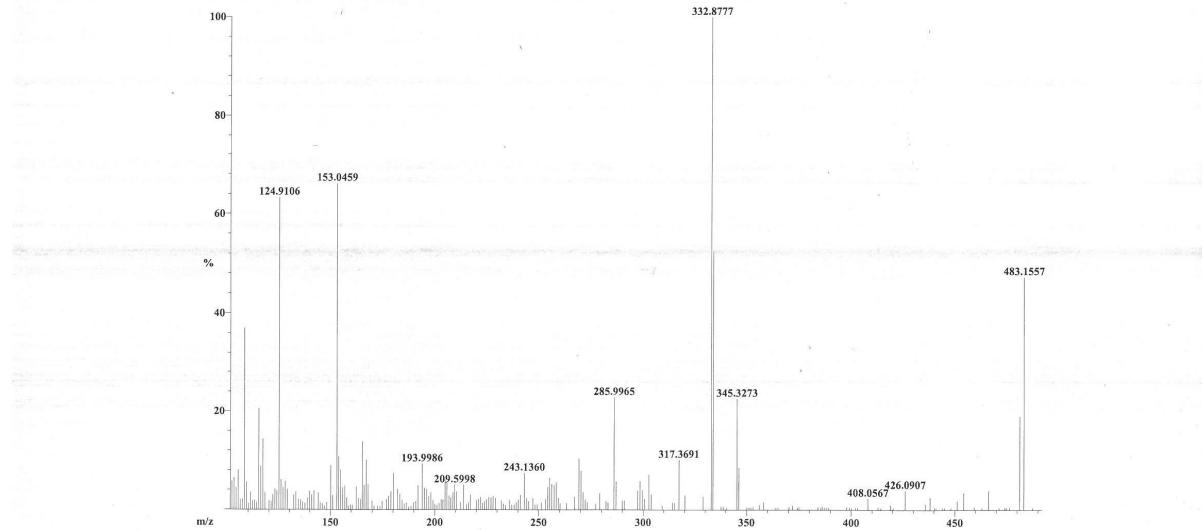
Ionization mode: EI+

Scan: 234

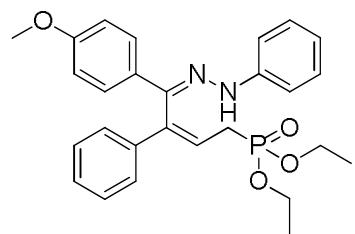
R.T.: 4.67

Base: m/z 333; 72.9%FS TIC: 8532288

#Ions: 299



diethyl ((2Z,4Z)-4-(4-methoxyphenyl)-3-phenyl-4-(2-phenylhydrazone)but-2-en-1-yl)phosphonate 7



C₂₇H₃₁N₂O₄P

M=478.2021 g.mol⁻¹

This compound was synthesized according to the general procedure **III**, using phosphonate adduct **5** (100 mg, 0.3 mmol) and (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine (80 mg, 0.3 mmol). Purification by flash chromatography with a gradient AcOEt/EP (40/60 to 60/40) gave the desired product in 42% isolated yield (65 mg, 0.1 mmol).

Aspect: green oil

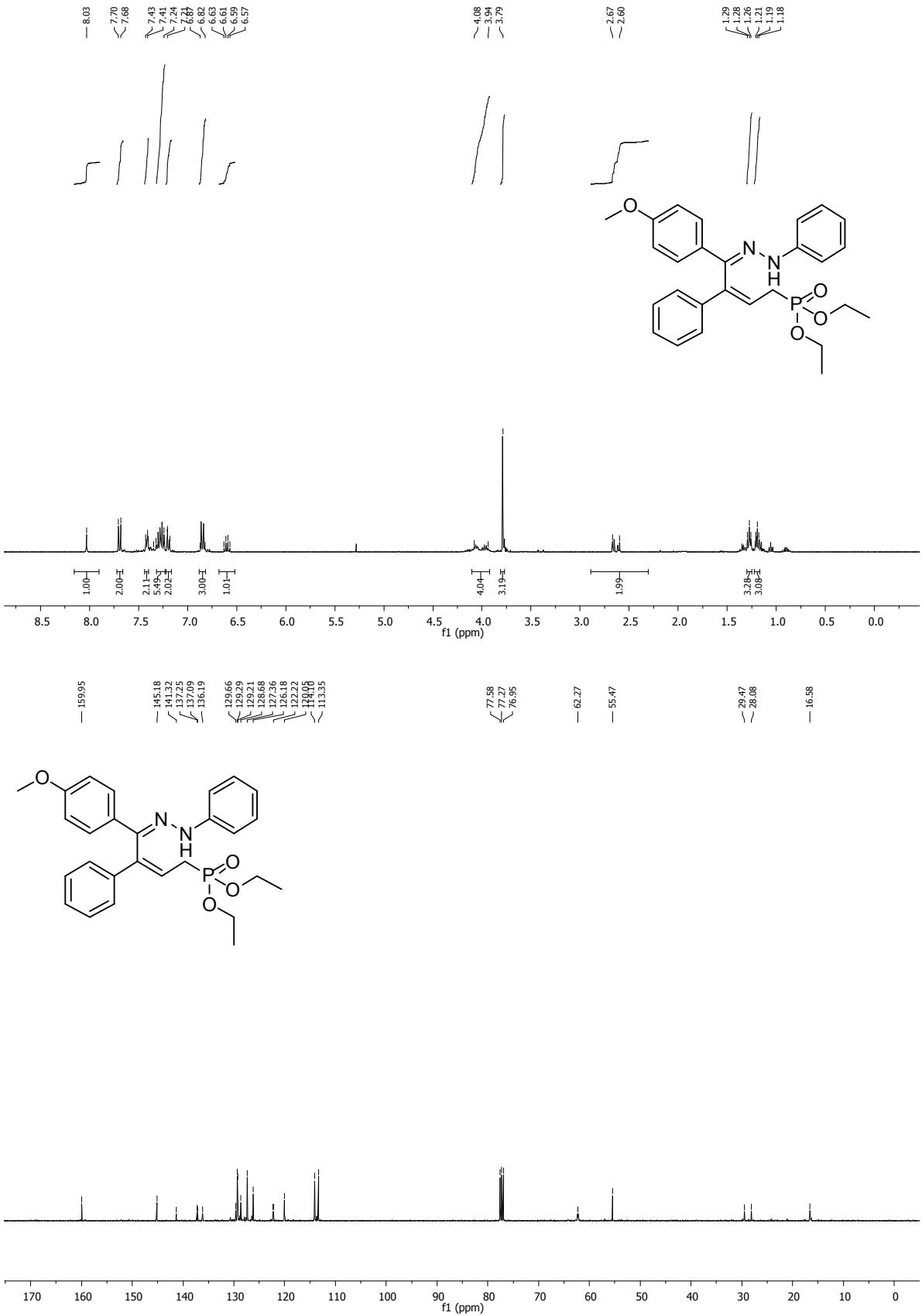
R_f: 0.23 (50:50 ethyl acetate / petroleum ether)

¹H NMR (CDCl₃, 400 MHz): δ 8.03 (s, 1H), 7.69 (d, *J* = 9.0 Hz, 2H), 7.44-7.40 (m, 2H), 7.32-7.23 (m, 5H), 7.21-7.18 (m, 2H), 6.88-6.82 (m, 3H), 6.60 (q, *J* = 7.6 Hz, 1H), 4.09-3.93 (m, 4H), 3.79 (s, 3H), 2.69-2.59 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (CDCl₃, 100.6 MHz): δ 159.9, 145.1, 141.3, 137.2, 137.0, 136.1, 129.6, 129.2, 129.2, 128.6, 127.3, 126.1, 122.3, 122.2, 120.0, 114.1, 113.3, 62.2, 55.4, 29.4, 28.0, 16.5.

HRMS: calculated for C₂₇H₃₁N₂O₄P: 478.2021, found: 478.2002.

I.R. (thin film): 2983, 2934, 2908, 2836, 1601, 1503, 1436, 1367, 1248, 1029, 972 cm⁻¹.



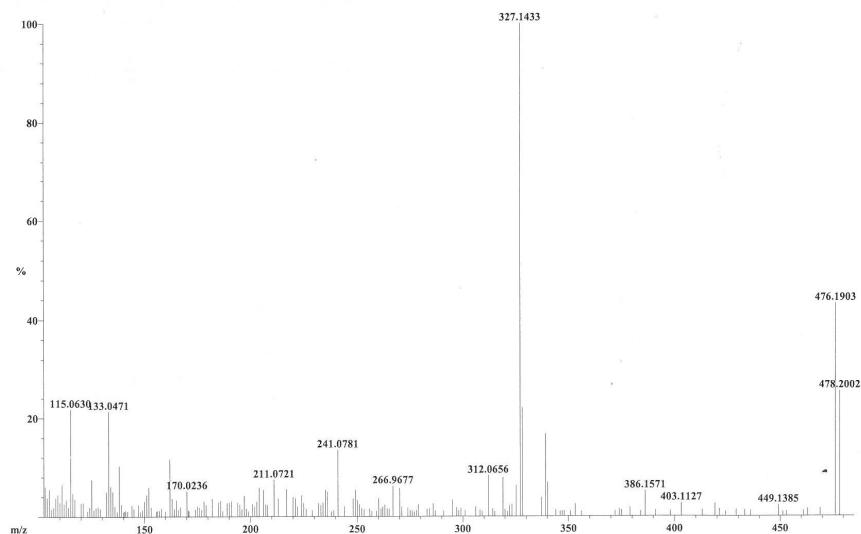
File: EE159
Sample:
Instrument: JEOL GCmate
Inlet: Direct Probe

Ionization mode: EI+

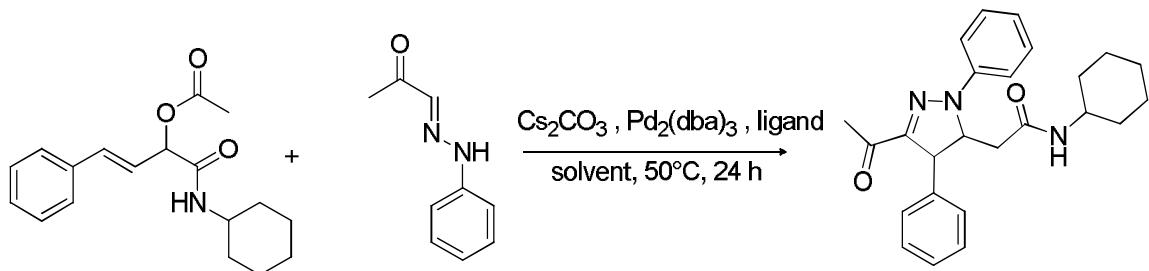
Scan: 219
Base: m/z 327; 29.4%FS TIC: 2370400

R.T.: 4.48

#Ions: 263



Enantioselective formation of 3a



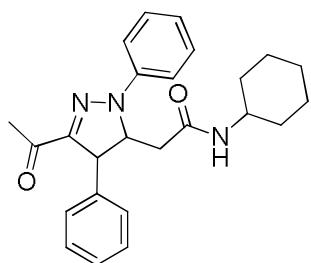
General procedure

Stirr $\text{pd}_2(\text{dba})_3$ (0.01 mmol, 0.05 eq) with chiral ligand (0.12 eq) in solvant (1 ml/0.2M) for 20 min at room temperature, followed by addition of **1a** (50 mg, 0.16 mmol), (1E)-1-(2-phenylhydrazin-1-ylidene)propan-2-one (29 mg, 0.18 mmol) and Cs_2CO_3 (54 mg, 0.16 mmol) and continue stirring for 24 hours at 50°C under argon. The solvent was removed afterwards under reduced pressure and the crude was purified by flash chromatography on silica gel.

Ligand	Solvent	Rdt	ee	Numbering
(r)-binaphane	toluene	67%	61%	1
	THF	60%	36%	2
(s)- <i>t</i> -Bu-PHOX	toluene	78%	57%	3
	THF	45%	52%	4
(s)-segphos	toluene	60%	42%	5
	THF	70%	50%	6
(r)-binap	toluene	55%	32%	7
	THF	45%	52%	8
(s)-I-Pr-phox	toluene	75%	42%	9
	THF	52%	40%	10
(r)-paracyclophane PHANPHOS	toluene	75%	20%	11
	THF	67%	10%	12
(s)-diop	toluene	85%	12%	13
	THF	60%	8%	14
DACH-naphthyl Trost	toluene	22%	51%	15
	THF	45%	34%	16

SFC conditions: [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm].

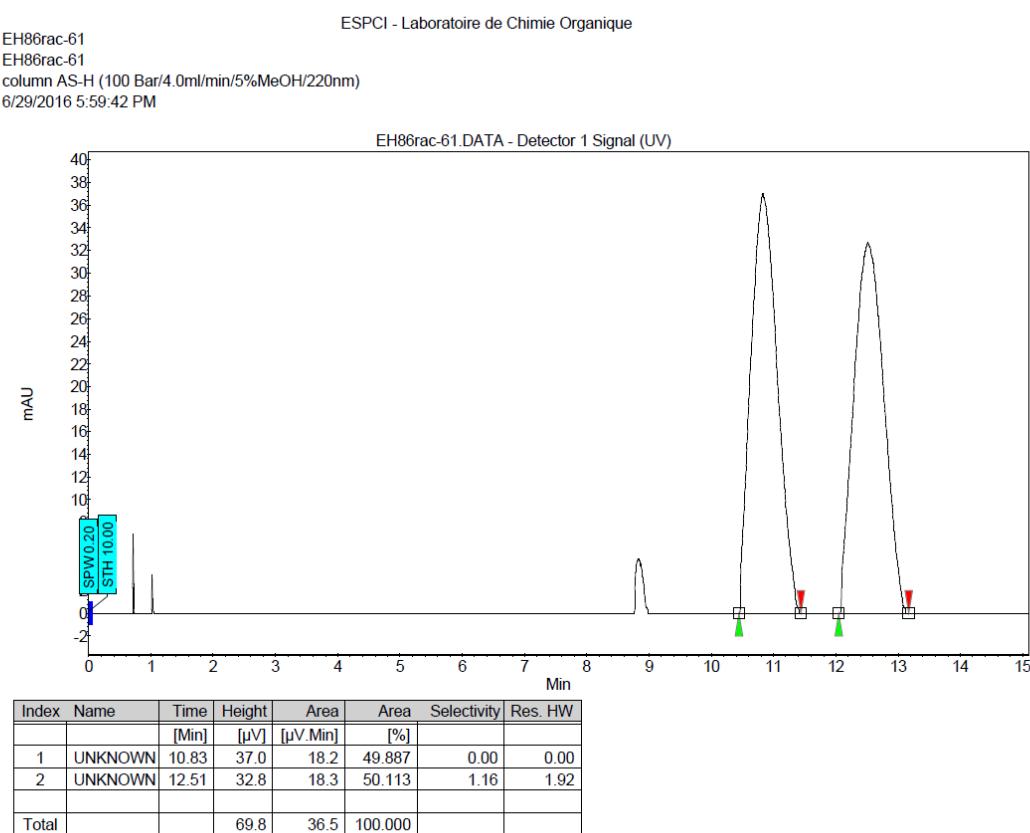
2-(3-acetyl-1,4-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-*N*-cyclohexylacetamide 1b



C₂₅H₂₉N₃O₂

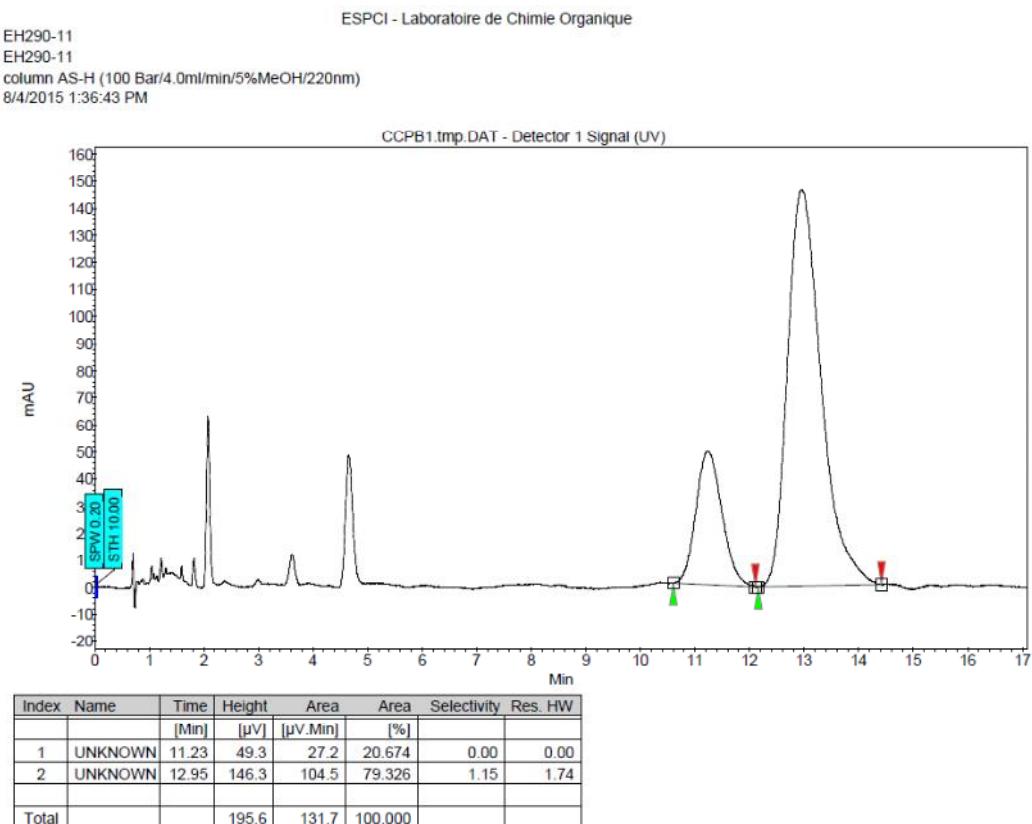
M=403.226 g.mol⁻¹

Racemic (2a) [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm; first enantiomer $t_R = 10.74$; second enantiomer $t_R = 12.42$ min].



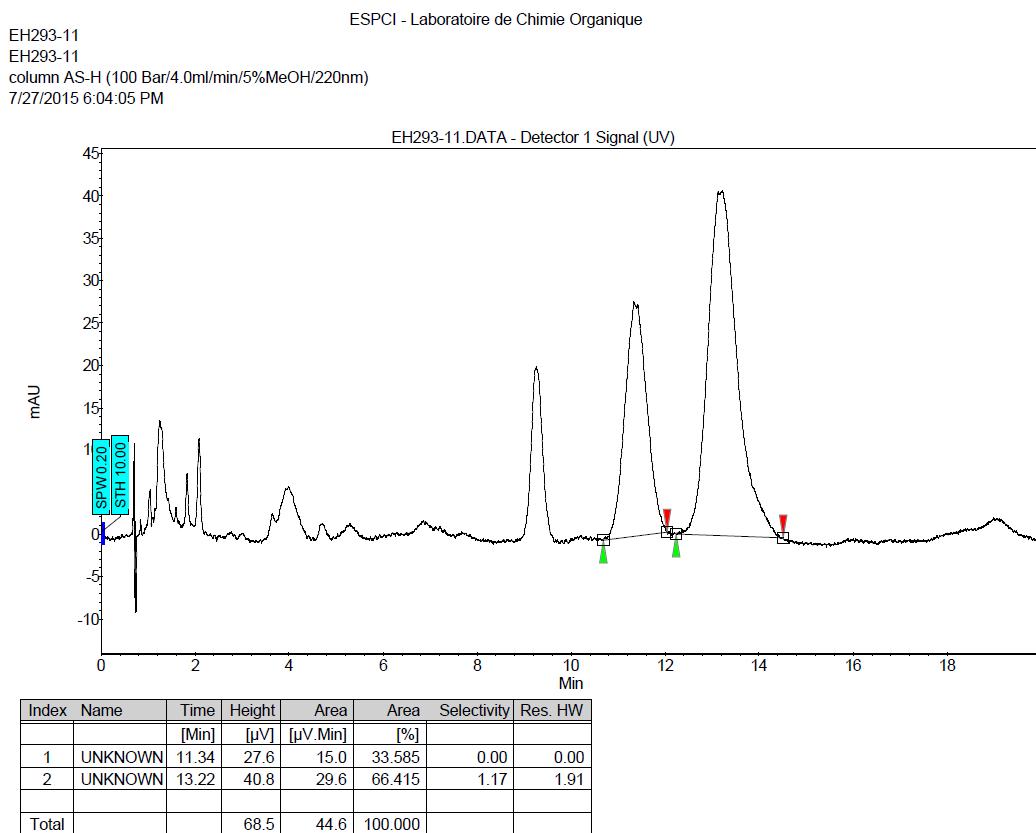
Condition N°1

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.95$ min; minor enantiomer $t_R = 11.23$ min].



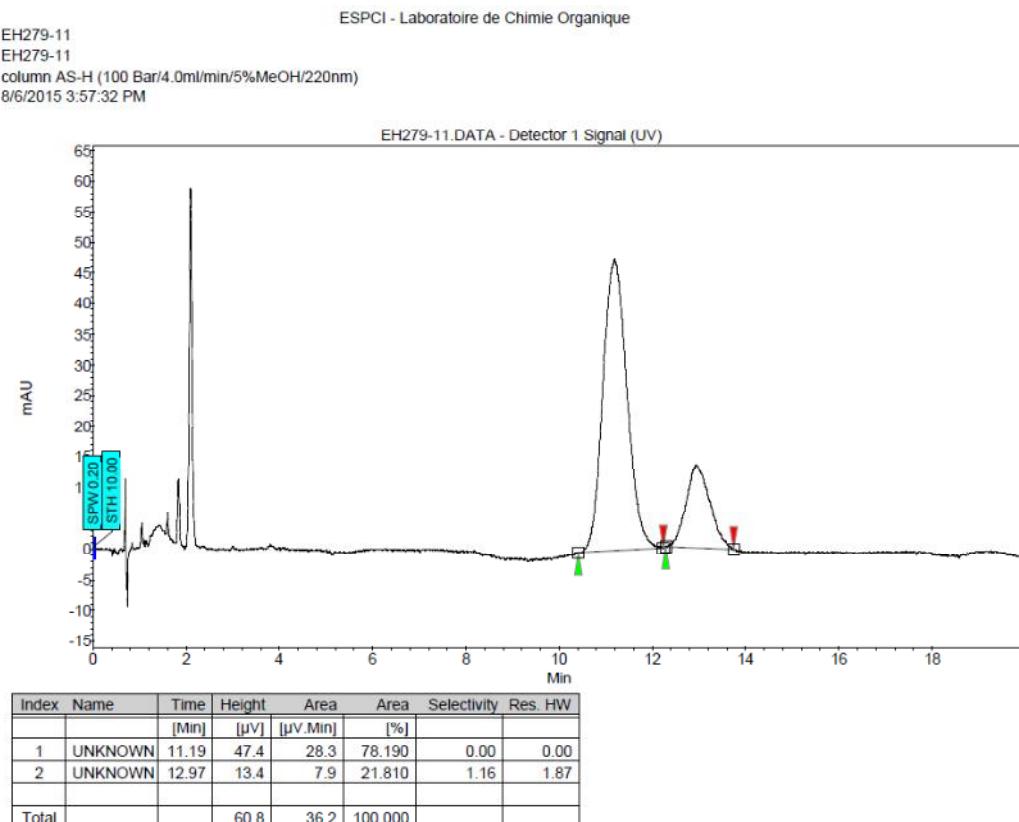
Condition N°2

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 13.22$ min; minor enantiomer $t_R = 11.34$ min].



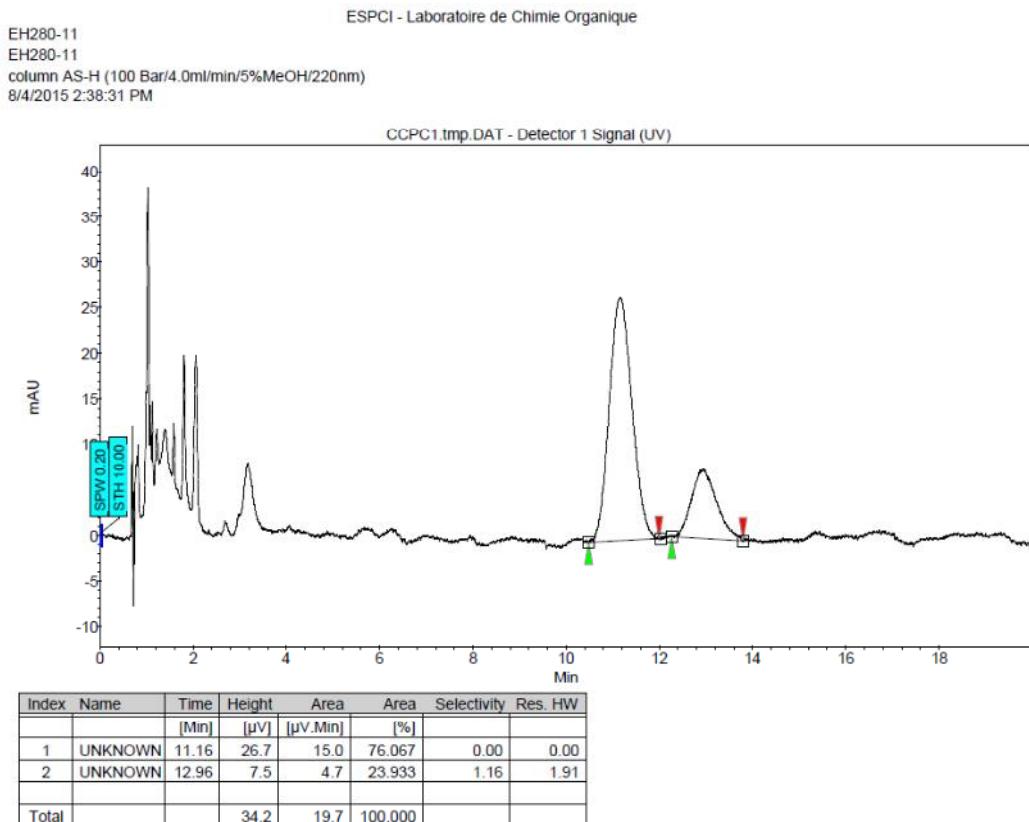
Condition N°3

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 11.19$ min; minor enantiomer $t_R = 12.97$ min].



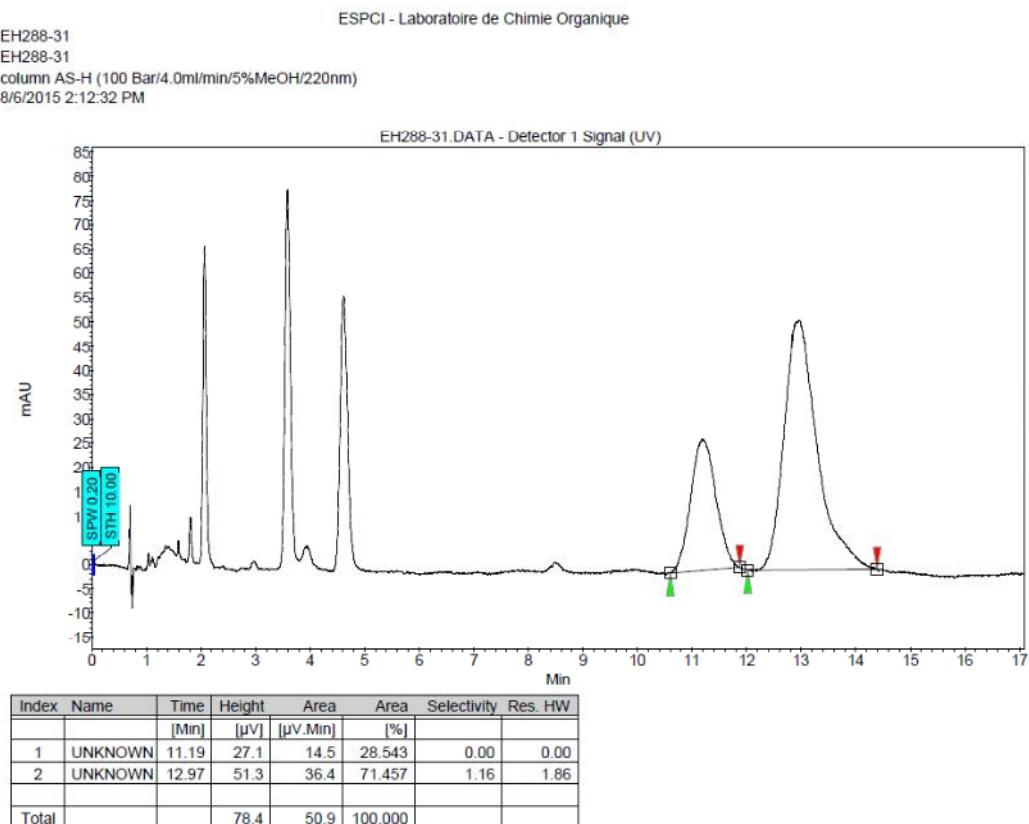
Condition N°4

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 11.16$ min; minor enantiomer $t_R = 12.96$ min].



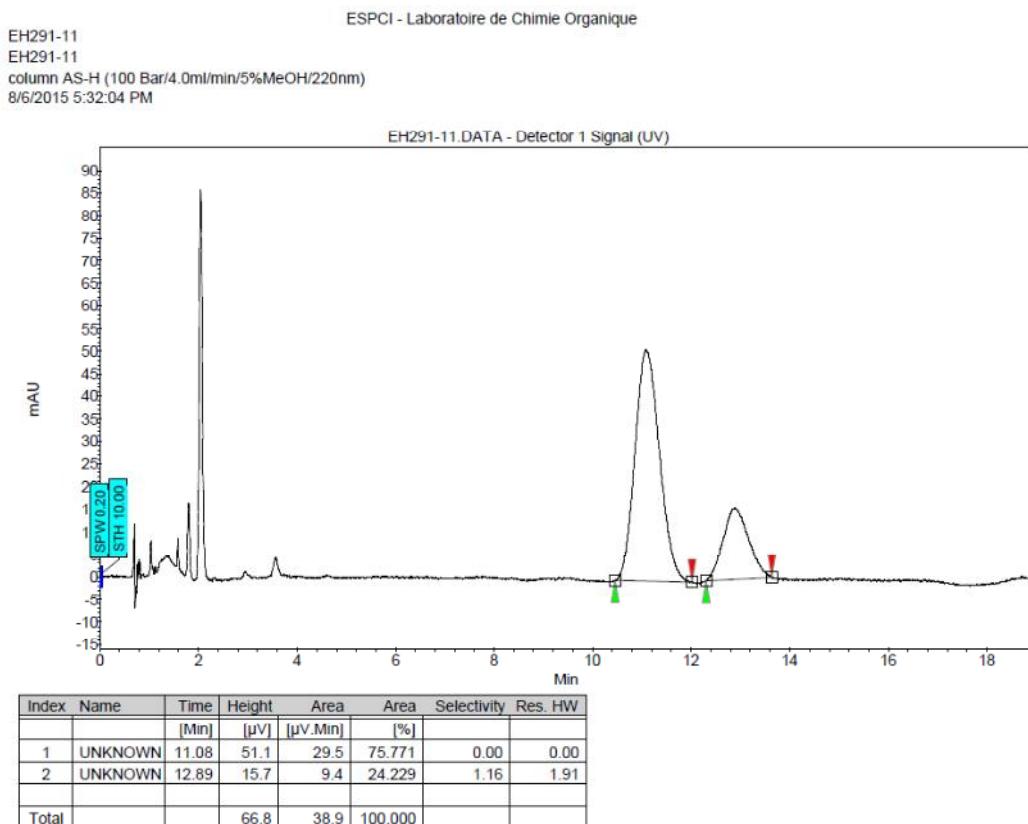
Condition N°5

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.97$ min; minor enantiomer $t_R = 11.19$ min].



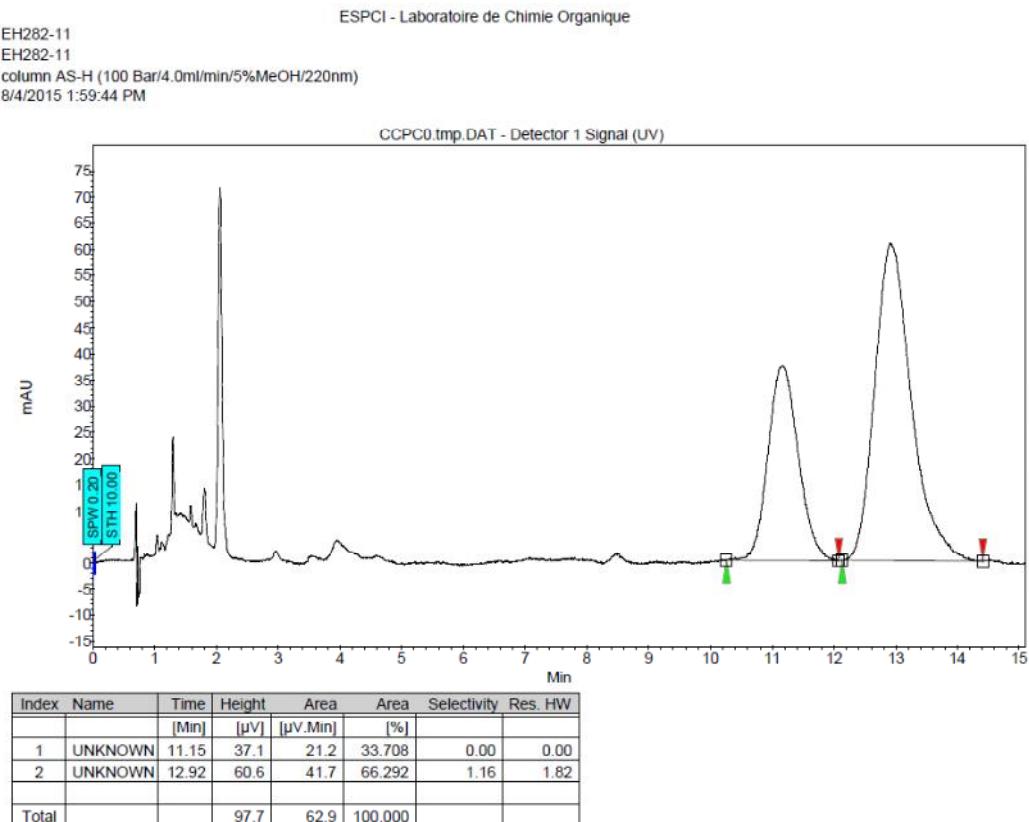
Condition N°6

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 11.08$ min; minor enantiomer $t_R = 12.89$ min].



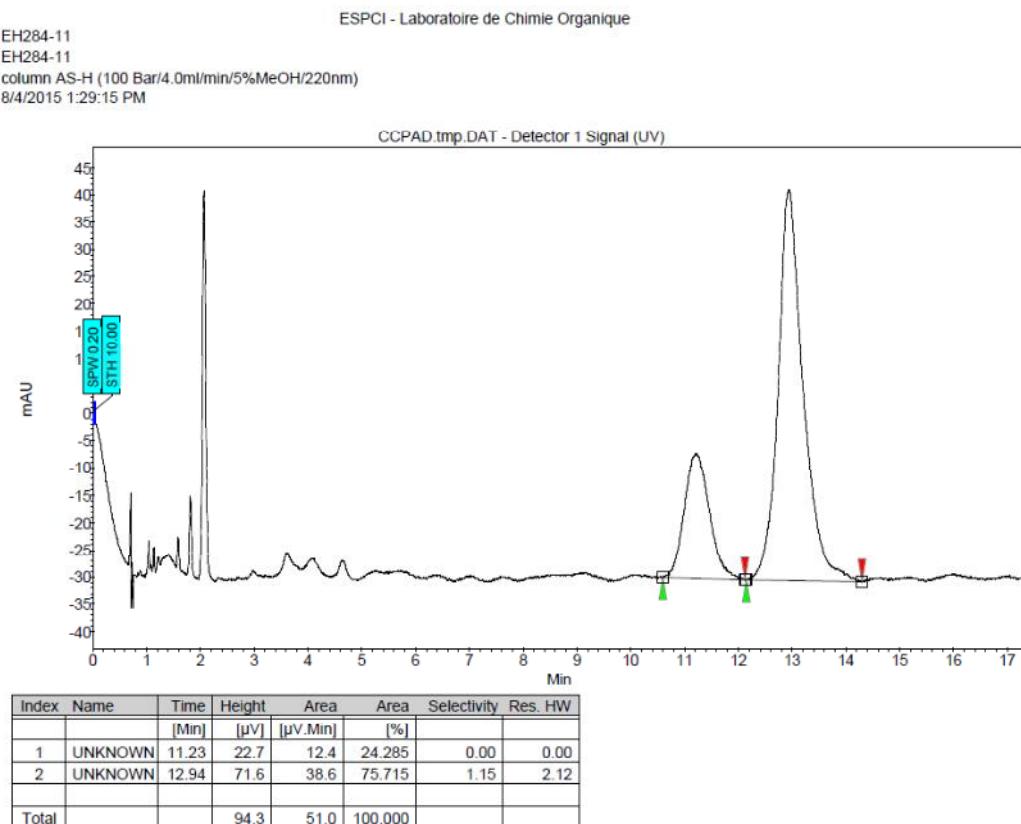
Condition N°7

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.92$ min; minor enantiomer $t_R = 11.15$ min].



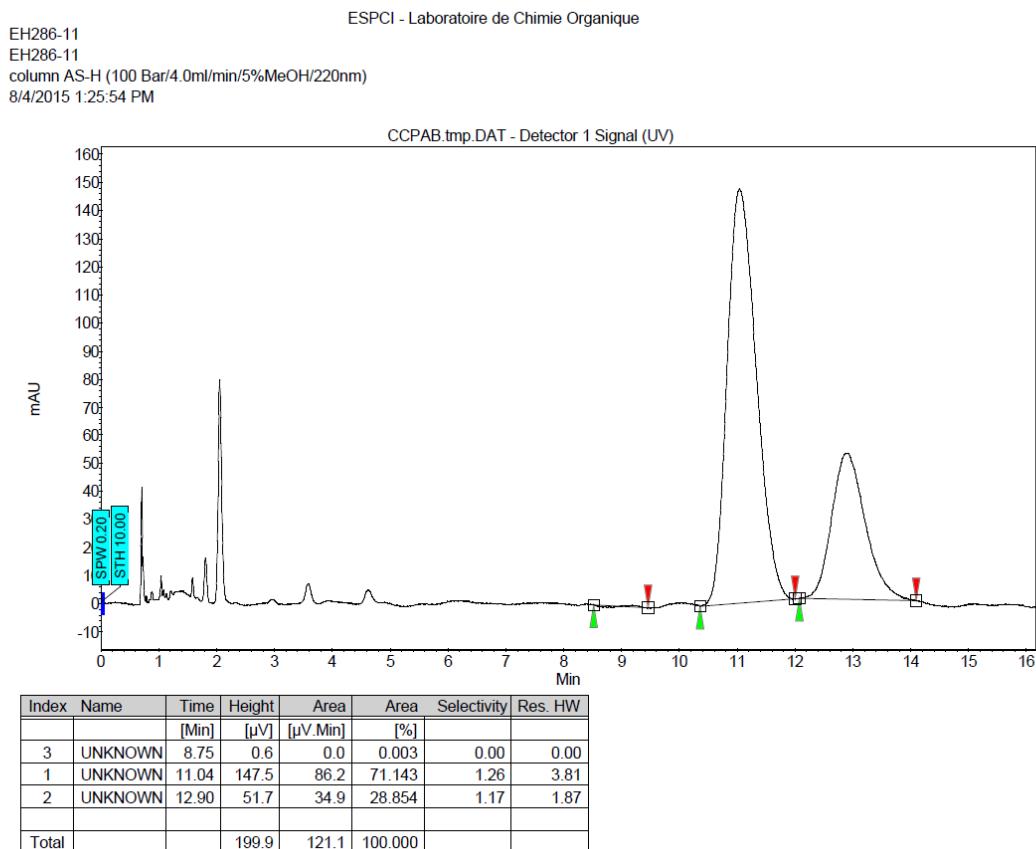
Condition N°8

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.94$ min; minor enantiomer $t_R = 11.23$ min].



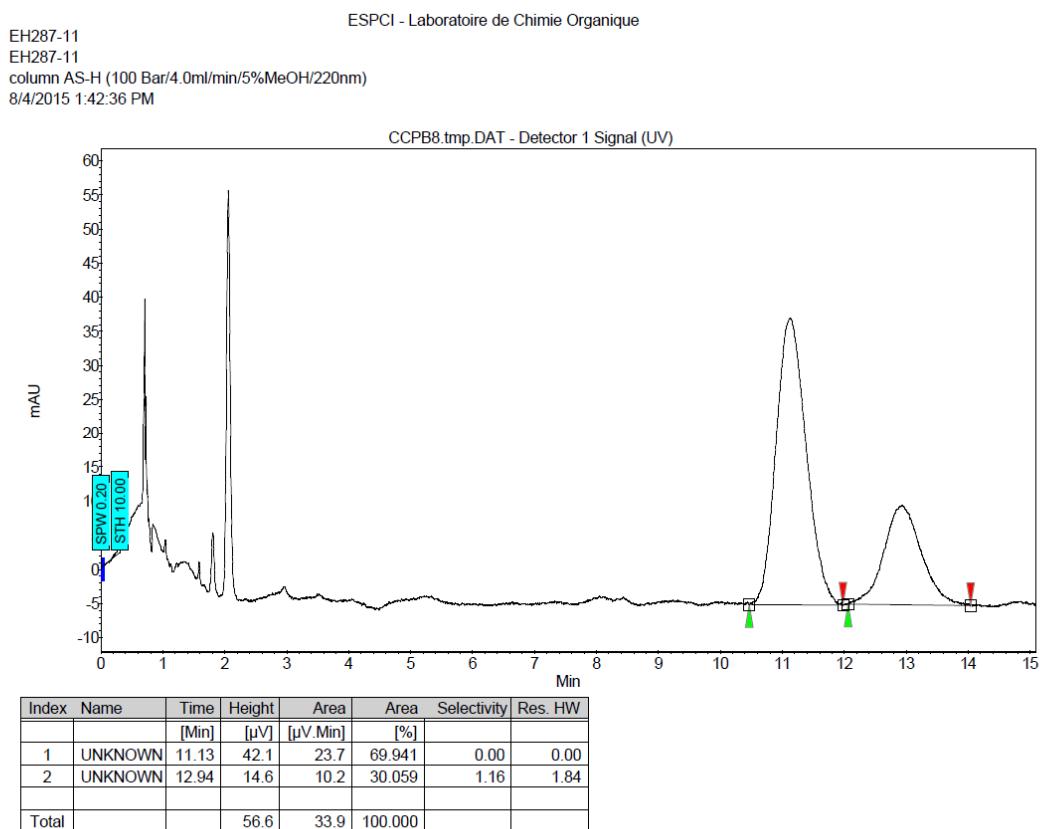
Condition N°9

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 11.04$ min; minor enantiomer $t_R = 12.90$ min].



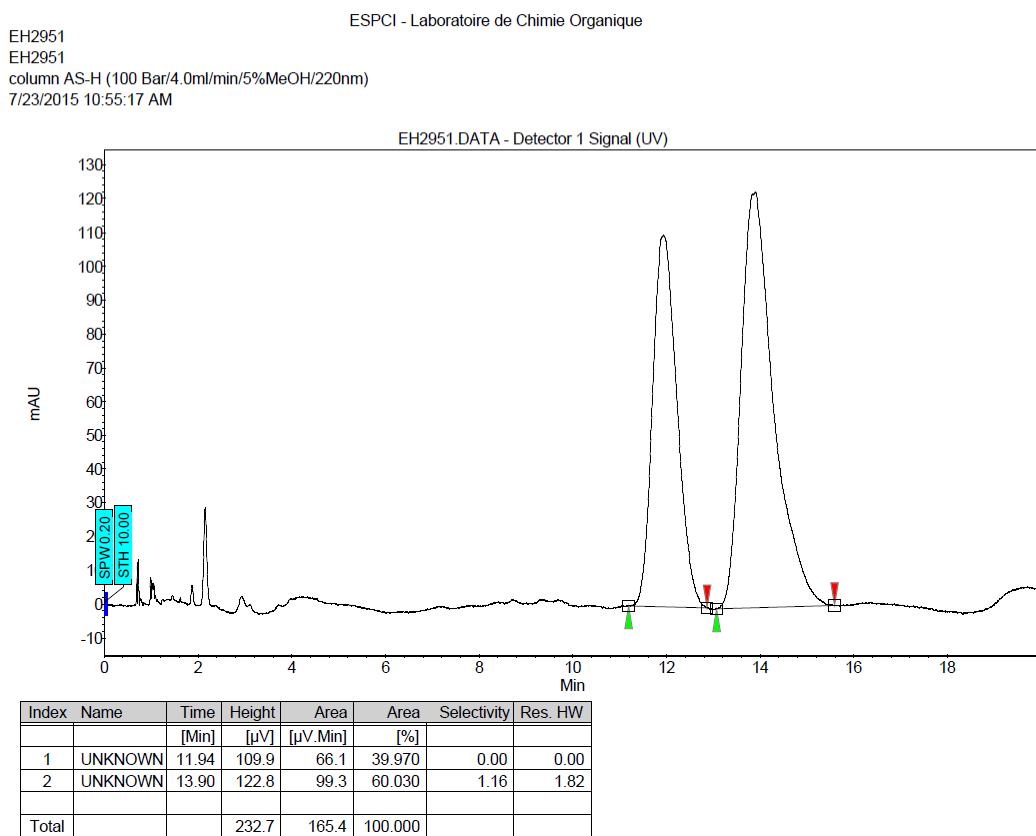
Condition N°10

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 11.13$ min; minor enantiomer $t_R = 12.94$ min].



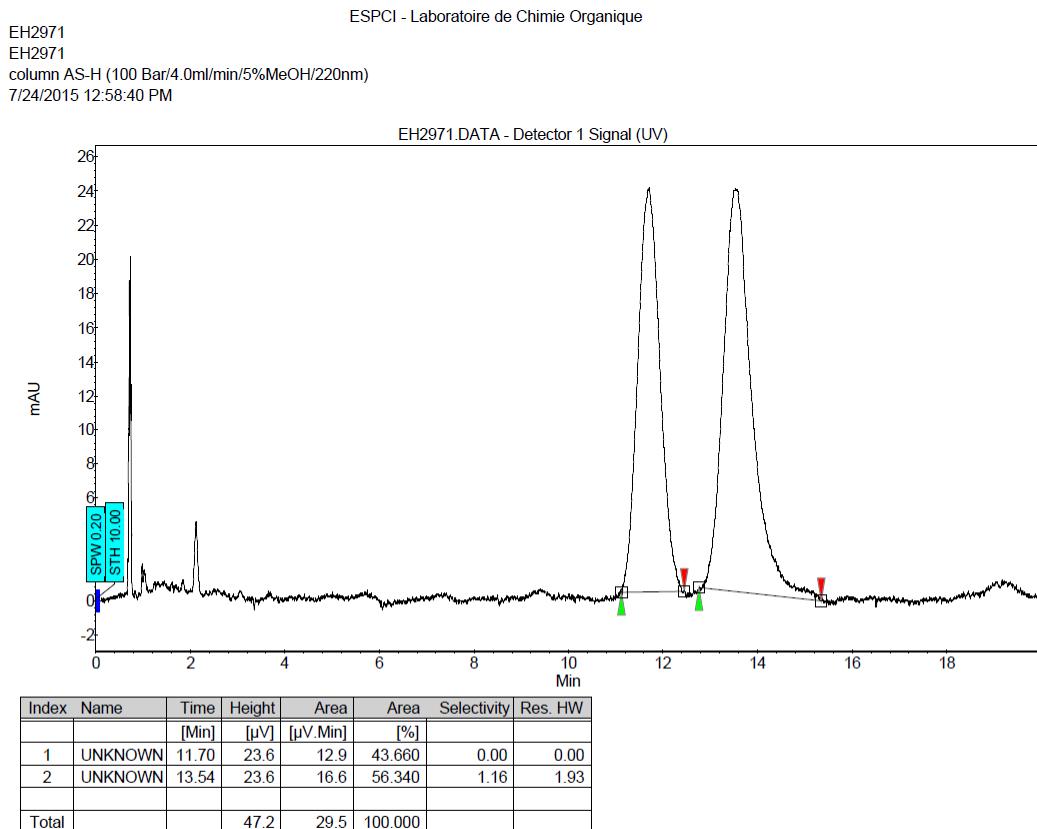
Condition N°11

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 13.90$ min; minor enantiomer $t_R = 11.94$ min].



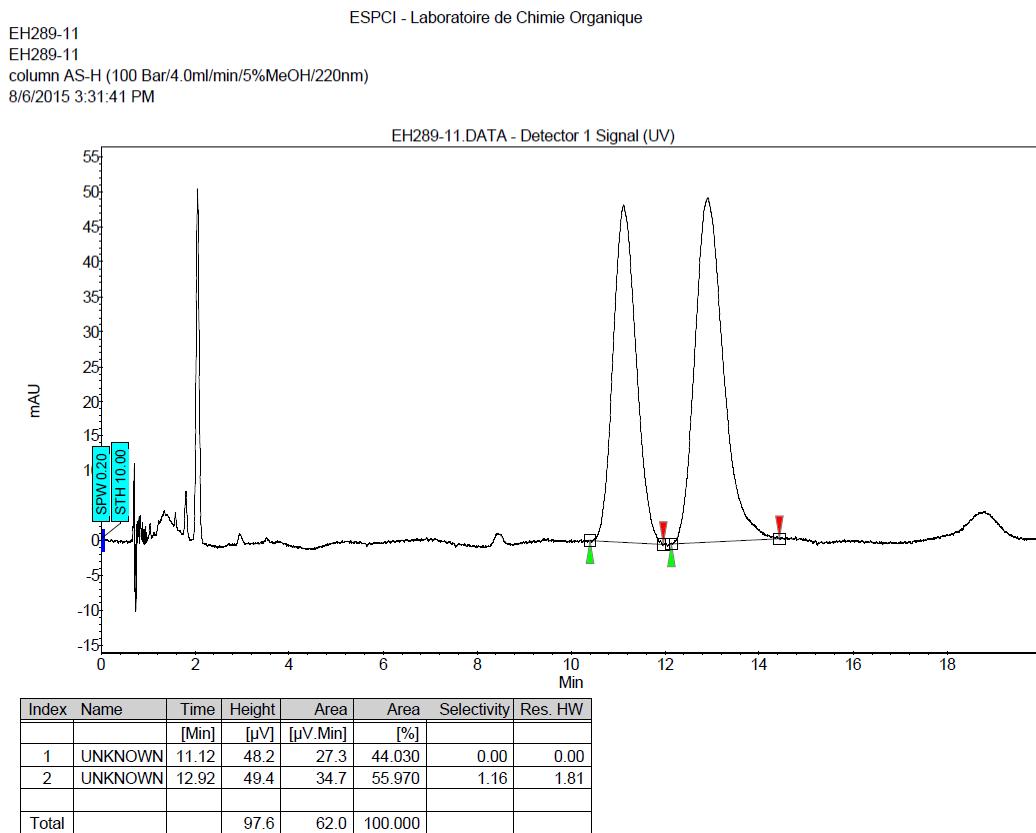
Condition N°12

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 13.54$ min; minor enantiomer $t_R = 11.70$ min].



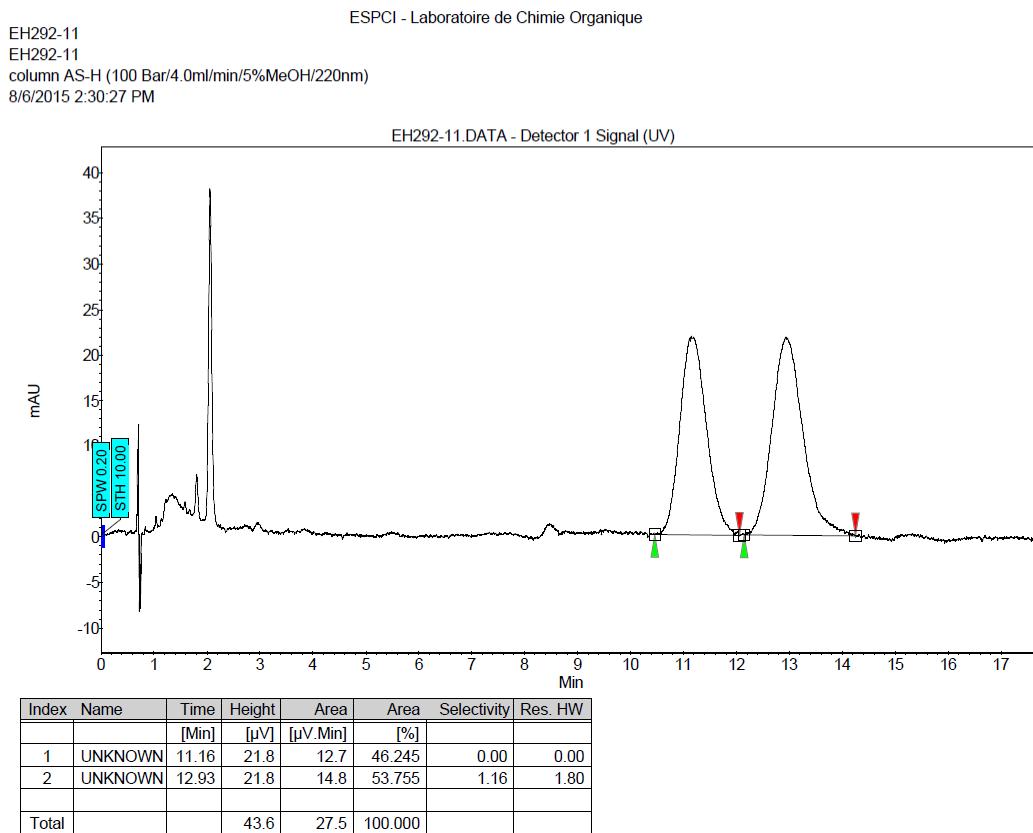
Condition N°13

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.92$ min; minor enantiomer $t_R = 11.12$ min].



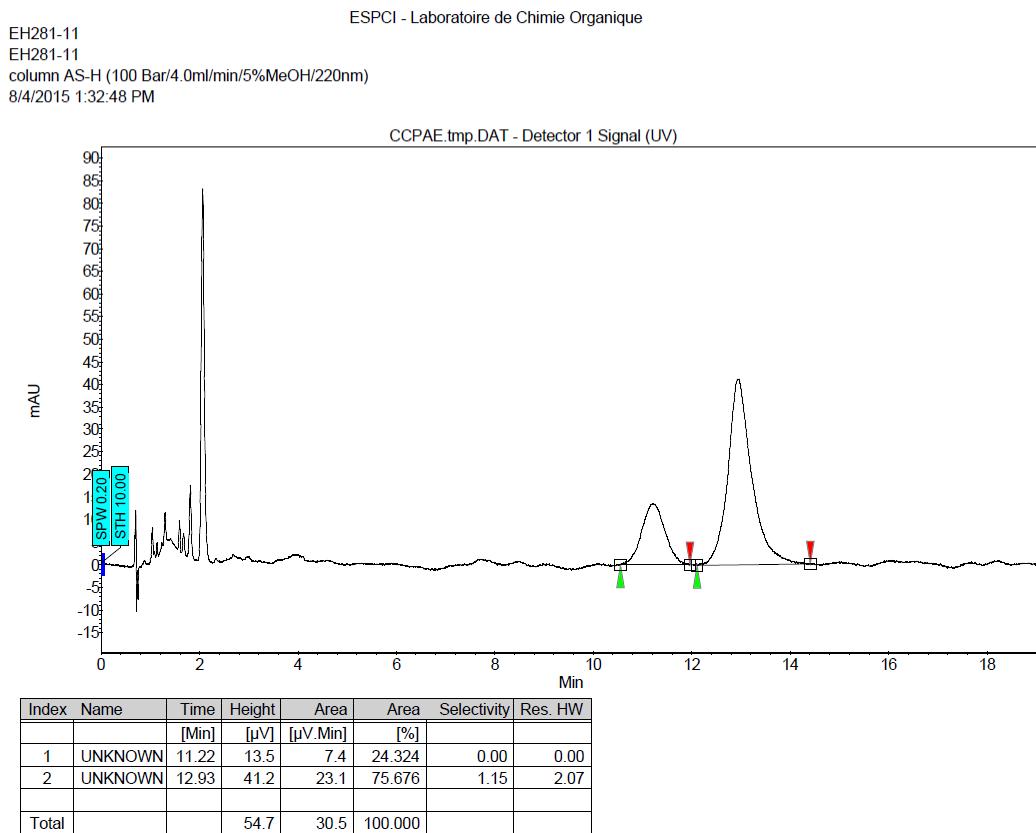
Condition N°14

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.93$ min; minor enantiomer $t_R = 11.16$ min].



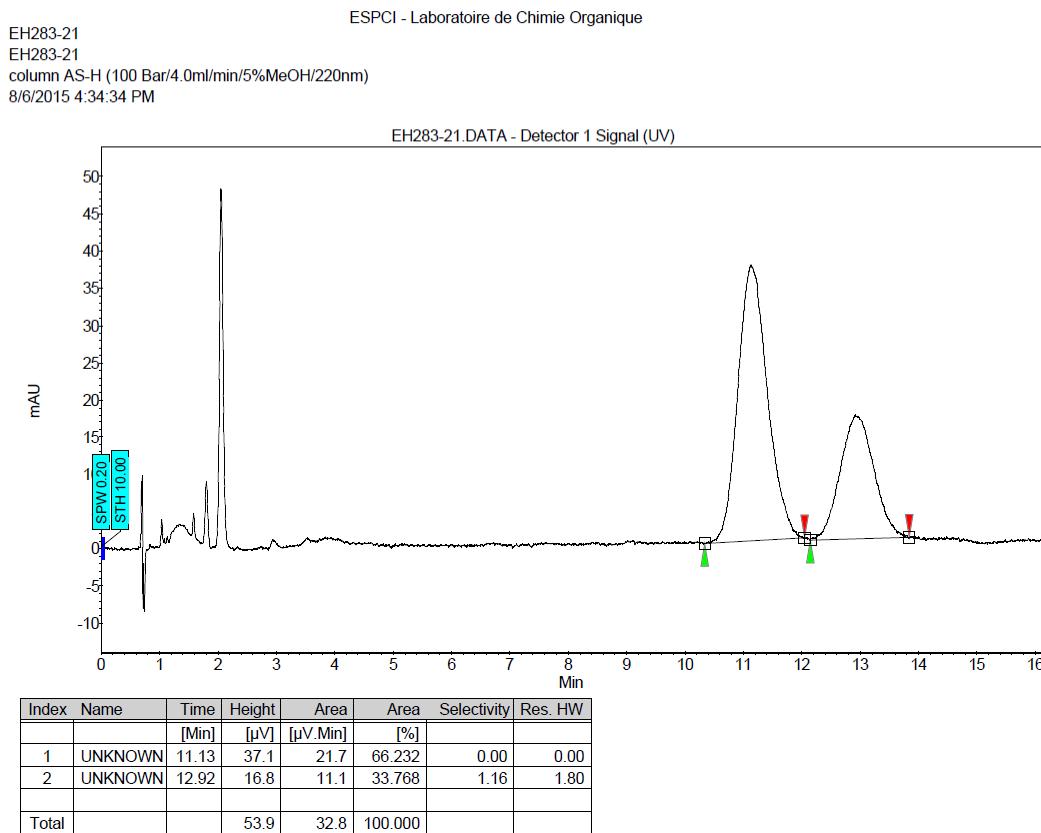
Condition N°15

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.93$ min; minor enantiomer $t_R = 11.22$ min].



Condition N°16

Following general procedure D [DAICEL AS-H column; 100 bar; flow: 4.0 mL/min; 5% MeOH; $\lambda = 220$ nm, major enantiomer $t_R = 12.92$ min; minor enantiomer $t_R = 11.13$ min].



Single crystal X-ray analysis

Single crystals of compounds **3e**, **3h** and **6f** were mounted on a kapton loop using Paratone® oil and cooled to 150 K in a nitrogen stream for X-ray structure determination.

The loop was transferred to a Nonius Kappa CCD diffractometer using Mo K α ($\lambda = 0.71069 \text{ \AA}$) X-ray source, a graphite monochromator and a Bruker APEX-II detector. Preliminary orientation matrixes and cell constants were determined by collection of 10 s frames, followed by spot integration and least-squares refinement. Data were integrated and corrected for Lorentz and polarization effects. The crystal structures were solved using SHELXT-2014 and refined in SHELXL-2014 by full-matrix least squares using anisotropic thermal displacement parameters for all non-hydrogen atoms. X-Ray structures show chirality at C7, C11 for **3e**, C9, C13, C35, C39 for **3h** and C9, C10 for **6f**. Constraints on bond lengths and angles were added to be able to describe the disorder located along the phosphonate chain of compound **6f**. ORTEP drawings were produced using Mercury with 50% probability thermal ellipsoids. CCDC 1495182-1495184.

Compound	Anisotropically refined hydrogens
3e	H12, H30, H31, H43, H61 et H62
3h	H1, H6A, H6B, H7 et H11
6f	H9, H10, H11A et H11B

Table 1: anisotropically refined hydrogens corresponding to C-H and N-H bonds of interest in the 3 compounds