Organocatalyzed Asymmetric Reactions via Microwave Activation

Sarah Mossé and Alexandre Alexakis*

Department of Organic Chemistry, University of Geneva, 30, quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

Supporting Information

Table of Contents

General Remarks. Concerning ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra, chemical shift (δ) are given in ppm relative to tetramethylsilane (0 ppm). Multiplicity is indicated as follows : s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants are reported in Hz. Optical rotations were measured at 25°C in a 10 cm cell in the stated solvent ; $[\alpha]_D$ values are given in 10^{-1} deg.cm^2 g^{-1} (concentration c given as g/100 mL). Enantiomeric excesses were determined by chiral Super Fluid Chromatography (SFC), with appropriated program using a gradient of methanol or by chiral Gas Chromatography (GC), with appropriated program using a gradient of temperature. Temperature programs are described as follows: initial temperature (°C) – initial time (min) – temperature gradient (°C/min) – final temperature (°C); retention times (R_T) are given in min. Flash chromatography was performed using silicagel 32-63 μm, 60 Å.

Evolution of reaction was followed by TLC. Benzaldehyde **2c** and isobutyraldehyde **4c** were freshly distilled before using. Cyclopentadiene monomer **7** was freshly used after cracking. (*S*,*S*)-*N*-Isopropyl-2,2'-bipyrrolidine (**iPBP**) was prepared as described in literature procedure.[1] (5*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one hydrochloride **9** was prepared as

[1] O. Andrey, A. Alexakis, A. Tomassini, G. Bernardinelli, *Adv. Synth. Catal.* **2004**, *346*, 1147.

described in literature.[2] All other reagents and solvents were purchased from commercial suppliers and used as received.

Microwave irradiation experiments.

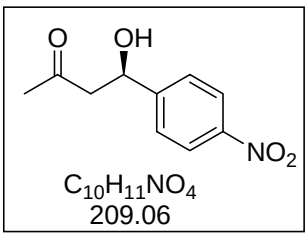
Microwave-assisted reactions were carried out using a focused microwave unit (Biotage Initiator™). The instrument consists of a continuous focused microwave power delivery system with operator selectable power output from 0-300 W. In all experiments, a constant power was applied to ensure reproducibility. Reactions were performed in glass vessels (2-5 mL) sealed with a septum. Pressure measurement is accomplished by a non-invasive sensor integrated into the cavity lid, which measures the deformation of the Teflon seal of the vessels (maximum 20 bar). Temperature controlled is achieved by means of an IR sensor and the indicated temperature corresponds to the maximal temperature reached during each experiment. The specified reaction time corresponds to the total irradiation time. Efficient cooling is accomplished by means of a pressurized air (with a pressure of 5 bar) during the entire experiment.

[2] Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243.

I. Aldol reactions

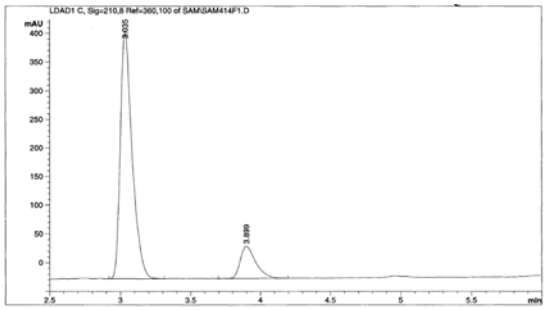
General procedure 1 under microwave irradiation. In a 2-5 mL vessel were introduced L-proline, DMSO (2.4 mL) and finally acetone **1** (20 vol %, 0.6 mL) and the mixture was stirred for 15 min under argon. Aldehyde was added (0.3 mmol) and the vessel was sealed with a septum and placed into the microwave cavity. The microwave source was then turned on. Constant microwave irradiation as well as simultaneous air-cooling (5 bar) were used during the entire reaction time. The evolution of the reaction was monitored by TLC. After cooling to room temperature, the mixture was quenched as described in literature procedure[3] using NH_4Cl aq. sat. and extracted with EtOAc (2x). The combined organic layers were washed successively with water and brine, dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash column chromatography on silica gel using a mixture of cyclohexane and ethyl acetate.

[3] a) List, B.; Lerner, R. A.; Barbas III, C. F. *J. Am. Chem. Soc*. **2000**, *22*, 2345. b) Sakthivel, K.; Notz, W.; Bui, T.; Barbas III, C. F. *J. Am. Chem. Soc*. **2001**, *23*, 5260.



(R)-4-hydroxy-4-(4-nitrophenyl)butan-2-one **3a** (Table 2, entry 1): From 4-nitrobenzaldehyde **2a** (1 eq., 0.3 mmol, 45.3 mg) and L-proline (0.2 eq., 0.06 mmol, 6.9 mg) according to *general procedure 1* (15 W, 0 bar, 35 °C) to give complete conversion after 15 min and to afford aldol product **3a** (43.3 mg, 69%). The enantiomeric excess was determined by chiral SFC (AS-H column, 2 mL/min, 200 bar, methanol 10%-2-1-25%, 30°C, R_t: 3.03 (*R*), 3.89 (*S*)). $[\alpha]_D^{20}$= +42.6 (*c* 1.035 , ee= 70%, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 8.22-8.20 (d, J= 8.60 Hz, 2H), 7.55-7.52 (d, J= 8.84 Hz, 2H), 5.28-5.24 (m, 1H), 3.56-3.55 (m, 1H), 2.86-2.84 (d, 2H), 2.22 (s, 3H). Other spectroscopic data are in agreement with published data.[3]

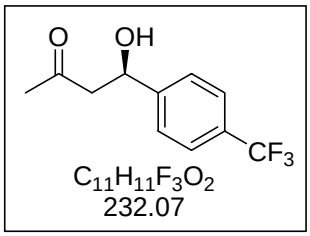


Area Percent Report

Sorted by Signal
Multiplier : 1.000000

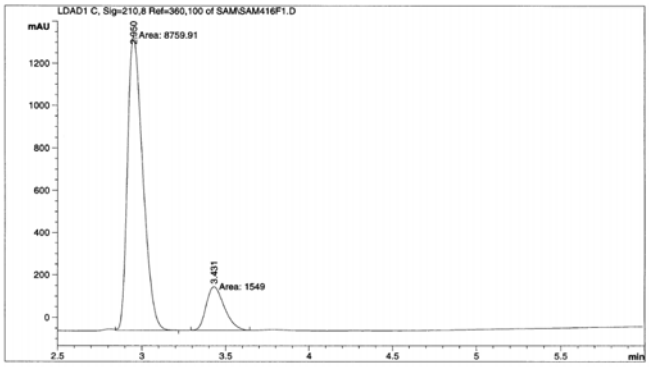
Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	3.035	BF	0.087	2502.18994	433.09723	84.9727
2	3.899	BV	0.117	442.50793	56.66236	15.0273



(R)-4-hydroxy-4-(4-(trifluoromethyl)phenyl)butan-2-one **3b** (Table 2, entry 2): From α,α,α-trifluoro-p-tolualdehyde **2b** (1 eq., 0.3 mmol, 52.23 mg) and L-proline (0.2 eq., 0.06 mmol, 6.9 mg) according to *general procedure 1* (15 W, 0 bar, 32 °C) to give complete conversion after 15 min and to afford aldol product **3b** (48.5 mg, 70%). The enantiomeric excess was determined by chiral SFC (AS-H column, 2 mL/min, 200 bar, methanol 2%-2-1-15%, 30°C, R_t: 2.95 (*R*), 3.43 (*S*)). $[\alpha]_D^{20}$= +32.6 (*c* 1.14 , ee= 70%, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.62-7.60 (d, J= 8.08 Hz, 2H), 7.49-7.47 (d, J= 8.08 Hz, 2H), 5.23-5.20 (m, 1H), 3.44-3.43 (m, 1H), 2.85-2.84 (d, 2H), 2.21 (s, 3H). Other spectroscopic data are in agreement with published data.[4]



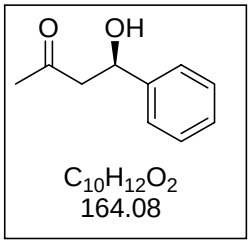
Area Percent Report

Sorted by Signal
Multiplier : 1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

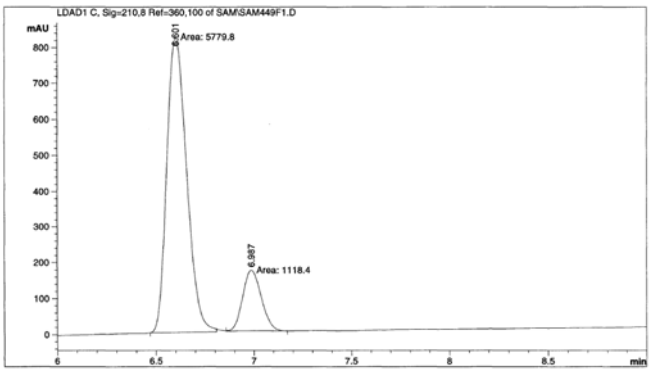
Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	2.950	MM	0.105	8759.90625	1394.90466	84.9742
2	3.431	MM	0.126	1548.99817	205.40544	15.0258

[4] Kotrusz, P.; Kmentová, I.; Gotov, B.; Toma, Š.; Solčániová, E. *Chem. Comm.* **2002**, 2510.



(R)-4-hydroxy-4-phenylbutan-2-one **3c** (Table 2, entry 3): From benzaldehyde **2c** (1 eq., 0.3 mmol, 30 μL) and L-proline (0.3 eq., 0.09 mmol, 10.3 mg) according to *general procedure 1* (15 W, 0 bar, 31 °C) to give 89% conversion after 1 h and to afford aldol product **3c** (34.2 mg, 70%). The enantiomeric excess was determined by chiral SFC (OD-H column, 2 mL/min, 200 bar, methanol 10%-2-1-25%, 30°C, R_t: 6.60 (*R*), 6.98 (*S*)). $[\alpha]_D^{20}$= +37.2 (*c* 0.575 , ee= 68%, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.36-7.30 (m, 4H), 7.29-7.26 (m, 1H), 5.17-5.14 (m, 1H), 3.29 (br, 1H), 2.92-2.79 (m, 2H), 2.19 (s, 3H). Other spectroscopic data are in agreement with published data.[3]

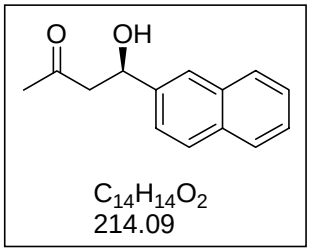


Area Percent Report

Sorted by Signal
Multiplier : 1.000000

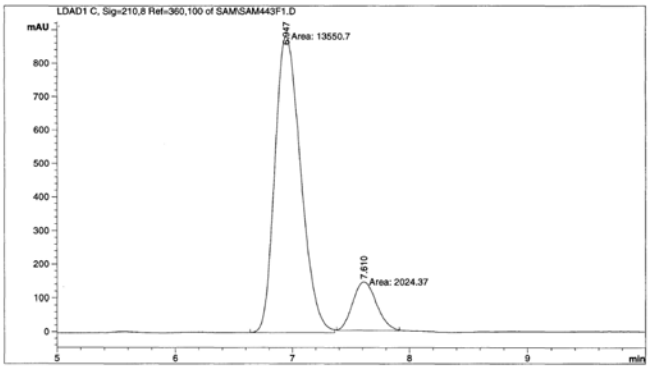
Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	6.601	MM	0.117	5779.79834	824.03949	83.7871
2	6.987	MM	0.110	1118.40088	169.07425	16.2129

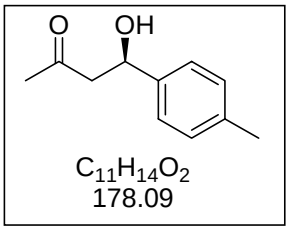


(R)-4-hydroxy-4-(naphthalen-2-yl)butan-2-one **3d** (Table 2, entry 4): From 2-naphtaldehyde **2d** (1 eq., 0.3 mmol, 46.9 mg) and L-proline (0.3 eq., 0.09 mmol, 10.3 mg) according to *general procedure 1* (15 W, 0 bar, 31 °C) to give 79% conversion after 1 h and to afford aldol product **3d** (35.9 mg, 56%). The enantiomeric excess was determined by chiral SFC (AD column, 2 mL/min, 200 bar, methanol 10%-2-1-25%, 30°C, R_t: 6.94 (*R*), 7.61 (*S*)). $[\alpha]_D^{20}$= +34.8 (*c* 0.525 , ee= 74%, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.85-7.83 (m, 4H), 7.50-7.45 (m, 3H), 5.35-5.31 (m, 1H), 3.39-3.38 (m, 1H), 2.96-2.93 (m, 2H), 2.21 (s, 3H). Other spectroscopic data are in agreement with published data.[3]

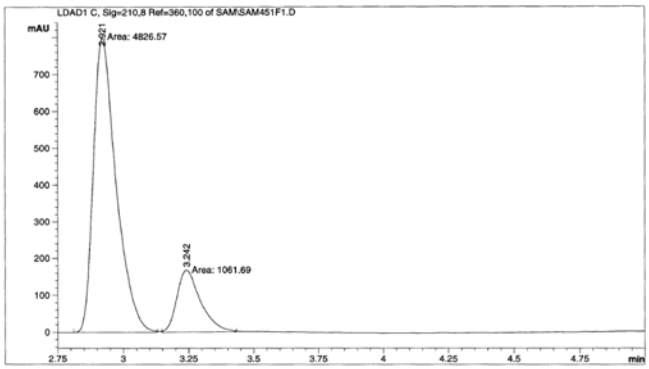



```
==================================================================
                    Area Percent Report
==================================================================

Sorted by Signal
Multiplier            :      1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

 Peak    RT      Type   Width     Area         Height       Area
  #     [min]           [min]   [mAU*sec]      [mAU]         %
|---|---------|------|-------|------------|------------|----------|
   1     6.947   MM     0.256  13550.65723    882.59186     87.0025
   2     7.610   MM     0.236   2024.37146    142.79712     12.9975
```



(R)-4-hydroxy-4-p-tolylbutan-2-one **3e** (Table 2, entry 5): From p-tolualdehyde **2e** (1 eq., 0.3 mmol, 35 μL) and L-proline (0.3 eq., 0.09 mmol, 10.3 mg) according to *general procedure 1* (15 W, 0 bar, 32 °C) to give 82% conversion (with 1:1 ratio of aldol product **3e** and α,β-unsaturated ketone derived from aldol product **3e**) after 1 h and to afford aldol product **3d** (20.3 mg, 38%). The enantiomeric excess was determined by chiral SFC (AS-H column, 2 mL/min, 200 bar, methanol 10%-2-1-25%, 30°C, R_t: 2.92 (*R*), 3.24 (*S*)). $[\alpha]_D^{20}$= +21.4 (*c* 0.41 , ee= 64%, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.25-7.23 (m, 2H), 7.17-7.15 (m, 2H), 5.13-5.11 (m, 1H), 3.17 (br, 1H), 2.92-2.77 (m, 2H), 2.33 (s, 3H), 2.19 (s, 3H). Other spectroscopic data are in agreement with published data.[5]

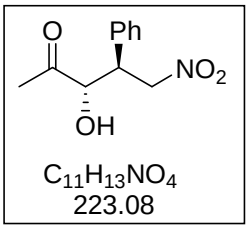



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted by Signal
Multiplier             :      1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

 Peak    RT      Type   Width     Area         Height        Area
  #     [min]           [min]   [mAU*sec]      [mAU]          %
|----|---------|------|-------|------------|------------|----------|
   1     2.921   MM     0.100   4826.57178   803.33917     81.9694
   2     3.242   MM     0.105   1061.68762   168.70941     18.0306
```

[5] Tang, Z.; Jiang, F.; Yu, L-T.; Cui, X.; Gong, L-Z.; Mi, A-Q.; Jiang, Y-Z.; Wu, Y-D. *J. Am. Chem. Soc*. **2003**, *25*, 5262.

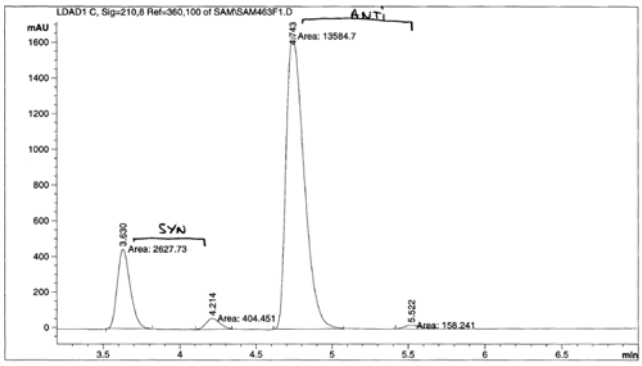
II. Conjugate Additions

General procedure 2 under microwave irradiation. In a 2-5 mL vessel were introduced (*R*,*R*)-***i*PBP** (0.15 eq. 0.05 mmol, 9.1 mg), $CHCl_3$ (2.5 mL), β-nitrostyrene (1 eq., 0.335 mmol, 50 mg) and finally the aldehyde or the ketone (10 eq., 3.35 mmol) and the vessel was sealed with a septum and placed into the microwave cavity. The microwave source was then turned on. Constant microwave irradiation as well as simultaneous air-cooling (5 bar) were used during the entire reaction time. The evolution of the reaction was monitored by TLC. After cooling to room temperature, the mixture was then hydrolyzed as described in literature procedure[1] using 1N HCl (2 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2x). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash column chromatography on silica gel using a mixture of cyclohexane and ethyl acetate.

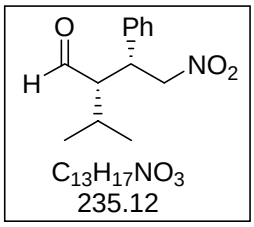


(3S,4S)-3-hydroxy-5-nitro-4-phenylpentan-2-one **6a** (Table 3, entry 2) : From hydroxyketone **4a** (10 eq., 3.35 mmol, 0.23 mL) according to *general procedure 2* (15 W, 0 bar, 28°C) to give complete conversion after 4 h and to afford Michael adduct **6a** as a mixture of two inseparable diastereoisomers (*syn*/*anti* 11:89) (62.3 mg, 83%). The enantiomeric excess was determined by chiral SFC (OJ column, 2 mL/min, 200 bar, methanol 5%-2-1-15%, 30°C, R_t: 4.7 (*S*,*S*), 5.5 (*R*,*R*)).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.41-7.23 (m, 5H), 4.84-4.79 (dd, J_1=6.04, J_2=13.36 Hz, 1H), 4.67-4.62 (dd, J_1=8.32, J_2=13.64 Hz, 1H), 4.40-4.39 (m, 1H), 3.83 (dt, J_1=6.04, J_2=8.32 Hz, 1H), 3.80-3.73 (m, 1H), 2.07 (s, 3H). Other spectroscopic data are in agreement with published data.[1]



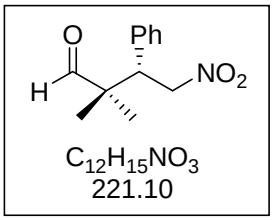

```
================================================================
                    Area Percent Report
================================================================

Sorted by Signal
Multiplier          :      1.000000

Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

 Peak    RT      Type   Width     Area        Height       Area
  #     [min]            [min]   [mAU*sec]     [mAU]        %
|----|--------|------|-------|-----------|-------------|----------|
   1    3.630   MM     0.097   2627.72754   450.12292     15.6644
   2    4.214   MM     0.108    404.45056    62.43424      2.4110
   3    4.743   MM     0.138  13584.70117  1642.41650     80.9812
   4    5.522   MM     0.122    158.24146    21.53666      0.9433
```



(2S,3R)-2-isopropyl-4-nitro-3-phenylbutanal **6b** (Table 3, entry 4) : From 3-methylbutyraldehyde **4b** (10 eq., 3.35 mmol, 0.36 mL) according to *general procedure 2* (15 W, 0 bar, 27°C) to give complete conversion after 1 h and to afford Michael adduct **6b** (76.4 mg, 97%). The enantiomeric excess was determined by chiral GC (Hydrodex-B-3P, iso 150°C, R_t: 38.48 (*R*,*S*), 39.61 (*S*,*R*)). $[\alpha]_D^{20}$= -51.6 (*c* 1.0 , ee= 78%, $CHCl_3$).

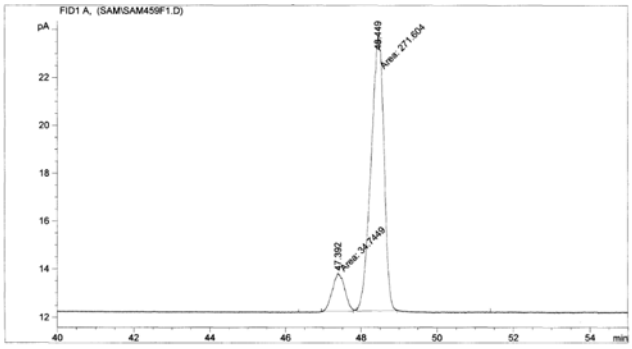
^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.93 (d, 1H, J = 2.2 Hz), 7.36-7.29 (m, 3H), 7.20-7.17 (m, 2H), 4.69-4.64 (dd, 1H, J= 4.32 Hz, J= 12.64 Hz), 4.60-4.54 (m, 1H), 3.92-3.86 (m, 1H), 2.79-2.75 (m, 1H), 1.75-1.67 (m, 1H), 1.10-1.09 (d, 3H, J= 7.08 Hz), 0.89-0.87 (d, 3H, J=7.08 Hz).Other spectroscopic data are in agreement with published data.[1]


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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]       %
----|-------|----|-------|----------|----------|--------|
   1  38.486 MM    0.2885   15.68239 9.05874e-1 10.35651
   2  39.611 MM    0.3099  135.74301    7.30098 89.64349
```



(S)-2,2-dimethyl-4-nitro-3-phenylbutanal **6c** (Table 3, entry 6) : From isobutyraldehyde **4c** (10 eq., 3.35 mmol, 0.30 mL) and according to *general procedure 2* (15 W, 0 bar, 27°C) to give 80% conversion after 2 h and to afford Michael adduct **6c** (56.7 mg, 76%). The enantiomeric excess was determined by chiral GC (Hydrodex-B-3P, iso 140°C, R_t: 47.39 (*R*), 48.44 (*S*)). $[\alpha]_D^{20}$= -6.7 (*c* 1.0 , ee= 77%, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.53 (s, 1H), 7.33-7.29 (m, 3H), 7.20-7.18 (m, 2H), 4.88-4.82 (m, 1H), 4.71-4.66 (m, 1H), 3.80 (m, 1H), 1.13 (s, 3H), 1.00 (s, 3H). Other spectroscopic data are in agreement with published data.[1]



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

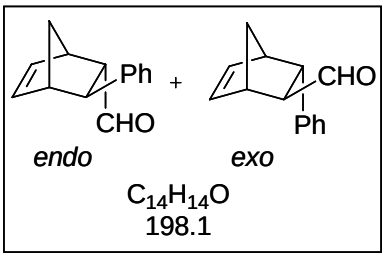
Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	47.392	MM	0.3715	34.74492	1.55857	11.34161
2	48.449	MM	0.3940	271.60416	11.48990	88.65839

III. Diels-Alder reaction

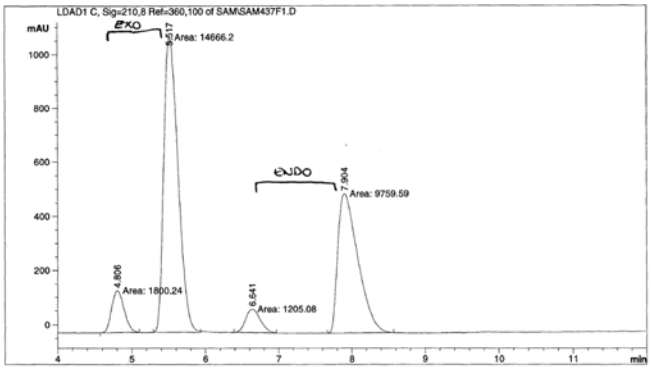
General procedure 3 under microwave irradiation. In a 2-5 mL vessel were introduced (5*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one hydrochloride **9** (0.05 eq. 0.095 mmol, 25 mg), MeOH/H_2O (95/5 v/v 2 mL), and (*E*)-cinnamaldehyde **8** (1 eq., 1.915 mmol, 0.25 mL). The solution was stirred 2 minutes under argon before addition of cyclopentadiene monomer **7** (3 eq., 5.745 mmol, 0.48 mL) and the vessel was sealed with a septum and placed into the microwave cavity. The microwave source was then turned on. Constant microwave irradiation as well as simultaneous air-cooling (5 bar) were used during the entire reaction time. The evolution of the reaction was monitored by TLC. After cooling to room temperature, the mixture was then quenched as described in literature procedure[2] diluting with Et_2O and washed successively with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered,

concentrated under reduced pressure. Hydrolysis of the product dimethyl acetal was performed by stirring the crude product mixture in TFA:H_2O:$CHCl_3$ (1:1:2, 12 mL) for 2 h at room temperature, followed by neutralization with sat. aq. $NaHCO_3$ and extraction with Et_2O. Purification of the Diels-Alder adduct was accomplished by silica gel chromatography using a mixture of cyclohexane and ethyl acetate.



(1*S*,2*S*,3*S*,4*R*)-3-phenylbicyclo[2.2.1]hex-5-ene-2-carboxaldehyde *endo*-**10** and (1*R*,2*S*,3*S*,4*S*)-3-phenylbicyclo[2.2.1]hex-5-ene-2-carboxaldehyde *exo*-**10** (Table 4, entry 3) : Prepared according to *general procedure 3* (50 W, 1 bar, 65 °C) to give 84% conversion after 1 h and to afford 1:1.2 *endo*-**10**/*exo*-**10** mixture as a pale yellow oil. Product ratio was determined by ^{1}H NMR on the crude material. The enantiomeric excess of each diatereoisomer was determined on the primary alcohols coming from the reduction of the aldehydes *endo*-**10**/*exo*-**10** mixture by SFC (chiralpak AD column, 2 mL/min, 200 bar, MeOH 10%-2-1-25%, 30°C, R_t: *exo* : 4.80 (*R*), 4.5.51 (*S*), and *endo* : 6.64 (*R*), 7.90 (*S*)).

Endo-10 : ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.61 (d, 1H, J=), 7.14-7.33 (m, 5H), 6.62-6.43 (m, 1H), 6.17-6.15 (m, 1H), 3.34 (br, 1H), 3.13 (br, 1H), 3.09 (m, 1H), 2.99 (m, 1H), 1.79-1.84 (m, 1H), 1.65-1.59 (m, 1H). Other spectroscopic data are in agreement with published data.[6]



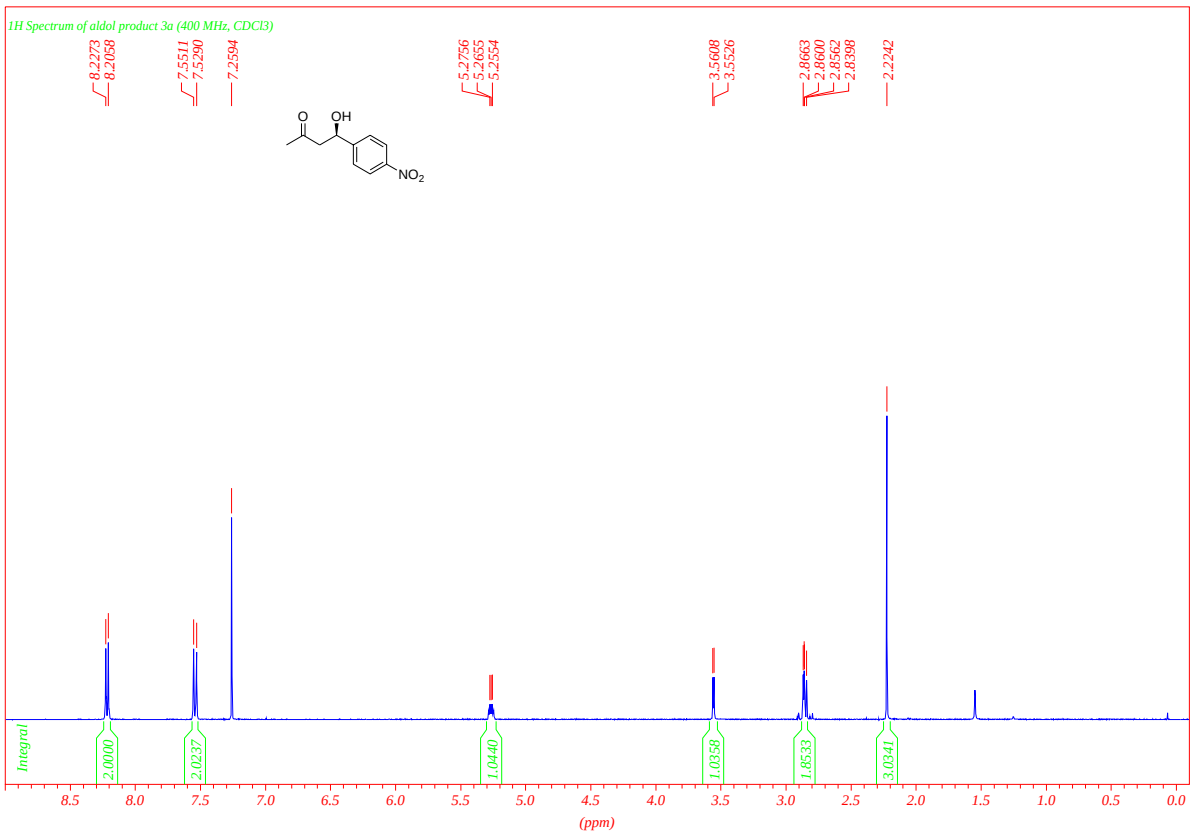
Area Percent Report

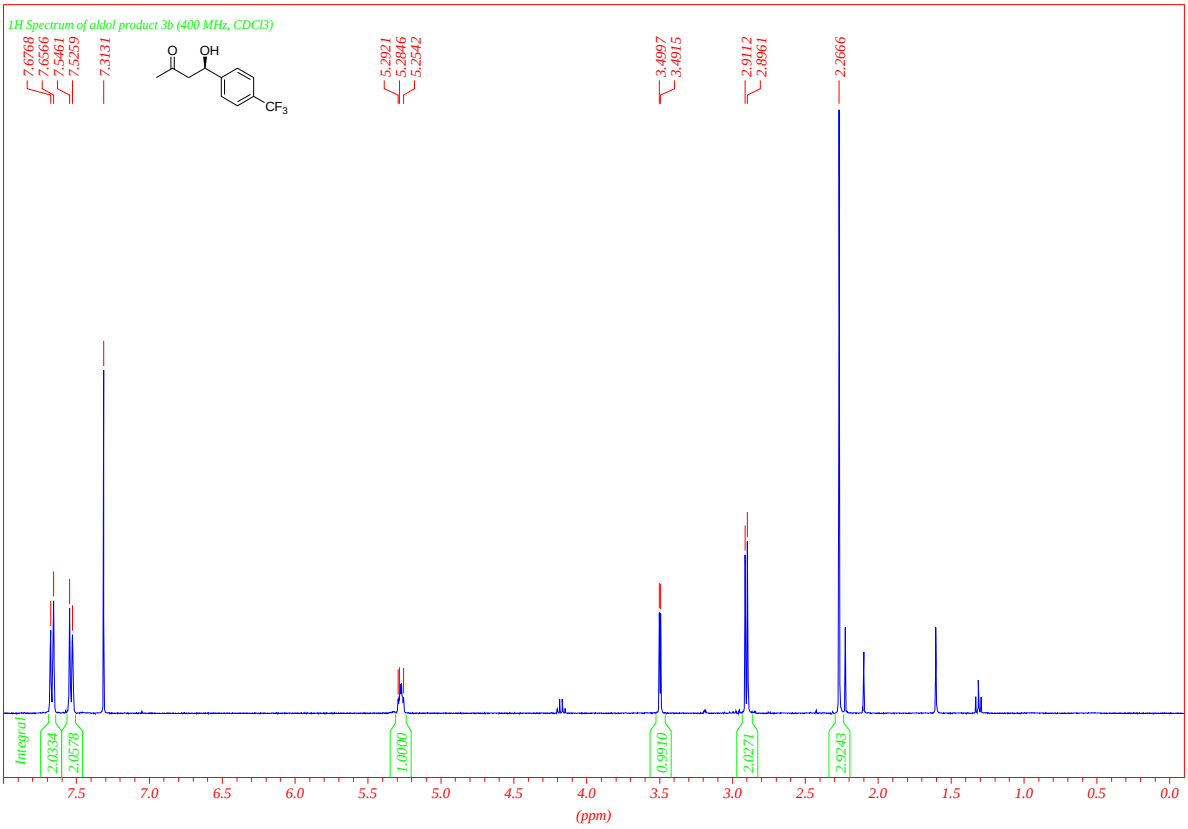
Sorted by Signal
Multiplier : 1.000000

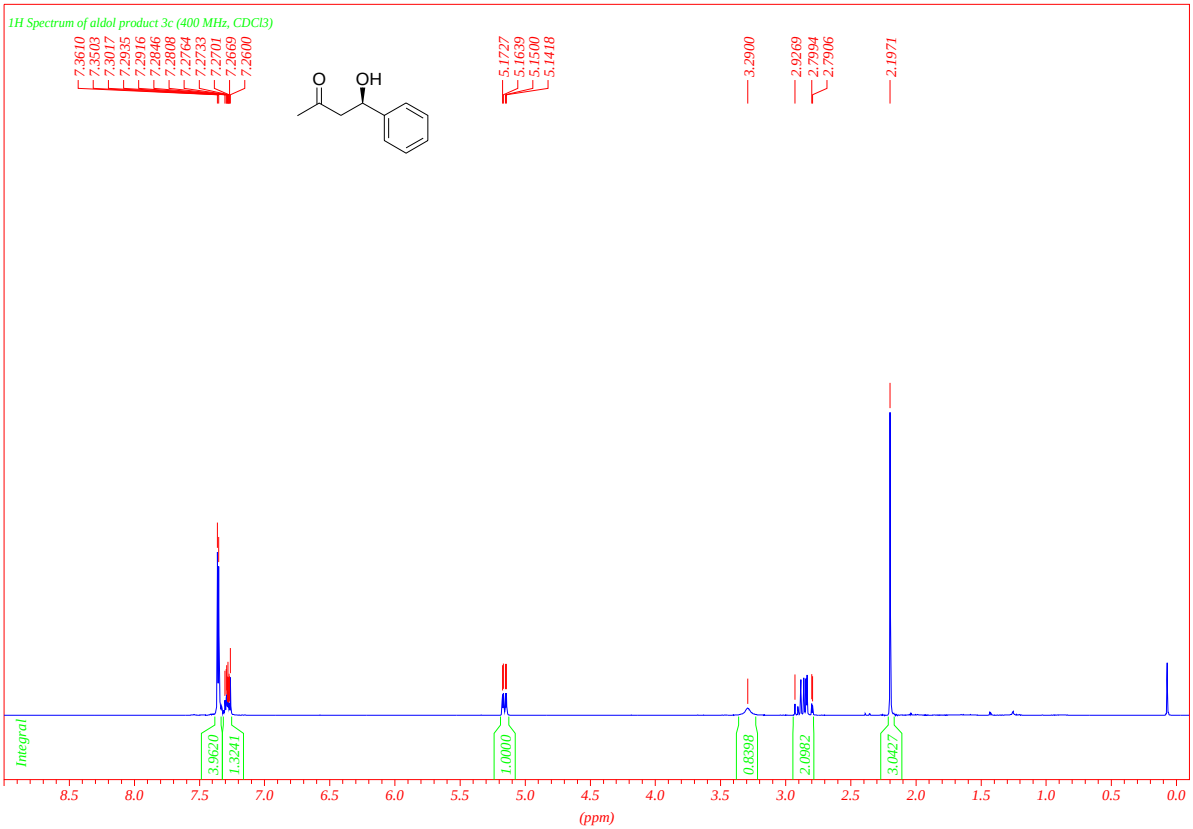
Signal 1: LDAD1 C, Sig=210,8 Ref=360,100

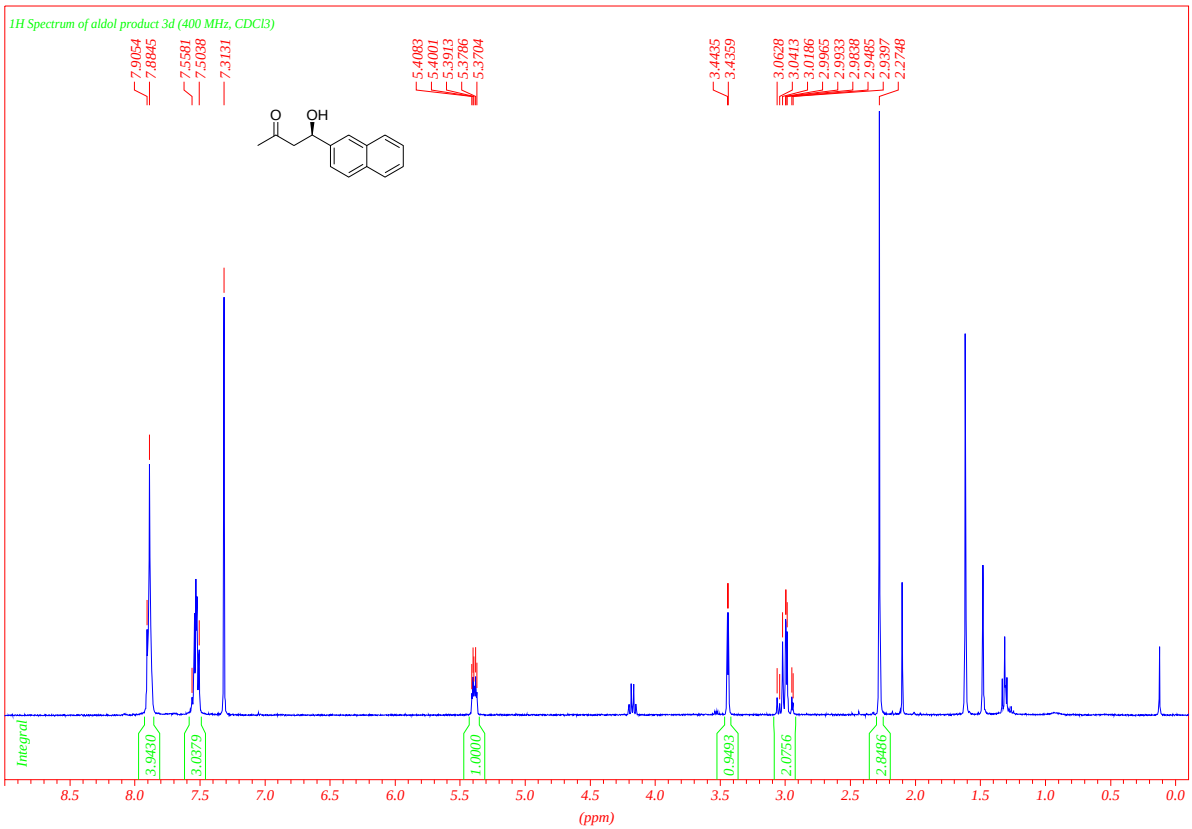
Peak #	RT [min]	Type	Width [min]	Area [mAU*sec]	Height [mAU]	Area %
1	4.806	MM	0.196	1800.23523	153.10909	6.5628
2	5.517	MM	0.224	14666.16406	1090.52527	53.4655
3	6.641	MM	0.236	1205.07861	84.94010	4.3931
4	7.904	MM	0.317	9759.58887	512.82208	35.5786

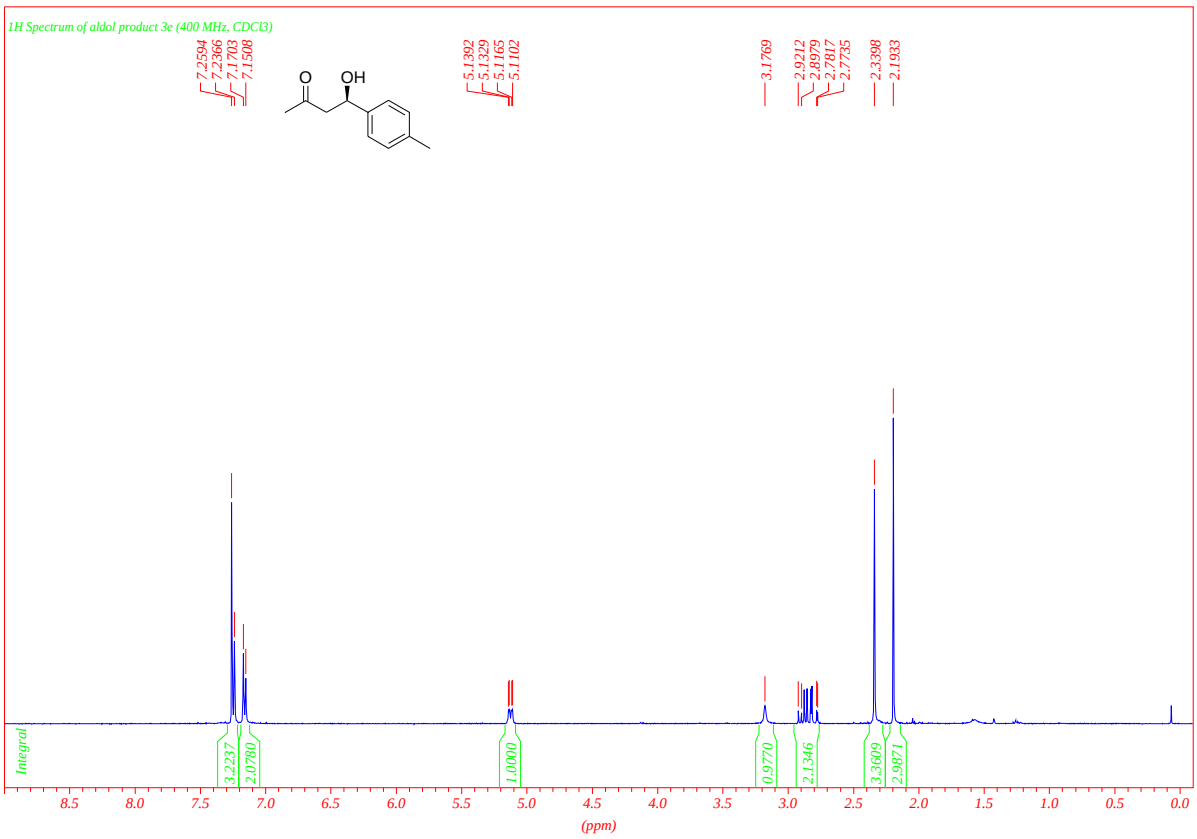
[6] Ishihara, K.; Kurihara, H.; Matsumoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1998**, *120*, 6920.

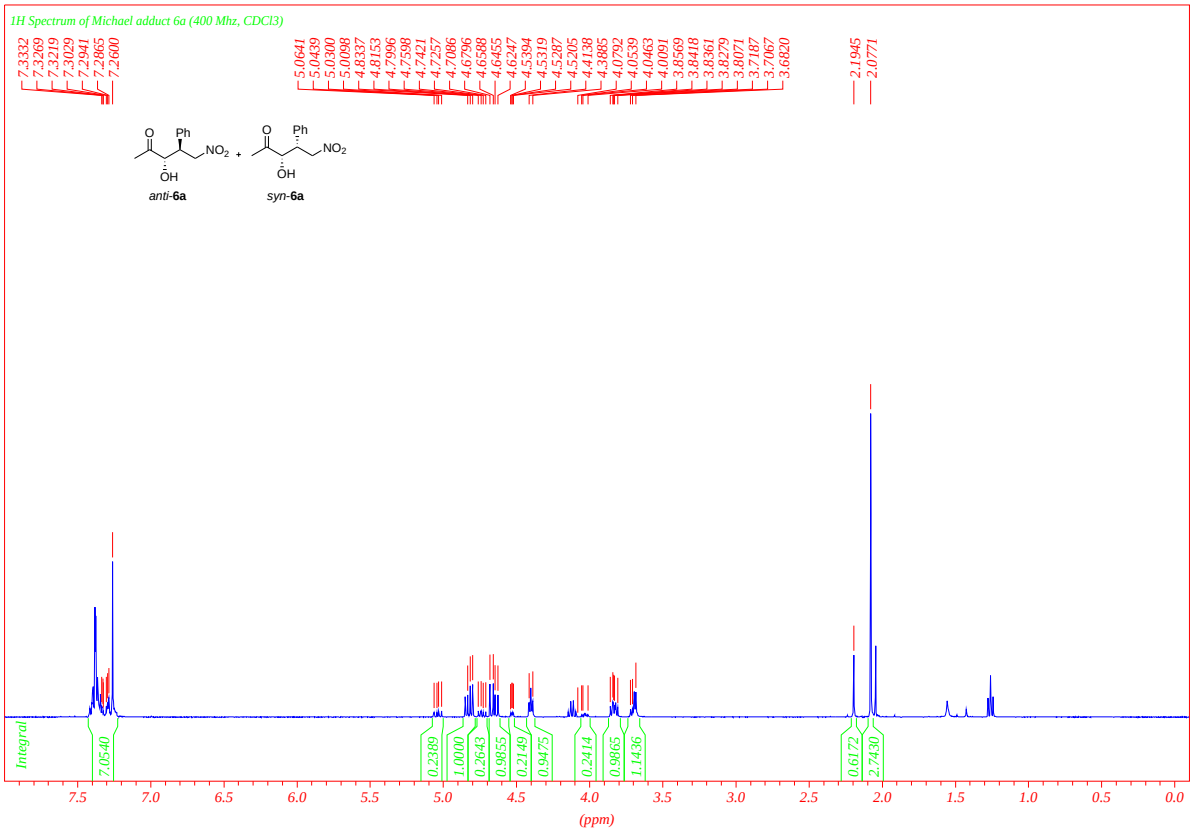

1H Spectrum of aldol product 3a (400 MHz, CDCl3)
8.2273
8.2058
7.5511
7.5290
7.2594
5.2756
5.2655
5.2554
3.5608
3.5526
2.8663
2.8600
2.8562
2.8398
2.2242
O
OH
NO2
Integral
2.0000
2.0237
1.0440
1.0358
1.8533
3.0341
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
(ppm)

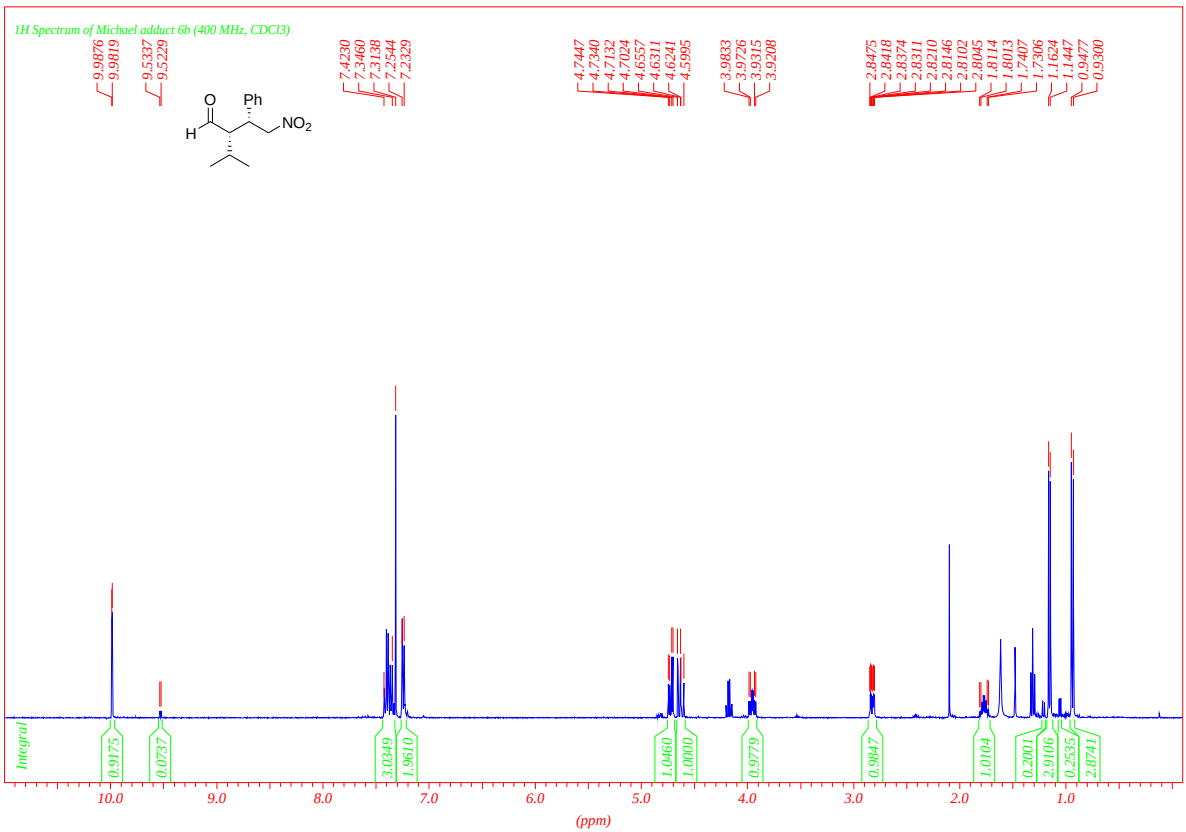

1H Spectrum of aldol product 3b (400 MHz, CDCl3)
7.6768
7.6566
7.5461
7.5259
7.3131
5.2921
5.2846
5.2542
3.4997
3.4915
2.9112
2.8961
2.2666
O
OH
CF3
Integral
2.0334
2.0578
1.0000
0.9910
2.0271
2.9243
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
(ppm)

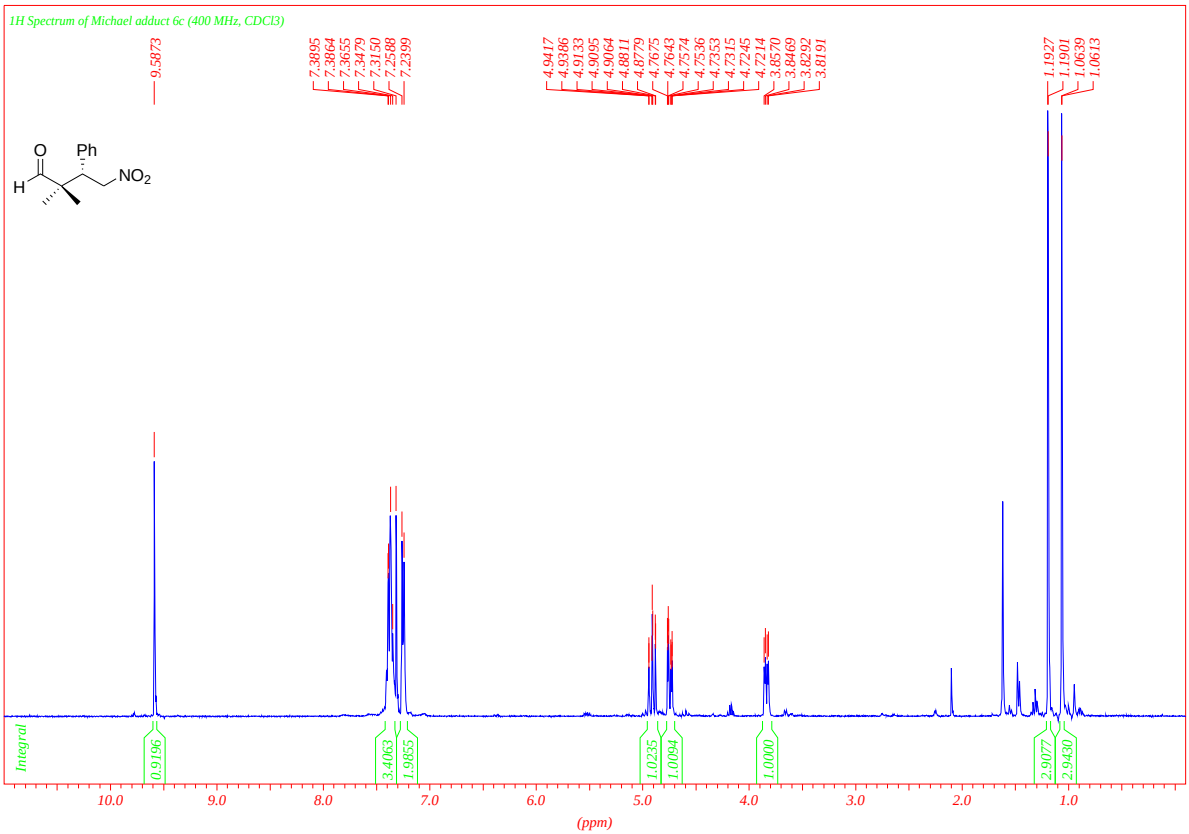

1H Spectrum of aldol product 3c (400 MHz, CDCl3)
7.3610
7.3503
7.3017
7.2935
7.2916
7.2846
7.2808
7.2764
7.2733
7.2701
7.2669
7.2600
5.1727
5.1639
5.1500
5.1418
3.2900
2.9269
2.7994
2.7906
2.1971
O
OH
Integral
3.9620
1.3241
1.0000
0.8398
2.0982
3.0427
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)

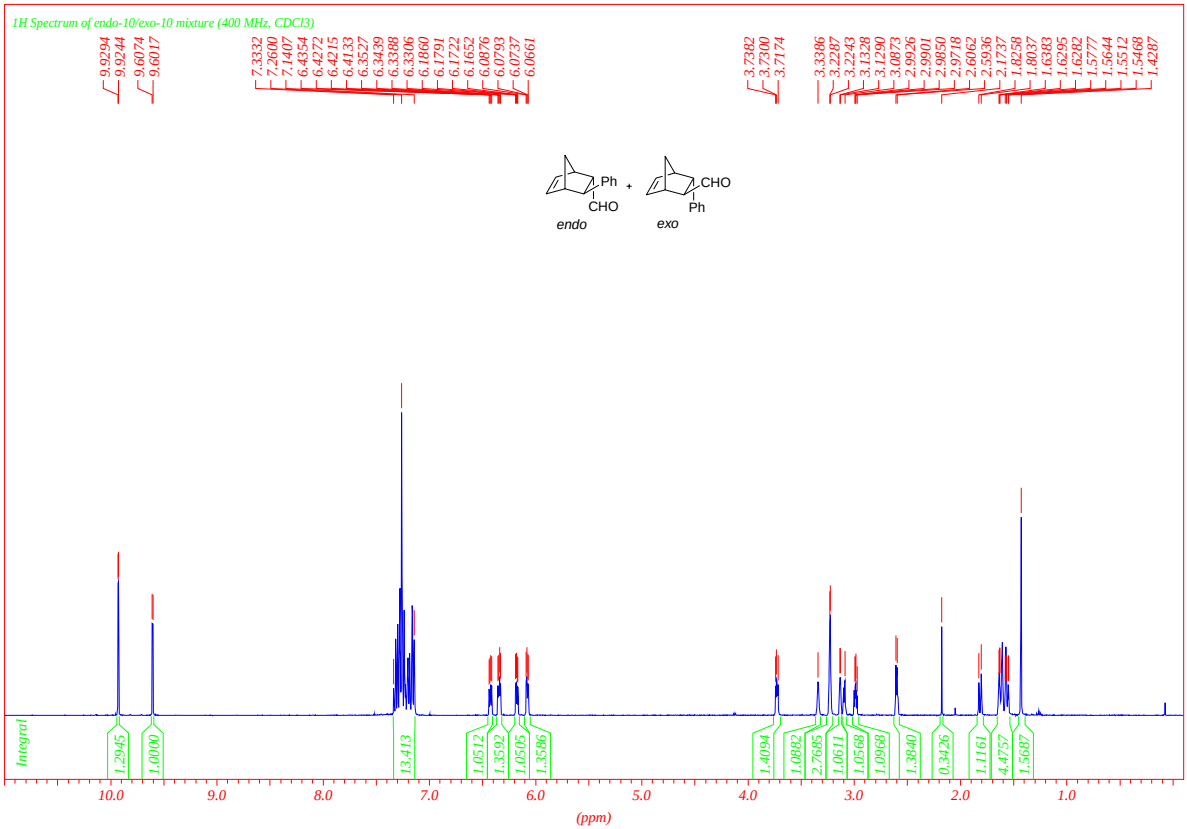

1H Spectrum of aldol product 3d (400 MHz, CDCl3)
7.9054
7.8845
7.5581
7.5038
7.3131
5.4083
5.4001
5.3913
5.3786
5.3704
3.4435
3.4359
3.0628
3.0413
3.0186
2.9965
2.9933
2.9838
2.9485
2.9397
2.2748
O
OH
Integral
3.9430
3.0379
1.0000
0.9493
2.0756
2.8486
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)


1H Spectrum of aldol product 3e (400 MHz, CDCl3)
7.2594
7.2366
7.1703
7.1508
5.1392
5.1329
5.1165
5.1102
3.1769
2.9212
2.8979
2.7817
2.7735
2.3398
2.1933
O
OH
Integral
3.2237
2.0780
1.0000
0.9770
2.1346
3.3609
2.9871
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)


1H Spectrum of Michael adduct 6a (400 Mhz, CDCl3)
7.3332
7.3269
7.3219
7.3029
7.2941
7.2865
7.2600
5.0641
5.0439
5.0300
5.0098
4.8337
4.8153
4.7996
4.7598
4.7421
4.7257
4.7086
4.6796
4.6588
4.6455
4.6247
4.5394
4.5319
4.5287
4.5205
4.4138
4.3885
4.0792
4.0539
4.0463
4.0091
3.8569
3.8418
3.8361
3.8279
3.8071
3.7187
3.7067
3.6820
2.1945
2.0771
Ph
NO2
OH
anti-6a
syn-6a
Integral
7.0540
0.2389
1.0000
0.2643
0.9855
0.2149
0.9475
0.2414
0.9865
1.1436
0.6172
2.7430
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)


1H Spectrum of Michael adduct 6b (400 MHz, CDCl3)
9.9876
9.9819
9.5337
9.5229
7.4230
7.3460
7.3138
7.2544
7.2329
4.7447
4.7340
4.7132
4.7024
4.6557
4.6311
4.6241
4.5995
3.9833
3.9726
3.9315
3.9208
2.8475
2.8418
2.8374
2.8311
2.8210
2.8146
2.8102
2.8045
1.8114
1.8013
1.7407
1.7306
1.1624
1.1447
0.9477
0.9300
O
Ph
H
NO2
Integral
0.9175
0.0737
3.0349
1.9610
1.0460
1.0000
0.9779
0.9847
1.0104
0.2001
2.9106
0.2535
2.8741
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)


1H Spectrum of Michael adduct 6c (400 MHz, CDCl3)
9.5873
7.3895
7.3864
7.3655
7.3479
7.3150
7.2588
7.2399
4.9417
4.9386
4.9133
4.9095
4.9064
4.8811
4.8779
4.7675
4.7643
4.7574
4.7536
4.7353
4.7315
4.7245
4.7214
3.8570
3.8469
3.8292
3.8191
1.1927
1.1901
1.0639
1.0613
O
Ph
H
NO2
Integral
0.9196
3.4063
1.9855
1.0235
1.0094
1.0000
2.9077
2.9430
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)

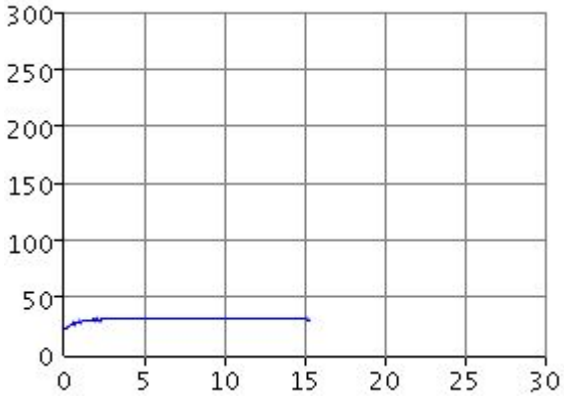

1H Spectrum of endo-10/exo-10 mixture (400 MHz, CDCl3)
9.9294
9.9244
9.6074
9.6017
7.3332
7.2600
7.1407
6.4354
6.4272
6.4215
6.4133
6.3527
6.3439
6.3388
6.3306
6.1860
6.1791
6.1722
6.1652
6.0876
6.0793
6.0737
6.0661
3.7382
3.7300
3.7174
3.3386
3.2287
3.2243
3.1328
3.1290
3.0873
2.9926
2.9901
2.9850
2.9718
2.6062
2.5936
2.1737
1.8258
1.8037
1.6383
1.6295
1.6282
1.5777
1.5644
1.5512
1.5468
1.4287
Ph
CHO
endo
CHO
Ph
exo
Integral
1.2945
1.0000
13.413
1.0512
1.3592
1.0505
1.3586
1.4094
1.0882
2.7665
1.0611
1.0568
1.0968
1.3840
0.3426
1.1161
4.4757
1.5687
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)

Temperature, pressure and microwave power profiles for the reaction mixture corresponding to Table 1, entry 10 (constant microwave power of 15 W during 15 min, using simultaneous cooling).

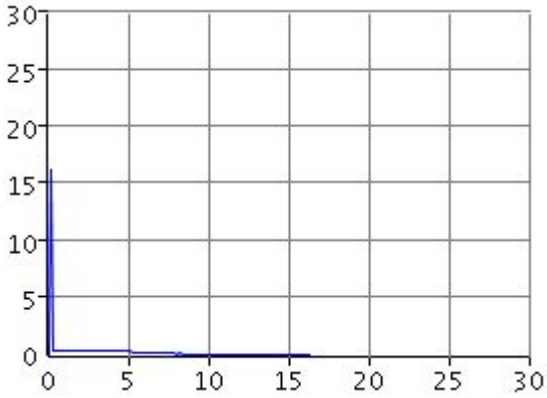
Status: OK
Absorption Level: Very High
Vial: 2.0-5.0 ml
Pre-stirring: 0
Initial power: 0

Step	Time	°C	bar	W	FHT	Cooling
1	00:15:00	Off	Off	15	On	On

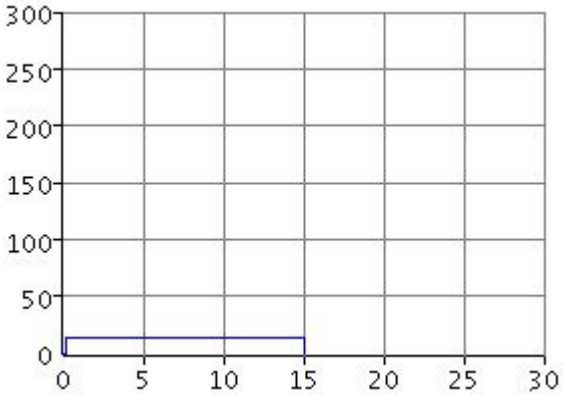
Temperature (°C)



Pressure (bar)



Power (W)

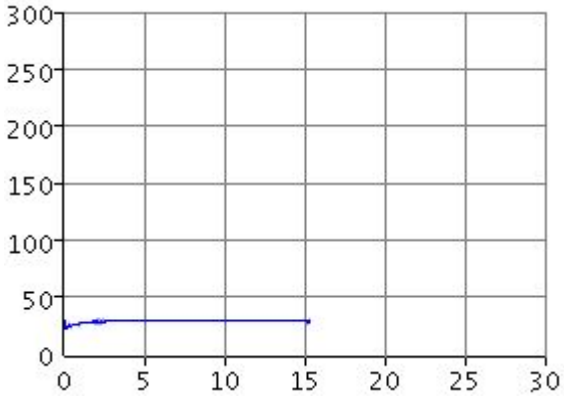


Temperature, pressure and microwave power profiles for the reaction mixture corresponding to Table 2, entry 1(constant microwave power of 15 W during 15 min, using simultaneous cooling).

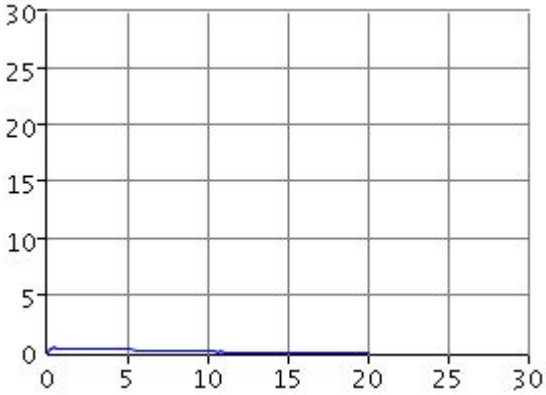
Status: OK
Absorption Level: Very High
Vial: 2.0-5.0 ml
Pre-stirring: 0
Initial power: 0

Step	Time	°C	bar	W	FHT	Cooling
1	00:15:00	Off	Off	15	On	On

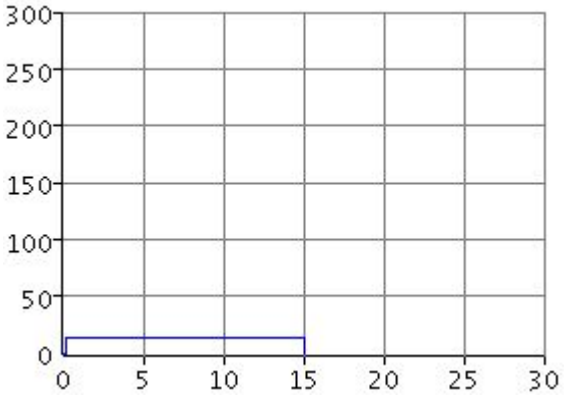
Temperature (°C)



Pressure (bar)



Power (W)

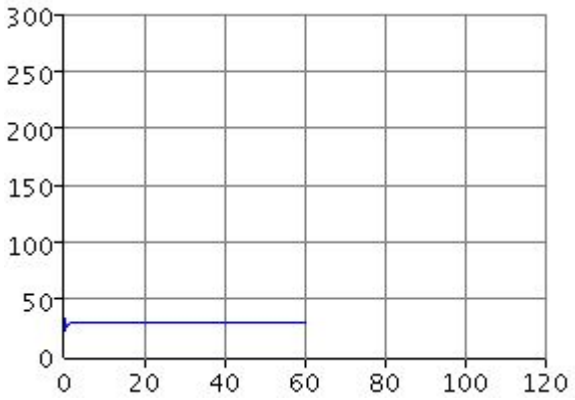


Temperature, pressure and microwave power profiles for the reaction mixture corresponding to Table 2, entry 3 (constant microwave power of 15 W during 1 h, using simultaneous cooling).

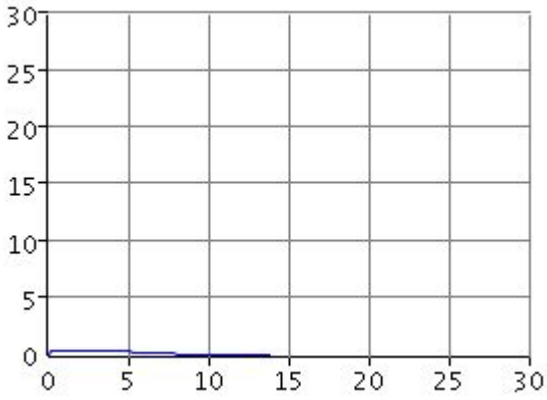
Status: OK
Absorption Level: Very High
Vial: 2.0-5.0 ml
Pre-stirring: 0
Initial power: 0

Step	Time	°C	bar	W	FHT	Cooling
1	01:00:00	Off	Off	15	On	On

Temperature (°C)



Pressure (bar)



Power (W)