Supporting Information

Continuous Synthesis of Homoallylic Ketones via Ketal–Claisen Rearrangement using Solid-Acid Catalysts

Kwihwan Kobayashi,*[a] Chie Negoro,[a] Junko Takaishi,[a] Koichiro Masuda,*[a] and Shū Kobayashi*[a,b]

a. Interdisciplinary Research Center for Catalytic Chemistry, National Institute of Advanced Industrial Science and Technology Central 5, Higashi 1-1-1, Tsukuba, Ibaraki 305-8565, Japan. E-mail: kobayashi-kwihwan@aist.go.jp, n-koumura@aist.go.jp, shu_kobayashi@chem.s.u-tokyo.ac.jp

b. Department of Chemistry, School of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 111-0033, Japan.

Contents

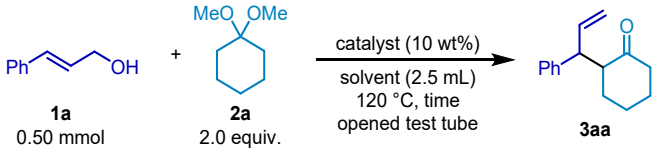
1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance NEO 400 MHz NMR spectrometer in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS) served as an internal standard ($\delta = 0$) for ^{1}H NMR, and $CDCl_3$ served as an internal standard ($\delta = 77.16$) for ^{13}C NMR. Gas chromatography was measured on a Shimadzu GC-2014 spectrometer with N_2 gas as a career, using Agilent Technologies DB-1 column (Length: 30 m, I.D.: 0.250 mm, Film: 0.25 μm). A dual plunger pump (UI-22 series) was purchased from FLOM, Inc., and flow reactor (LCR-1000), column (CLM-1010) and fraction collector (DC-1000) were purchased from EYELA. Other chemicals and solvents were purchased from Tokyo Chemical Industry Co., Ltd, FUJIFILM Wako pure chemicals, Kishida chemical Co., Ltd., and Sigma-Aldrich. IR spectra were recorded by Shimadzu IRSpirit. ESI high-resolution mass spectra (HRMS) were measured by JEOL JMS-700T MStation. JAI LaboAce LC-5060 Plus II was used for a recycling preparative GPC. Particle size distribution was measured by MICROTRACBELL MT3000II. SEM was measured by JEOL JSM-

IT800.

2. Procedure and results for the catalyst screening under batch conditions (Table 1)

A reaction mixture of a cinnamyl alcohol (**1a**; 0.50 mmol, 67.1 mg), cyclohexanone dimethyl ketal (**2a**; 1.0 mmol, 144.2 mg), and catalyst (10 wt%, 6.7 mg) in solvent (2.5 mL) was heated at 120 °C and stirred in an opened test tube. The reaction mixture was cooled to room temperature and filtered through a filter with ethyl acetate. Obtained filtrates were concentrated in vacuo and analyzed by ^{1}H NMR to determine yield and diastereomeric ratio.

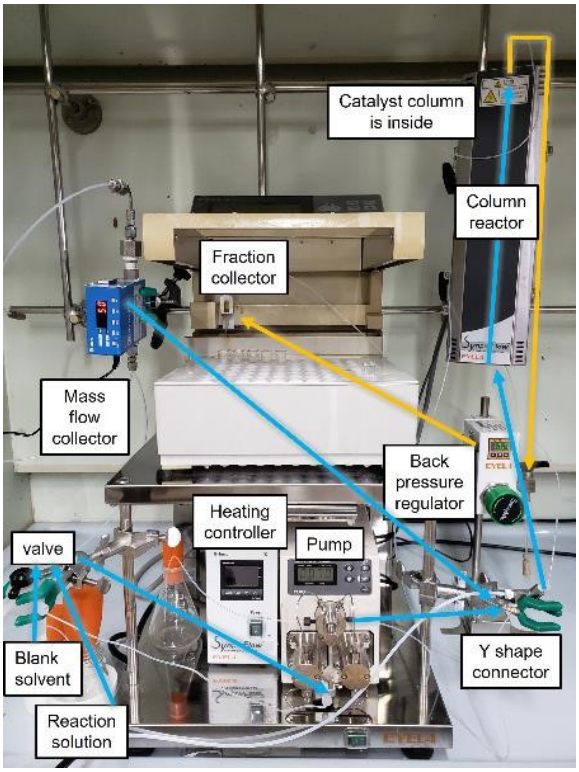


entry	catalyst	solvent	time	yield [d.r.]
1	zeolite Hβ	toluene	4 h	3%
2	CO_2H-SiO_2	toluene	4 h	0%
3	8% PO_4-ZrO_2	toluene	4 h	2%
4	10% WO_3-ZrO_2	toluene	4 h	8%
5	JRC-TIO10	toluene	4 h	0%
6	Amberlyst 15	toluene	4 h	23% [4.0/1]
7	SO_3H-SiO_2	toluene	4 h	46% [5.6/1]
8	SO_3H-ZrO_2	toluene	4 h	58% [7.7/1
9	SO_3H-ZrO_2	toluene	21 h	71% [7.1/1]
10	SO_3H-ZrO_2	AcO^nBu	21 h	88% [6.7/1]
11	SO_3H-ZrO_2	CPME	21 h	77% [4/1]
12 [a]	SO_3H-ZrO_2	CPME	21 h	40% [4.1/1]
13[b]	SO_3H-ZrO_2	CPME	21 h	49% [4.1/1]

[a] The reaction was conducted using sealed test tube. [b] The reaction was carried out using 10 mmol of **1a**, 20 mmol of **2a**, 10wt% of SO_3H-ZrO_2, and 50 mL of CPME.

Zeolite Hβ (HSZ-900, Tosoh corporation), CO_2H-SiO_2 (CHROMATOREX COOH MB100-75/200, FUJI SILYSIA CHEMICAL LTD.), Amberlyst 15 (hydrogen form, Merck), SO_3H-SiO_2 (CHROMATOREX SO_3H MB100-75/200, FUJI SILYSIA CHEMICAL LTD.), and SO_3H-ZrO_2 (Sulfated Zirconia, FUJIFILM Wako Chemicals), 8% PO_4-ZrO_2 (Catalysis Society of Japan), 10% WO_3-ZrO_2 (Catalysis Society of Japan), and JRC-TIO10 (Catalysis Society of Japan).

3. Experimental setup for the flow reaction



Pump: UI-22 110P, EYELA

Flow reactor (heating controller and column reactor): LCR-1000, EYELA

Back pressure regulator: BPR-1000B, EYELA

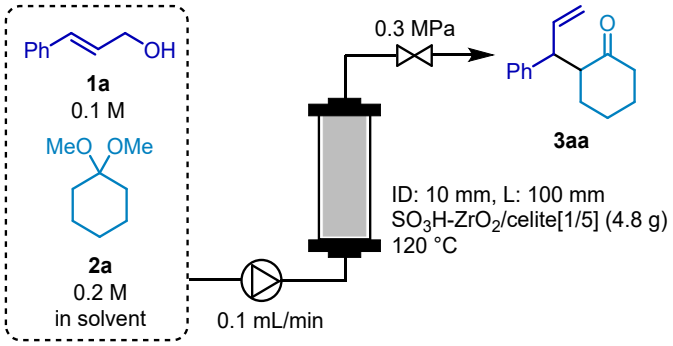
Mass Flow Controller: 8500MC, KOFLOC

Fraction collector: DC-1000, EYELA

The volume of total tubes connecting apparatuses was 2.81 mL (ID: 1 mm tube 250 cm, ID: 2 mm tube 10 cm).

4. Procedure and results for the flow ketal-Claisen rearrangement without N_2 gas (Table 2)

SO_3H-ZrO_2 was pre-mixed with celite (0.8/4.0g) and then packed into a column (I.D. φ10×100 mm, CLM-1010, EYELA). The catalyst column was set onto the reactor, and solvent was flowed at designed flow rate (0.1 mL/min, pump: UI-22 110P, EYELA) for 30 min to remove residual air inside. The catalyst column was heated at 120 °C (heating controller and column reactor: LCR-1000, EYELA) with solvent flow under 0.3 MPa of back pressure (BPR-1000B, EYELA), after stabilization the reaction was started by changing into feed solution of cinnamyl alcohol (**1a**; 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in solvent. The resulted solution was fractionated for every 1 hours (6 mL) (Fraction collector: DC-1000, EYELA), and selected fractions were analyzed ^{1}H NMR to determine yields.



entry	solvent	yield of 1a	yield of 3aa	main product
1	toluene	20–30%	3–4%	Ph, Me **4** 35–40% yield
2	AcO^{n}Bu	20–30%	3–4%	Ph, O^{n}Bu **5** 36–38% yield
3	CPME	20–30%	3–4%	Ph, OMe **6** 33–37% yield

5. Procedure for the amine-treatment of SO_3H-ZrO_2

SO_3H-ZrO_2 (900 mg) was added to the amine (12 mL) at room temperature. After stirring for 3 hours, the suspension was filtered through a filter with ethyl acetate. Filtrated solid catalyst was dried in vacuo, amine-treated SO_3H-ZrO_2 was obtained.

6. Results of elemental analysis

Et_3N-treated SO_3H-ZrO_2

C	H	N
1.1%	0.3%	0.3%

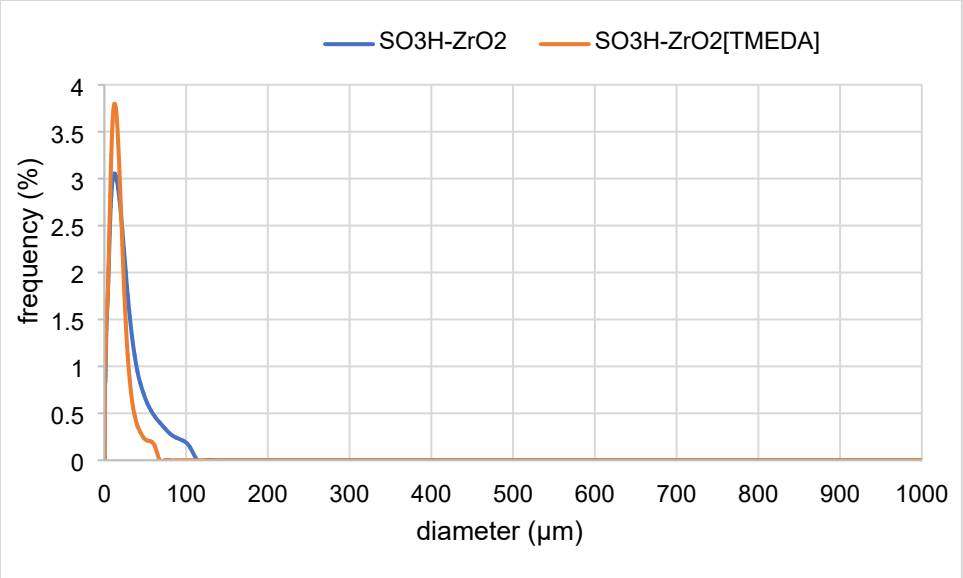
The amount of Et_3N on the SO_3H-ZrO_2 was 0.178 mmol/g.

TMEDA-treated SO_3H-ZrO_2

C	H	N
1.1%	0.3%	0.5%

The amount of TMEDA on the SO_3H-ZrO_2 was 0.178 mmol/g.

7. Results of particle size distribution

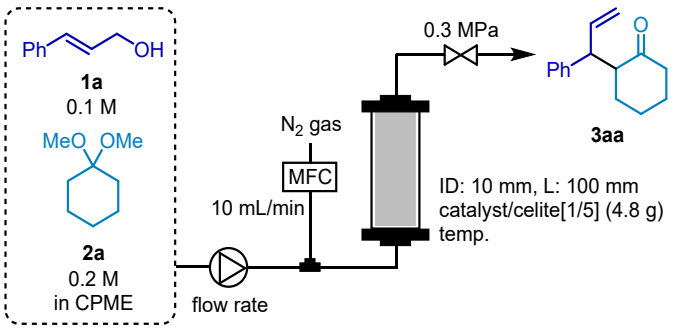


	MV (um)	MN (um)	MA (um)	CS
SO_3H-ZrO_2	12.13	0.41	2.34	2.56
SO_3H-ZrO_2[TMEDA]	9.42	0.63	2.73	2.20

MV: Mean volume diameter, MN: mean number diameter, MA: mean area diameter, CS: specific surface area.

8. Procedure and results for the catalyst screening under flow conditions with N_2 gas (Table 3)

A catalyst was pre-mixed with celite (0.8/4.0g) and then packed into a column (I.D. φ10×100 mm, CLM-1010, EYELA). The catalyst column was set onto the reactor, and CPME was flowed at designed flow rate (0.1 or 0.05 mL/min, pump: UI-22 110P, EYELA) for 30 min to remove residual air inside. N_2 gas was flowed with CPME at 10 mL/min (Mass Flow Controller: 8500MC, KOFLOC). The catalyst column was heated at 120 or 140 °C (heating controller and column reactor: LCR-1000, EYELA) with CPME and N_2 gas flow under 0.3 MPa of back pressure (BPR-1000B, EYELA), after stabilization the reaction was started by changing into feed solution of cinnamyl alcohol (**1a**; 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in solvent. The resulted solution was fractionated for every 1 hours (3 or 6 mL) (Fraction collector: DC-1000, EYELA), and selected fractions were analyzed ^{1}H NMR to determine yields.



entry	catalyst	temp. (°C)	flow rate (mL/min)	yield of 3aa (%)

1	SO_3H-ZrO_2	120	0.1	28–30
2	SO_3H-ZrO_2[Et_3N]	120	0.1	28–30
3	SO_3H-ZrO_2[Et_3N]	140	0.1	51–53
4	SO_3H-ZrO_2[Et_3N]	140	0.05	70–75
5	SO_3H-ZrO_2[DIPEA]	140	0.05	57–58
6	SO_3H-ZrO_2[Et_2NH]	140	0.05	74–75
7	SO_3H-ZrO_2[TMEDA]	140	0.05	77–78
8	SO_3H-ZrO_2[TEEDA]	140	0.05	56–57
9	SO_3H-ZrO_2[DETA]	140	0.05	0–1
10	SO_3H-ZrO_2[pyridine]	140	0.05	60–62
11	SO_3H-ZrO_2[hexylamine]	140	0.05	55–74
12	SO_3H-ZrO_2[octylamine]	140	0.05	70–74

DIPEA: *N*,*N*-Diisopropylethylamine, TMEDA: *N*,*N*,*N*',*N*'-Tetramethylethylenediamine, TEEDA: *N*,*N*,*N*',*N*'-Tetraethylethylenediamine, DETA: Diethylenetriamine,

9. Procedure and calculation for the void volume of the catalyst column.

A TMEDA-treated SO_3H-ZrO_2 (1.0 g) was pre-mixed with celite (3.8 g) and then packed into a column (I.D. φ10×100 mm, EYELA, CLM-1010). The catalyst column was sealed with plugs and weighted (237.06 g). Sealed plugs were removed, and the catalyst column was set onto a flow reactor (heating controller and column reactor: LCR-100, EYELA). The catalyst column was filled with CPME by a pump (UI-22 110P, EYELA) at 1.0 mL/min for 1 hours. After solvent filling, the catalyst column was sealed with plugs again and weighted (242.06 g). Therefore, the void volume of the catalyst column was calculated as follows with the density of CPME at 20 °C (0.86 g/mL); (242.06 – 237.06)/0.86 = 5.81 mL. If only CPME at 0.05 mL/min is used, the residence time is 5.81/0.05 = 116.2 min.

10. General Procedure for the substrate scope (Table 4)

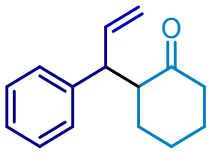
TMEDA-treated SO_3H-ZrO_2 was pre-mixed with celite (1.0/3.8g) and then packed into a column (I.D. φ10×100 mm, CLM-1010, EYELA). The catalyst column was set onto the reactor, and CPME was flowed at designed flow rate (0.05 mL/min, pump: UI-22 110P, EYELA) for 30 min to remove residual air inside. N_2 gas was flowed with CPME at 10 mL/min (Mass Flow Controller: 8500MC, KOFLOC). The catalyst column was heated at 140 °C (heating controller and column reactor: LCR-1000, EYELA) with CPME and N_2 gas flow under 0.3 MPa of back pressure (BPR-1000B, EYELA), after stabilization the reaction was started by changing into feed solution of allylic alcohol (**1**; 0.1 M) and dimethyl ketal (**2**, 0.2 M) in solvent. The resulted solution was fractionated for every 1 hours (3 mL) (Fraction collector: DC-1000, EYELA), and selected fractions were analyzed ^{1}H NMR to determine yields. Fractions were collected for the described time. After evaporation of solvent, the product was isolated over silica-gel column chromatography to obtain desired homoallylic ketones. If silica-gel column chromatography was not able to completely purify, the yield of product was determined by ^{1}H NMR analysis and the product was purified by recycling preparative GPC (chloroform) using part of reaction mixture.

11. Long-term operation for the flow ketal-Claisen rearrangement (Figure 2)

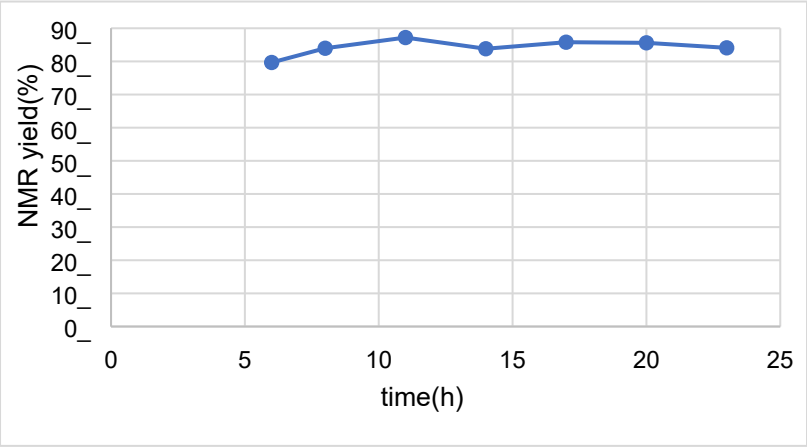
TMEDA-treated SO_3H-ZrO_2 was pre-mixed with celite (0.8/4.0g) and then packed into a column (I.D. φ10×100 mm, CLM-1010, EYELA). The catalyst column was set onto the reactor, and CPME was flowed at designed flow rate (0.05 mL/min, pump: UI-22 110P, EYELA) for 30 min to remove residual air inside. N_2 gas was flowed with CPME at 10 mL/min (Mass Flow Controller: 8500MC, KOFLOC). The catalyst column was heated at 140 °C (heating controller and column reactor: LCR-1000, EYELA) with CPME and N_2 gas flow under 0.3 MPa of back pressure (BPR-1000B, EYELA), after stabilization the reaction was started by changing into feed solution of allylic alcohol (**1**; 0.1 M) and dimethyl ketal (**2**, 0.2 M) in solvent. The resulted solution was fractionated for every 1 hours (3 mL) (Fraction collector: DC-1000, EYELA), and selected fractions were analyzed ^{1}H NMR to determine yields. Fractions were collected from 7 to 156 hours. After evaporation of solvent, the product was isolated over column chromatography to obtain **3aa** (72% yield, 6.5 g). The space-time yield was 0.135 kg/L day.

12. Spectroscopic data of nitriles and the results of continuous-flow reactions

2-(1-Phenylallyl)cyclohexan-1-one (3aa)



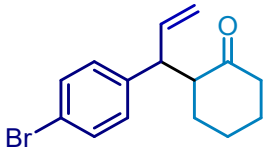
According to General Procedure, a solution of cinnamyl alcohol (**1a**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 6 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3aa** was obtained in 84% yield (d.r.: 4.5/1, 972.1 mg, 4.5 mmol) as a pale yellow oil.



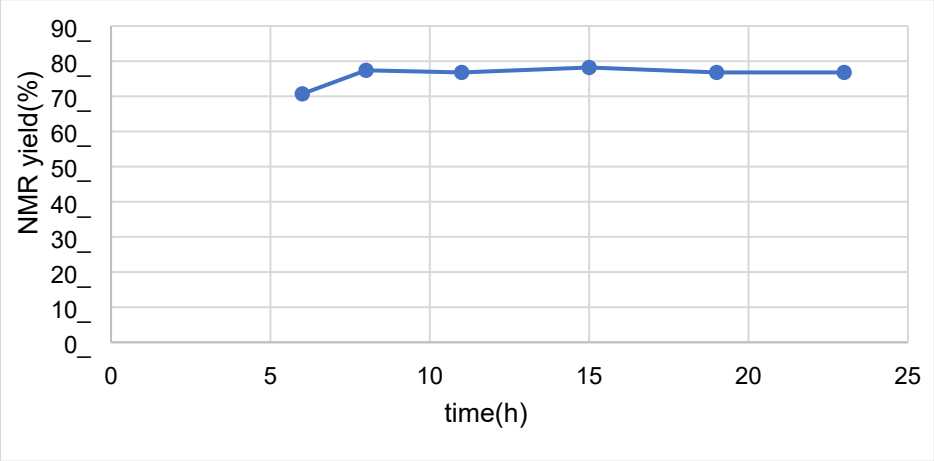
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (m, 2H), 7.23–7.16 (m, 3H), 6.04 (ddd, *J* = 17.2, 10.0, 7.2 Hz, 0.84H), 5.88 (ddd, *J* = 17.2, 10.4, 9.2 Hz, 0.15H), 5.11–5.07 (m, 0.13H), 5.03–4.95 (m, 1.72H), 3.81 (t, *J* = 8.8 Hz, 0.15H), 3.72 (t, *J* = 8.8 Hz, 0.87H), 2.82–2.75 (m, 1H), 2.45–232 (m, 1.83H), 2.28–2.15 (m, 0.27H), 1.97–1.90 (m, 1.22 H), 1.84–1.53 (m, 3.87H), 1.39–1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.6, 211.6, 143.3, 141.7, 140.1, 139.2, 128.6, 128.5, 128.4, 127.9, 126.5, 126.2, 116.2, 114.9, 55.4, 55.3, 49.3, 49.0, 42.3, 42.1, 31.9, 31.6, 28.5, 28.4, 24.4,

23.8. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that of reference 1.

2-(1-(4-Bromophenyl)allyl)cyclohexan-1-one (3ba)

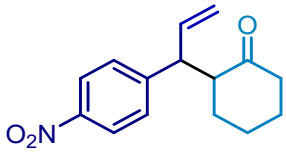


According to General Procedure, a solution of 4-bromocinnamyl alcohol (**1b**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 6 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3ba** was obtained in 70% yield (d.r.: 3.3/1, 1.1 g, 3.8 mmol) as a pale yellow oil.



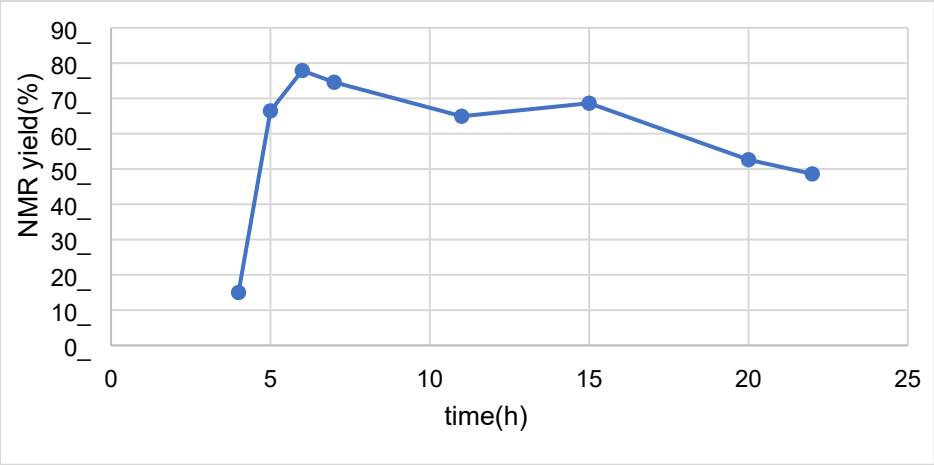
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.38 (m, 2H), 7.10–7.05 (m, 2H), 6.02 (ddd, J = 17.2, 10.4, 7.2 Hz, 0.89H), 5.83 (ddd, J = 17.2, 10.4, 9.2 Hz, 0.11H), 5.09–5.07 (m, 0.17H), 5.06–4.94 (m, 1.86H), 3.71 (t, J = 8.8 Hz, 1H), 2.77–2.71 (m, 1H), 2.43–2.31 (m, 2H), 1.99–1.83 (m, 1H), 1.82–1.54 (m, 4H), 1.35–1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.0, 211.4, 142.5, 140.8, 139.6, 138.8, 131.6, 131.5, 130.3, 129.6, 120.3, 120.0, 116.6, 115.4, 55.1(2C), 49.0, 48.2, 42.5, 42.2, 32.0, 31.9, 28.4(2C), 24.6, 24.1. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that of reference 2.

2-(1-(4-Nitrophenyl)allyl)cyclohexan-1-one (3ca)



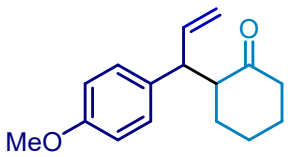
According to General Procedure, a solution of 4-nitrocinnamyl alcohol (**1c**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 5 h to 20 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3ca** was obtained in 45% yield (d.r.: 4.7/1, 560.1 mg, 2.2 mmol) as a pale

yellow oil.

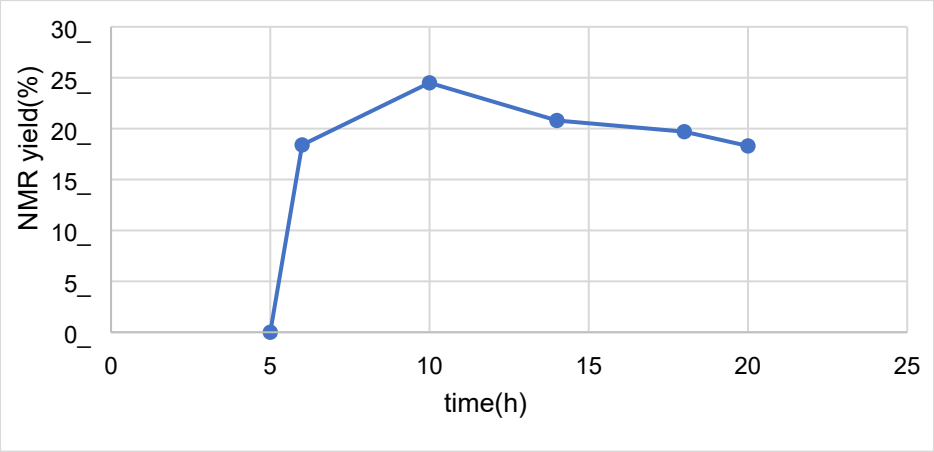


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17–8.12 (m, 2H), 7.39–7.37 (m, 2H), 6.08 (ddd, *J* = 17.2, 10.4, 7.2 Hz, 0.83H), 5.83 (ddd, *J* = 17.2, 10.4, 9.2 Hz, 0.17H), 5.14–5.09 (m, 1.18H), 5.05–5.00 (m, 0.85H), 3.89 (t, *J* = 7.8 Hz, 0.85H), 3.82 (t, *J* = 9.2 Hz, 0.17H), 2.86–2.80 (m, 1H), 2.45–2.33 (m, 2H), 2.05–1.99 (m, 1H), 1.84–1.60 (m, 4H), 1.35–1.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1, 211.0, 151.5, 149.7, 146.7, 146.4, 138.5, 137.9, 129.5, 128.6, 123.7, 123.7, 117.5, 116.6, 54.9(2C), 49.8, 48.6, 42.7, 42.4, 32.4, 32.1, 28.4, 28.2, 25.0, 24.5.; IR (ATR) cm^{-1}: 3079, 2937, 2862, 1708, 1638, 1603, 1596, 1559, 1514, 1464, 1463, 1448, 1431, 1414, 1342, 1257, 1243, 1206, 1181, 1157, 1125, 1109, 1066, 1014; ESI-HRMS m/z: 259.1208 ([M]+); Calcd. for $C_{15}H_{17}NO_3$: 259.1208.

2-(1-(4-Methoxyphenyl)allyl)cyclohexan-1-one (**3da**)

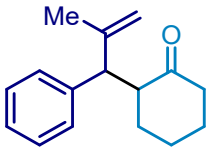


According to General Procedure, a solution of 4-methoxycinnamyl alcohol (**1d**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 6 h to 20 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3da** was obtained in 15% yield (d.r.: 2.3/1, 164.9 mg, 0.68 mmol) as a pale yellow oil. Further purification was performed by recycling preparative GPC (column: JAIGEL-2HR Plus, chloroform), and purified **3da** (single diastereomer) was obtained.

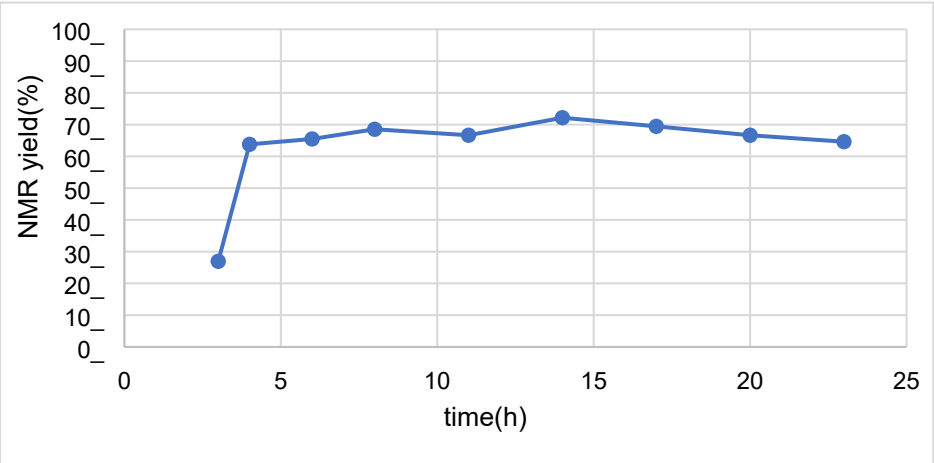


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 6.02 (ddd, J = 16.8, 10.4, 7.6 Hz, 1H), 5.01–4.93 (m, 2H), 3.78 (s, 3H), 3.68 (t, J = 1H), 2.76–2.70 (m, 1H), 2.45–2.31 (m, 2H), 1.96–1.89 (m, 1H), 1.82–1.66 (m, 3H), 1.62–1.53 (m, 1H), 1.39–1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.8, 158.2, 140.4, 133.7, 129.4, 114.6, 114.0, 55.5. 55.2, 48.1, 42.0, 31.8, 28.5, 23.7. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that of reference 2.

2-(2-Methyl-1-phenylallyl)cyclohexan-1-one (3ea)



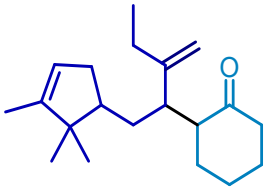
According to General Procedure, a solution of 2-methyl-3-phenyl-2-propen-1-ol (**1e**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 4 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3ea** was obtained in 58% yield (d.r.: 4.6/1, 794.6 mg, 3.5 mmol) as a pale yellow oil.



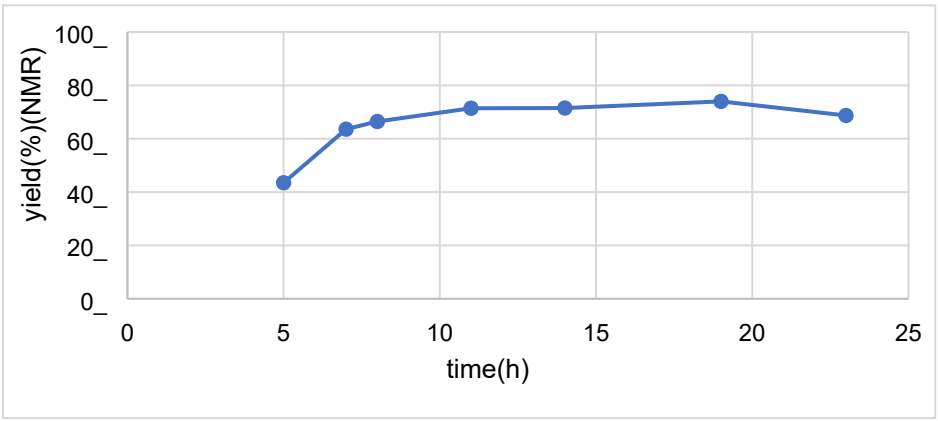
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.26 (m, 2H), 7.22–7.17 (m, 3H), 4.79 (s, 2H), 3.55 (d, J = 10.8 Hz, 1H), 3.08–3.01 (m, 1H), 2.48–2.34 (m, 2H), 2.03–1.56 (m, 1H), 1.79–1.51 (m, 7H), 1.31–1.22 (m, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 212.9, 147.7 141.1, 128.6, 128.4, 126.6, 108.9, 54.0, 51.9, 42.3, 33.1, 29.2, 24.4, 22.6. Spectroscopic data of ^1H and ^{13}C NMR were identical to that of reference 3.

2-(3-Methylene-1-(2,2,3-trimethylcyclopent-3-en-1-yl)pentan-2-yl)cyclohexan-1-one (3fa)

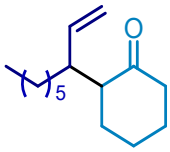


According to General Procedure, a solution of 2-(3-methylene-1-(2,2,3-trimethylcyclopent-3-en-1-yl)pentan-2-yl)cyclohexan-1-one (**1f**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 8 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3fa** was obtained in 45% yield (d.r.: 2.3/1, 623.1 mg, 2.2 mmol) as a pale yellow oil.



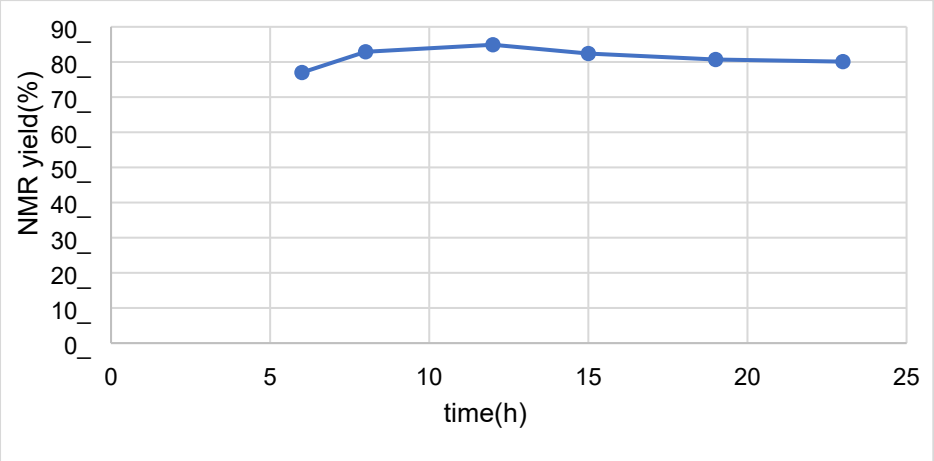
^1H NMR (400 MHz, $CDCl_3$): δ 5.24 (br, 0.70H), 5.20–5.19 (m, 0.29H), 4.84–4.74 (m, 2H), 2.73–2.68 (m, 1H), 2.45–2.20 (m, 4H), 2.01–1.58 (m, 13H), 1.45–1.239 (m, 2H), 1.04–1.00 (m, 3H), 0.98–0.91 (m, 3H), 0.80–0.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.9, 212.6, 152.5, 151.0, 148.6, 148.5, 122.0, 121.9, 109.5, 108.9, 54.2, 54.0, 49.3, 47.1, 47.0, 46.7, 43.3, 42.4, 41.6, 41.4, 36.7, 35.1, 29.9, 29.0, 28.4, 28.4, 27.6, 27.6, 27.3, 26.0, 25.4, 24.0, 23.3, 19.8, 19.4, 12.6, 12.6, 12.2, 12.1.; IR (ATR) cm^{-1}: 3649, 3080, 3033, 2934, 1748, 1734, 1708, 1671, 1664, 1654, 1641, 1623, 1618, 1559, 1540, 1521, 1517, 1507, 1490, 1448, 1437, 1405, 1395, 1382, 1375, 1359, 1339, 1312, 1289, 1260, 1233, 1219, 1201, 1128, 1115, 1072, 1051, 1012; ESI-HRMS m/z: 288.2453 ([M]+); Calcd. for $C_{20}H_{32}O$: 288.2453.

2-(Non-1-en-3-yl)cyclohexan-1-one (3ga)



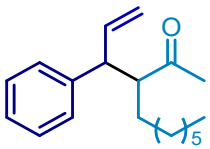
According to General Procedure, a solution of *trans*-2-nonen-1-ol (**1g**, 0.1 M) and cyclohexanone dimethyl ketal (**2a**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 6 h to 23 h. After evaporation of solvent and purification over silica-gel column

chromatography (ethyl acetate/hexane), **3ga** was obtained in 50% yield (d.r.: 2.8/1, 600.4 mg, 2.7 mmol) as a pale yellow oil.

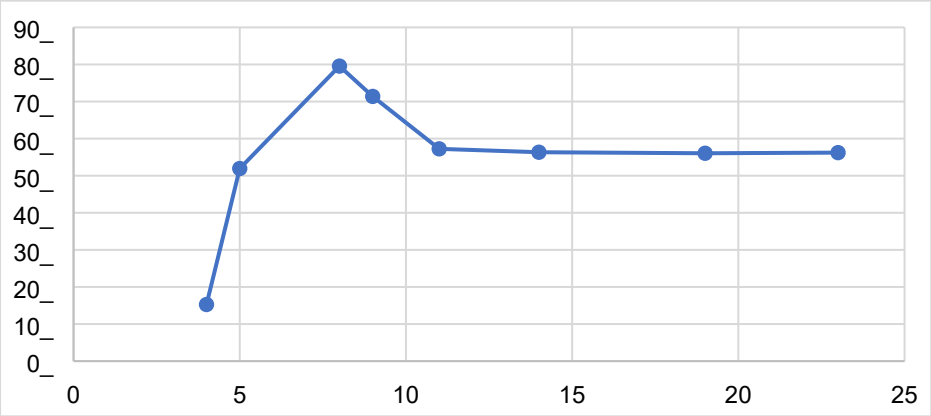


^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (ddd, *J* = 16.8, 10.4, 9.2 Hz. 0.80H), 5.47 (ddd, *J* = 17.2, 10.4, 9.2 Hz, 0.19H), 5.07–5.03 (m, 0.28H), 5.00–4.93 (m, 1.71H), 2.42–2.21 (m, 4H), 1.97–1.55 (m, 7H), 1.43–1.19 (m, 10H), 0.89–0.56 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.2, 212.3, 140.7, 140.1, 116.2, 115.2, 55.1, 54.8, 43.5, 42.9, 42.2, 41.9, 32.4, 31.8, 31.8, 31.1, 30.7, 29.6, 29.3, 29.2, 28.0, 27.6, 27.5, 27.3, 24.3, 23.8, 22.7(2C), 14.1(2C).; IR (ATR) cm^{-1}: 3074, 2927, 2856, 1709, 1638, 1464, 1450, 1428, 1378, 1338, 1312, 1276, 1260, 1223, 1206, 1127, 1062; ESI-HRMS m/z: 222.1989 ([M]+); Calcd. for $C_{15}H_{26}O$: 222.1984.

3-(1-phenylallyl)decan-2-one (**3ab**)

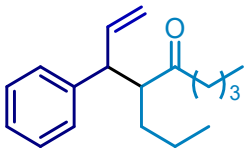


According to General Procedure, a solution of cinnamyl alcohol (**1a**, 0.1 M) and 2,2-dimethoxydecane (**2b**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 5 h to 23 h. After evaporation of solvent, the yield of **3ab** (60%, d.r.: 3.2/1) was determined ^{1}H NMR using ethylene carbonate as an internal standard. Purified **3ab** (d.r.: 1/1) was obtained by recycling preparative GPC (column: JAIGEL-2HR Plus, chloroform) using part of reaction mixture as a pale yellow oil.

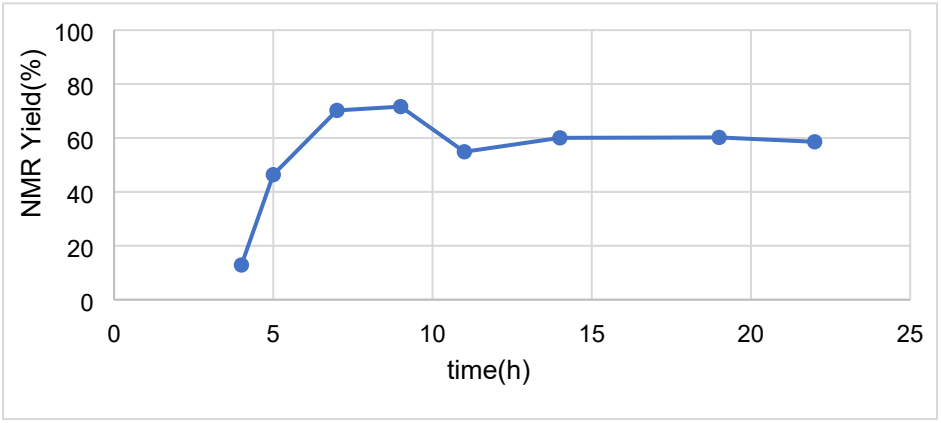


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.14 (m, 5H), 5.98–5.85 (m, 1H), 5.12–4.97 (m, 2H), 3.43–3.37 (m, 1H), 2.93–2.85 (m, 1H), 2.11 (s, 1.48H), 1.77 (s, 1.56H), 1.67–1.58 (m, 1H), 1.29–1.13 (m, 11H), 0.89–0.81 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.3, 212.2, 142.3, 141.8, 139.5, 139.4, 128.7, 128.7, 127.9, 127.7, 126.7, 126.6, 116.3, 115.7, 58.2, 57.7, 53.4, 53.1, 31.8, 31.7, 31.0, 30.8, 30.6, 30.5, 29.7, 29.4, 29.1, 29.0, 27.5, 27.3, 22.6, 22.6, 14.1, 14.0.; IR (ATR) cm^{-1}: 3080, 3063, 3030, 3001, 2954, 2925, 2856, 1711, 1638, 1602, 1493, 1454, 1418, 1353, 1243, 1160, 1132, 1075, 1029; ESI-HRMS m/z: 272.2144 ([M]+); Calcd. for $C_{19}H_{28}O$: 272.2140.

3-Phenyl-4-propylon-1-en-5-one (**3ac**)

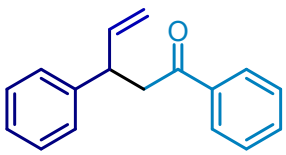


According to General Procedure, a solution of cinnamyl alcohol (**1a**, 0.1 M) and 5,5-dimethoxynonane (**2c**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 7 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3ac** was obtained in 52% yield (d.r.: 1/1, 685.3 mg, 2.7 mmol) as a pale yellow oil.

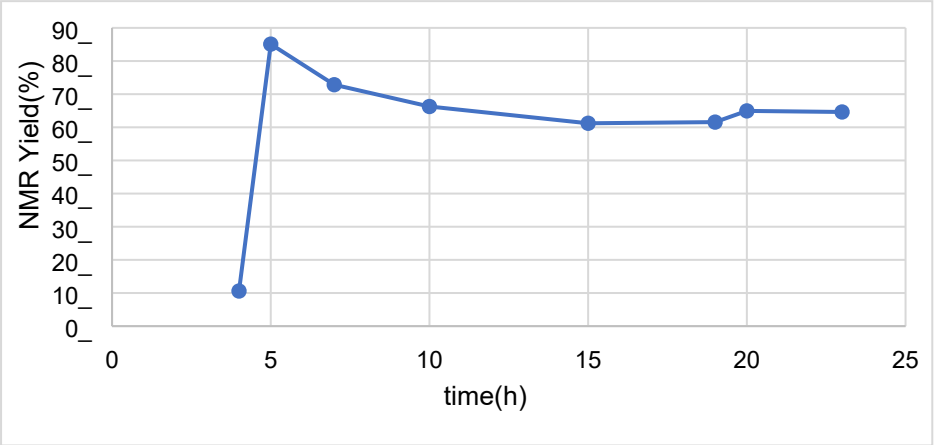


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.14 (m, 5H), 5.98–5.88 (m, 1H), 5.12–4.95 (m, 2H), 3.44–3.38 (m, 1H), 2.93–2.85 (m, 1H), 2.38 (t, *J* = 7.4 Hz, 1H), 2.14–2.06 (m, 0.47H), 1.88–1.80 (m, 0.47H), 1.63–0.97 (m, 8H), 0.92–0.87 (m, 3H), 0.76–0.70 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.3, 214.2, 142.5, 142.0, 139.5(2C), 128.7, 128.6, 127.9, 127.8, 126.6, 126.5, 116.3, 115.8, 57.1, 57.0, 53.4, 53.2, 44.6, 44..4, 33.2, 33.0, 25.0, 24.8, 22.3, 22.0, 20.7, 20.6, 14.3, 14.1, 13.9, 13.7. ; IR (ATR) cm^{-1}: 3080, 3063, 3030, 2958, 2932, 2873, 1708, 1671, 1638, 1602, 1493, 1464, 1454, 1404, 1378, 1300, 1256, 1240, 1165, 1124, 1071, 1043; ESI-HRMS m/z: 258.1981 ([M+H]+); Calcd. for $C_{18}H_{26}O$: 258.1984.

1,3-Diphenylpent-4-ene-1-one (**3ad**)

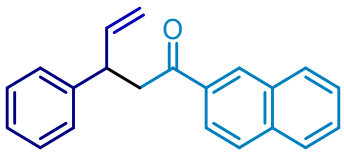


According to General Procedure, a solution of cinnamyl alcohol (**1a**, 0.1 M) and (1,1-dimethyletheyl)benzene (**2d**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 5 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3ad** was obtained in 66% yield (889.0 mg, 3.8 mmol) as a pale yellow oil.

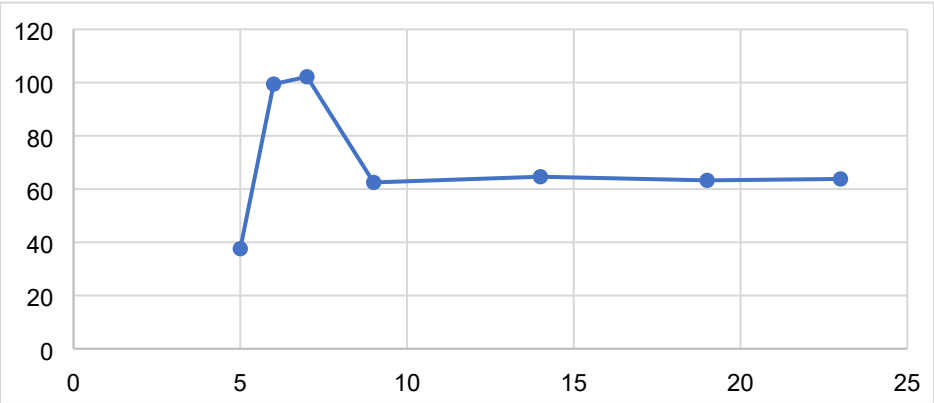


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.91 (m, 2H), 7.56–7.52 (m, 1H), 7.45–7.42 (m, 2H), 7.32–7.24 (m, 4H), 7.22–7.18 (m, 1H), 6.05 (ddd, J = 17.2, 10.0, 6.4 Hz, 1H), 5.08–5.01 (m, 2H), 4.13 (q, J = 6.9 Hz, 1H), 3.47–3.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 143.2, 140.7, 137.2, 133.0, 128.6, 128.1, 127.7, 126.6, 114.7, 44.6, 44.1. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that of reference 4.

1-(Naphthalen-2-yl)-3-phenylpent-4-en-1-one (**3ae**)

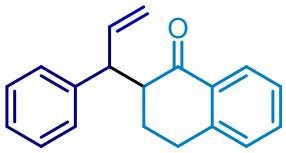


According to General Procedure, a solution of cinnamyl alcohol (**1a**, 0.1 M) and 2-(1,1-dimethoxyethyl)naphthalene (**2e**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 7 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3ae** was obtained in 62% yield (905.5 mg, 3.2 mmol) as a pale yellow solid.

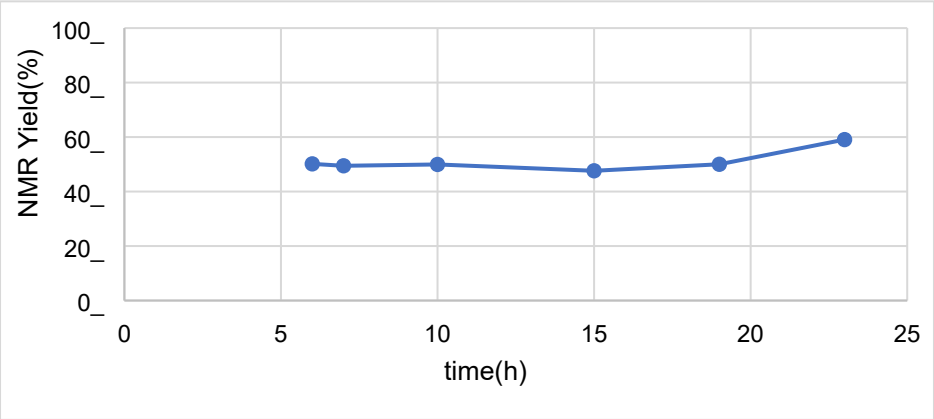


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 8.00 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.89–7.86 (m, 2H), 7.62–7.53 (m, 2H), 7.32–7.30 (m, 4H), 7.23–7.19 (m, 1H), 6.09 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.10–5.04 (m, 2H), 4.23–4.18 (m, 1H), 3.61–3.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 143.3, 140.8, 135.6, 134.6, 132.6, 129.8, 129.6, 128.7, 128.5, 127.9, 127.8, 126.8, 126.7, 124.0, 114.9, 44.8, 44.2. Spectroscopic data of ^{1}H and ^{13}C NMR were identical to that of reference 5.

2-(1-Phenylallyl)-3,4-dihydronaphthalen-1(*2H*)-one (3af)



According to General Procedure, a solution of cinnamyl alcohol (**1a**, 0.1 M) and 4-methoxy-1,2-dihydronaphthalene (**2f**, 0.2 M) in CPME (100 mL) was prepared. The profile about NMR yields of product was indicated as below. Fractions were collected from 6 h to 23 h. After evaporation of solvent and purification over silica-gel column chromatography (ethyl acetate/hexane), **3af** was obtained in 56% yield (d.r.: 5.6/1, 793.4 mg, 3.0 mmol) as a pale yellow oil.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.45 (ddd, *J* = 7.4, 7.4, 1.4 Hz, 1H), 7.32–7.19 (m, 7H), 6.17 (ddd, *J* = 15.6, 10.4, 8.0 Hz, 0.90H), 6.07 (ddd, *J* = 17.2, 10.4, 8.8 Hz, 0.08H), 5.20 (ddd, *J* = 17.2, 2.0, 1.2 Hz, 0.09H), 5.15 (ddd, *J* = 10.4, 1.2, 1.2 Hz, 0.09H), 5.07 (ddd, *J* = 10.4, 1.2, 1.2 Hz, 0.91H), 4.97 (ddd, *J* = 17.2, 1.2, 1.2 Hz, 0.91H), 4.29 (dd, *J* = 8.4, 5.2 Hz, 0.08H), 4.01 (dd, *J* = 8.0, 8.0 Hz, 0.92H) , 3.06–2.84 (m, 3H), 2.22–2.16 (m, 0.09H), 2.15–2.09 (m, 0.98H), 1.78–1.69 (m, 1H);^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 197.3, 142.8, 142.5, 142.1, 139.1, 136.5, 132.3, 132.3, 132.1, 131.8, 127.8(2C), 127.7, 127.6, 127.6, 127.2, 126.8, 126.7, 125.8(2C), 125.7, 125.5, 116.7, 114.4, 52.4, 51.3, 47.4, 47.2, 27.6,. 26.4, 24.8, 23.9.; IR (ATR) cm^{-1}: 3062, 3027, 2978, 2866, 2838, 1679, 1638, 1599, 1491, 1453, 1434, 1417, 1352, 1328, 1305, 1287, 1275, 1239, 1220, 1196, 1184, 1155, 1112, 1023; ESI-HRMS m/z: 262.1360 ([M]+); Calcd. for $C_{19}H_{18}O$: 262.1358.

13. References

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2. Jian-Ping Chen, Qian Peng, Bai-Lin Lei, Xue-Long Hou, and Yun-Dong Wu, *J. Am. Chem. Soc.* **2011**, *133*. 14180–14183.

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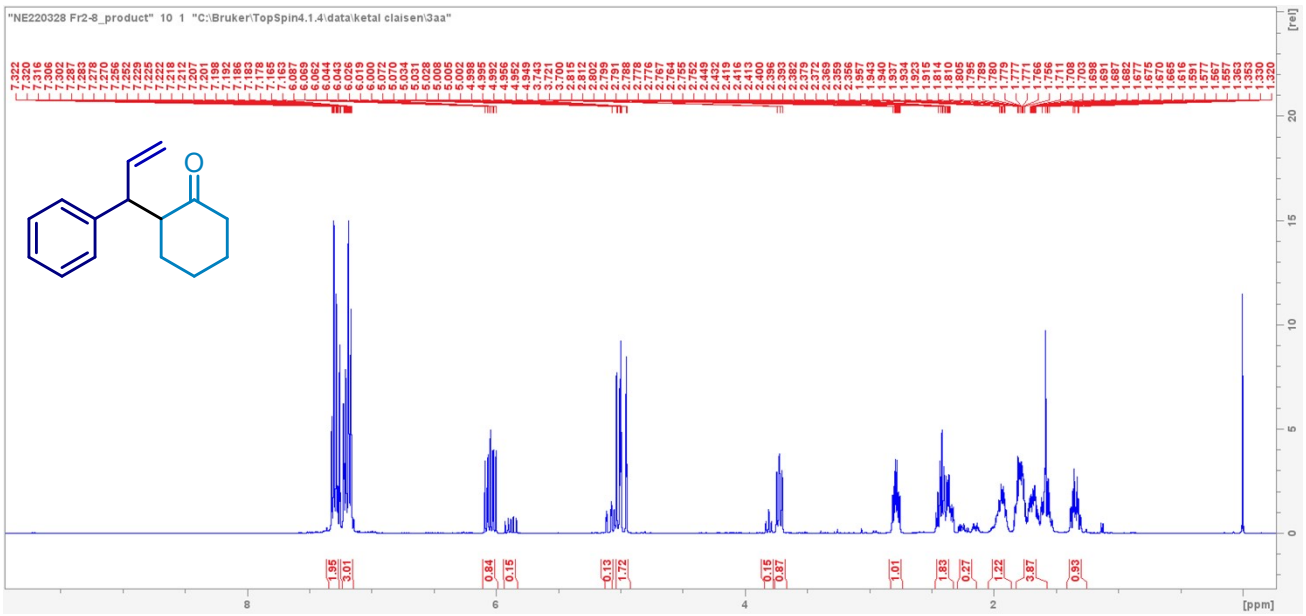
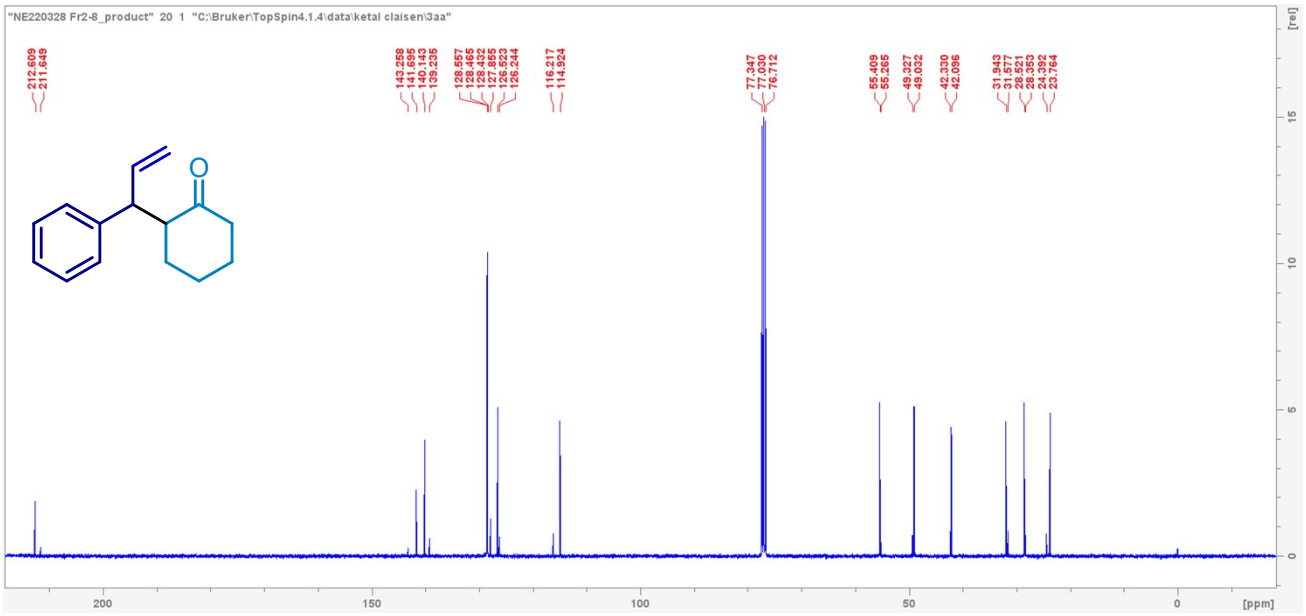
14. ^{1}H and ^{13}C NMR spectra

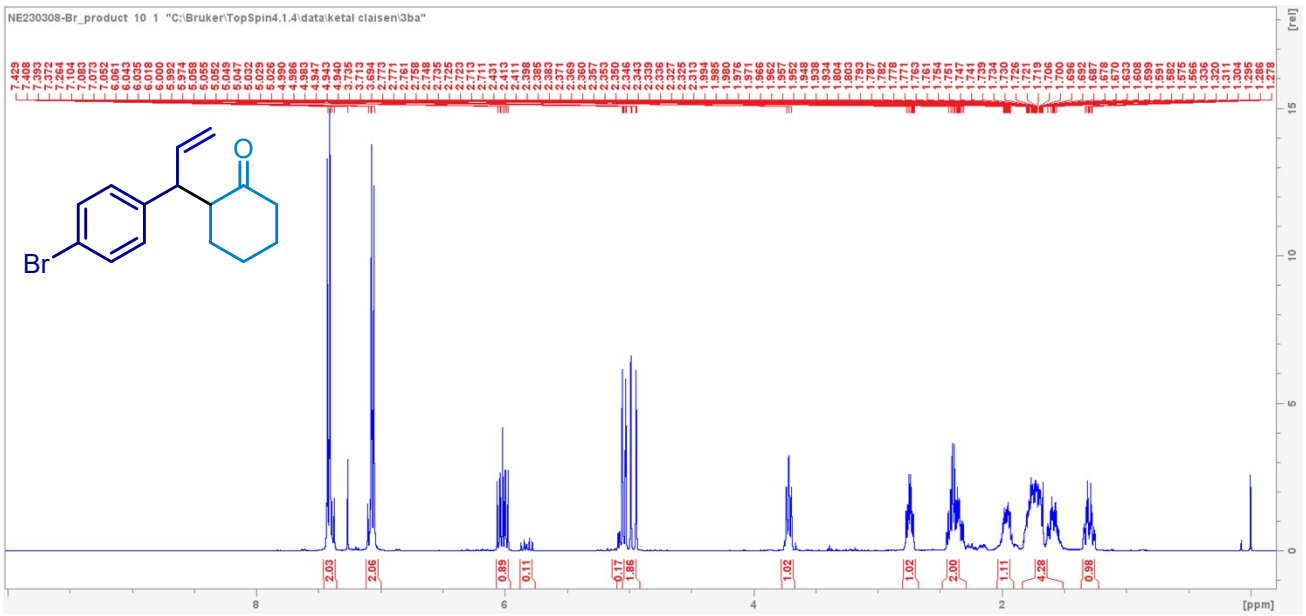
^{1}H NMR of **3aa** ($CDCl_3$, 400 Hz)



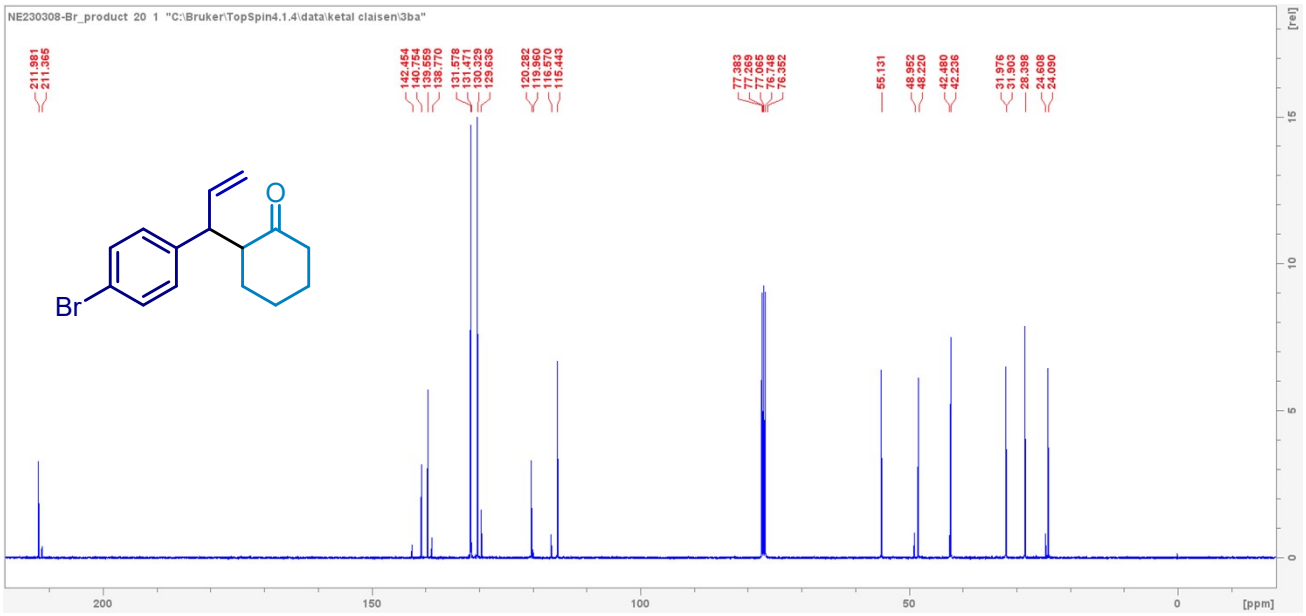
^{13}C NMR of **3aa** ($CDCl_3$, 100 Hz)



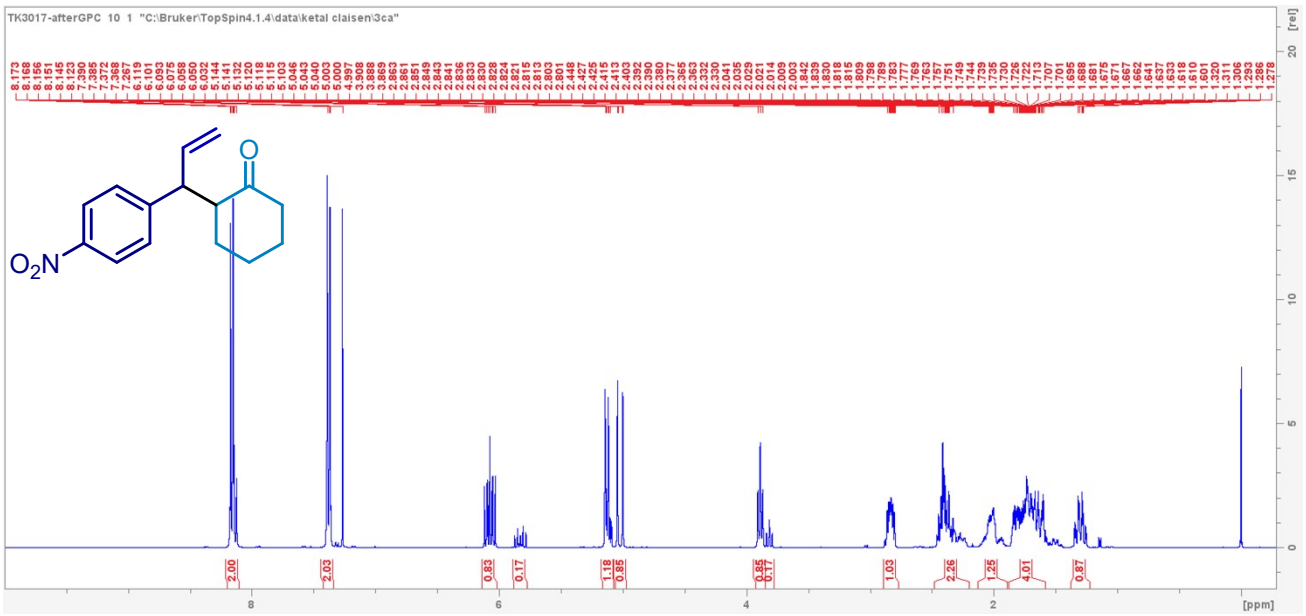
^{1}H NMR of **3ba** ($CDCl_3$, 400 Hz)



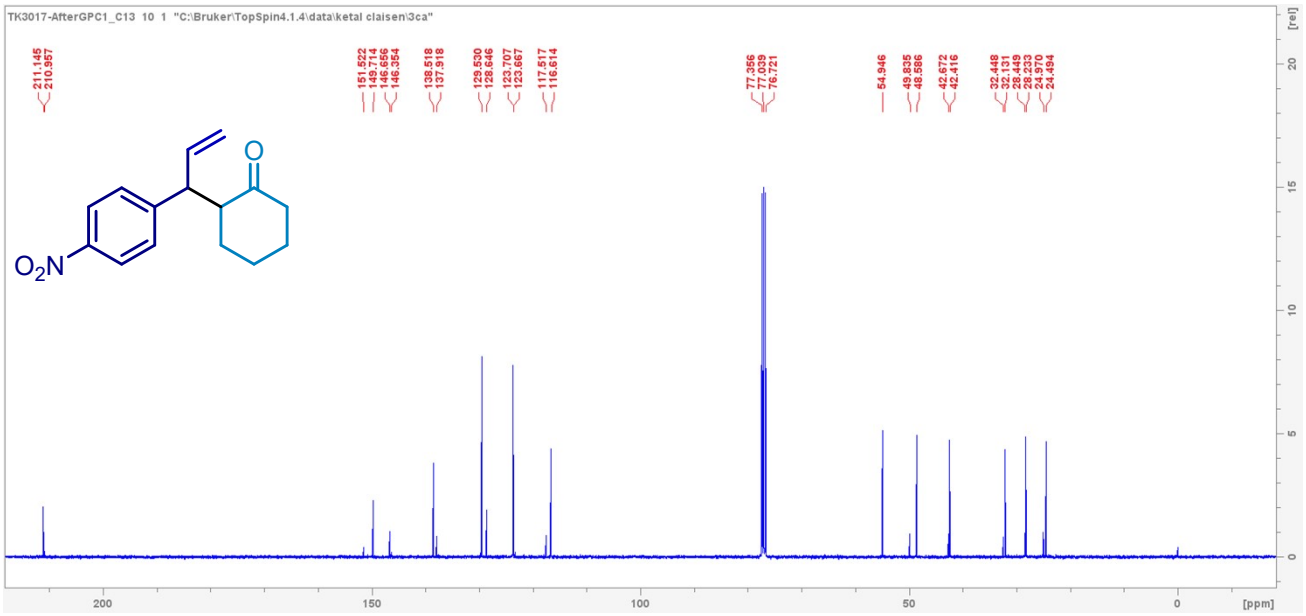
^{13}C NMR of **3ba** ($CDCl_3$, 100 Hz)



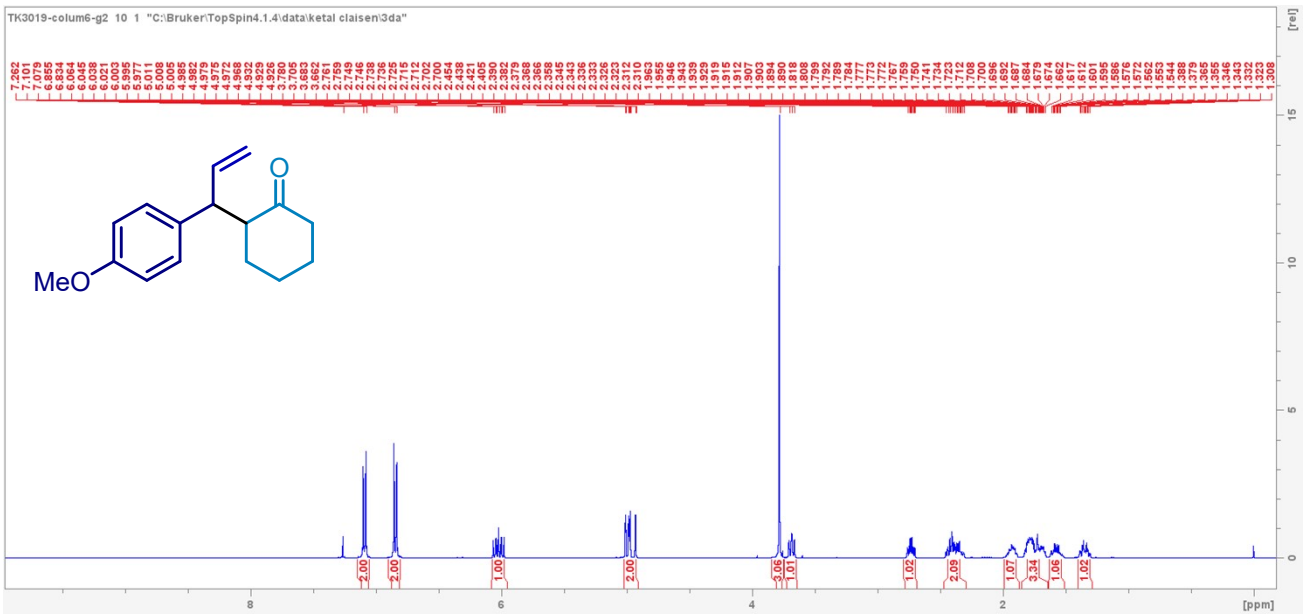
^{1}H NMR of **3ca** ($CDCl_3$, 400 Hz)



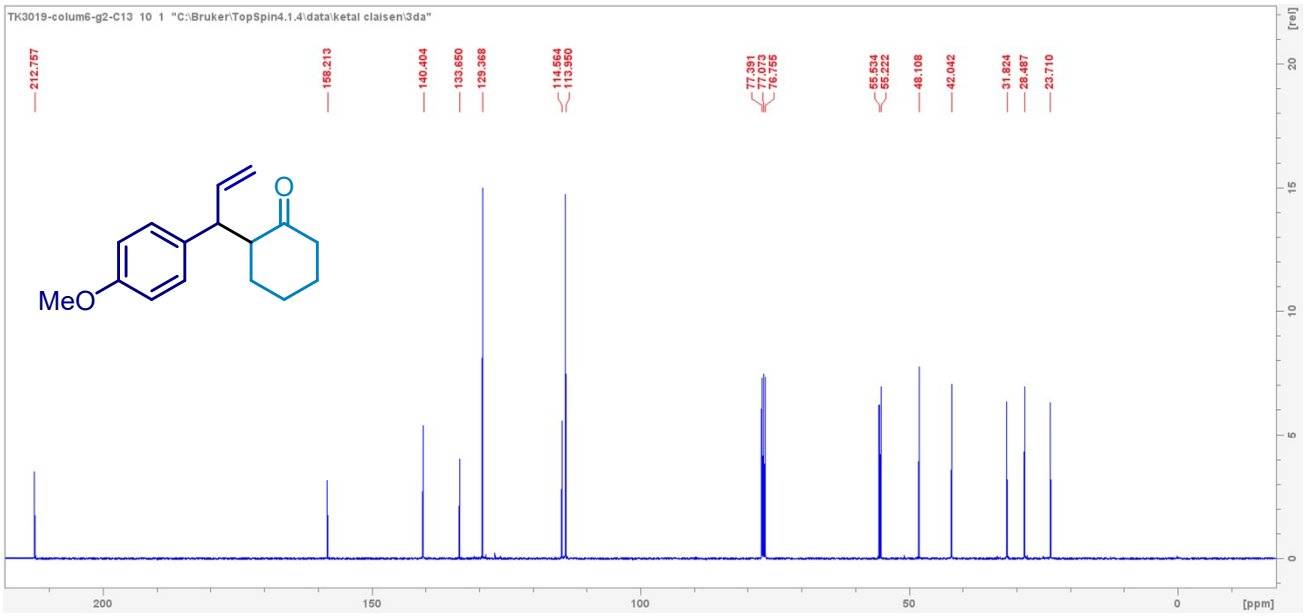
^{13}C NMR of **3ca** ($CDCl_3$, 100 Hz)



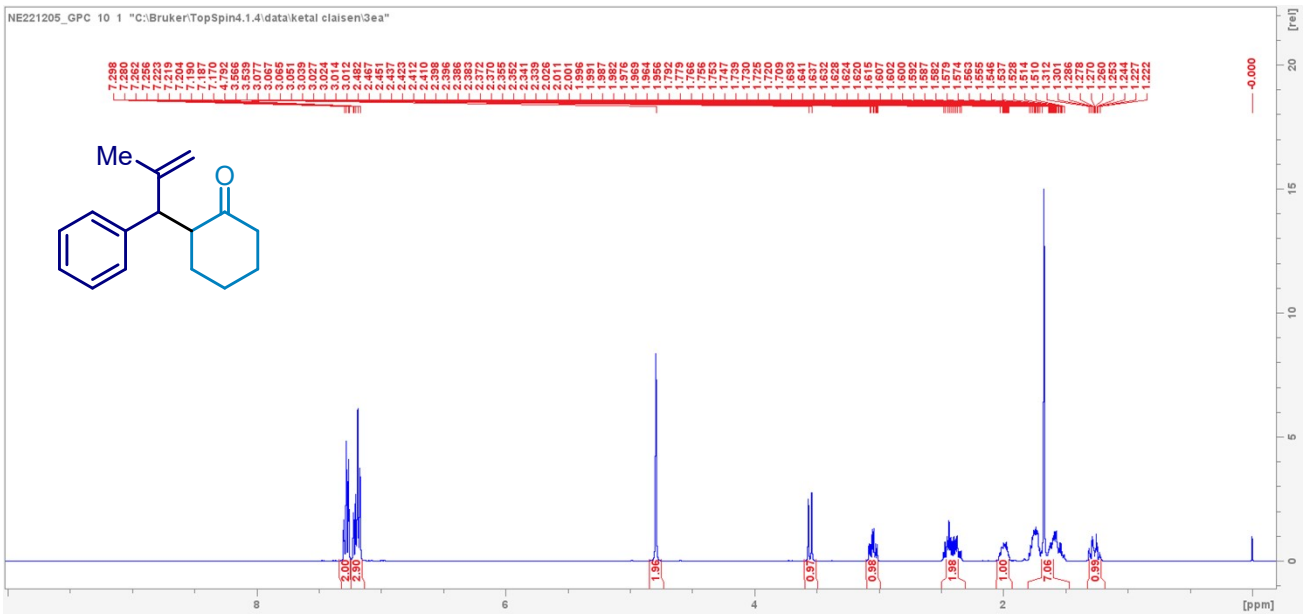
^{1}H NMR of **3da** ($CDCl_3$, 400 Hz)



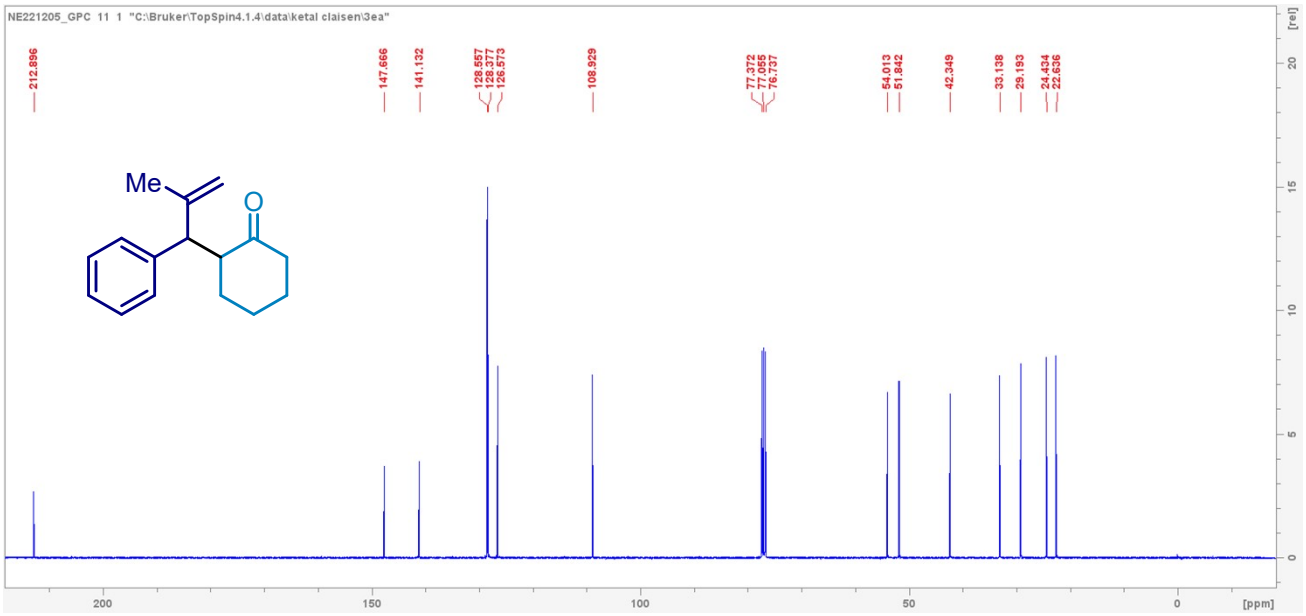
^{13}C NMR of **3da** ($CDCl_3$, 100 Hz)



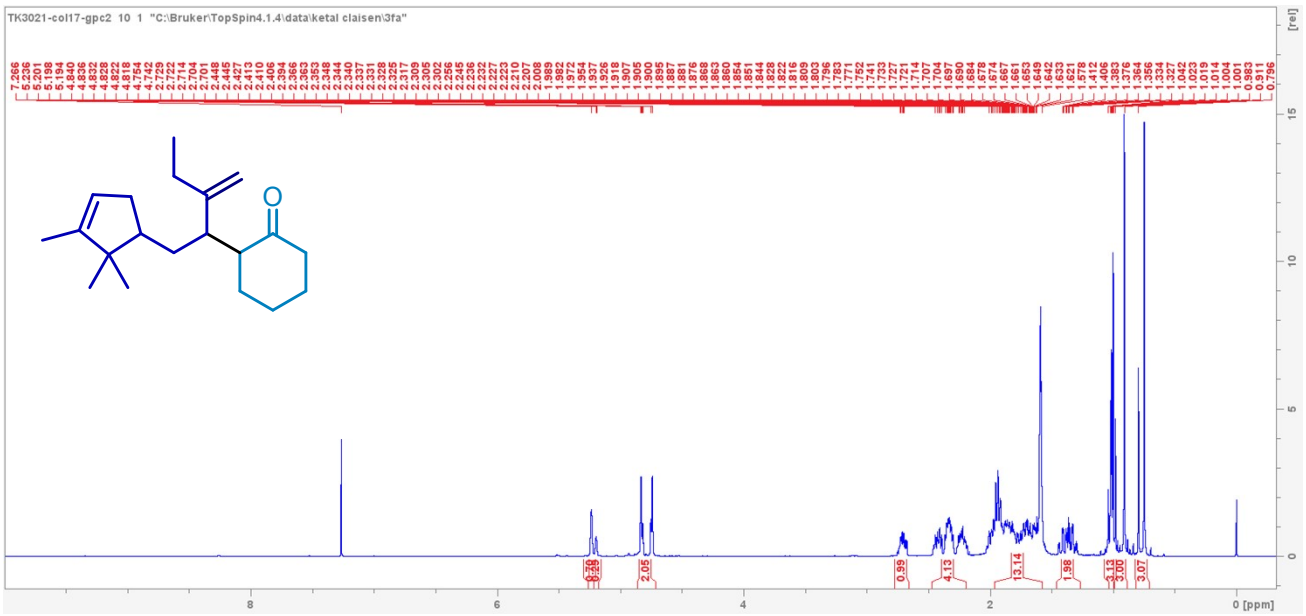
^{1}H NMR of **3ea** ($CDCl_3$, 400 Hz)



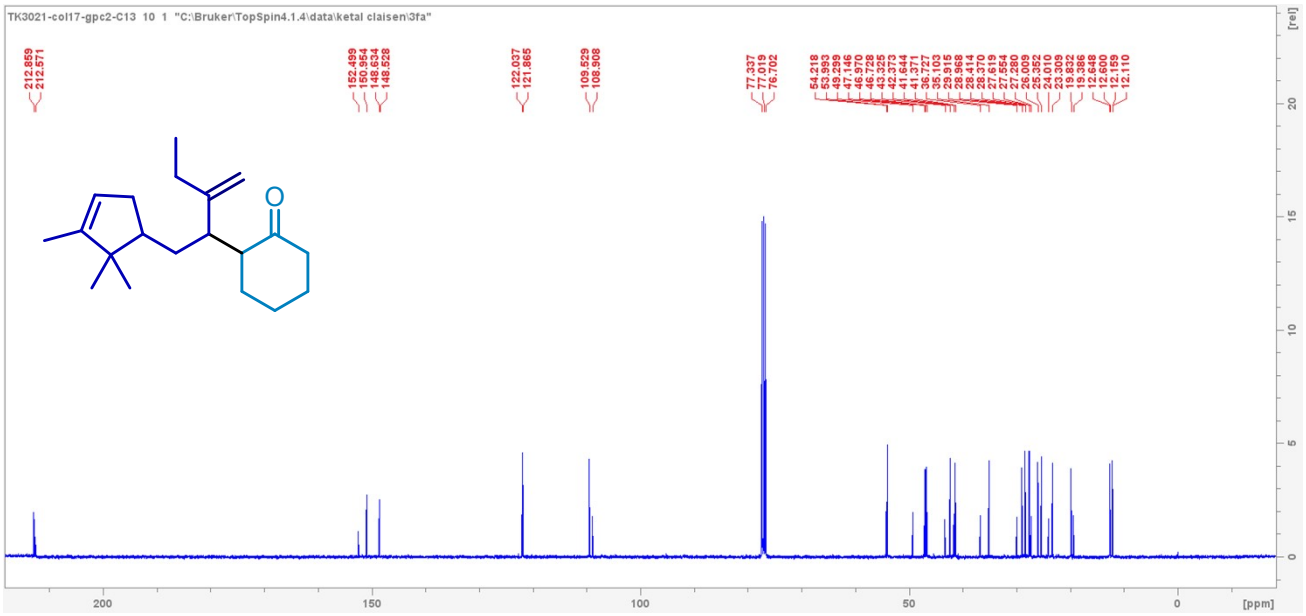
^{13}C NMR of **3ea** ($CDCl_3$, 100 Hz)



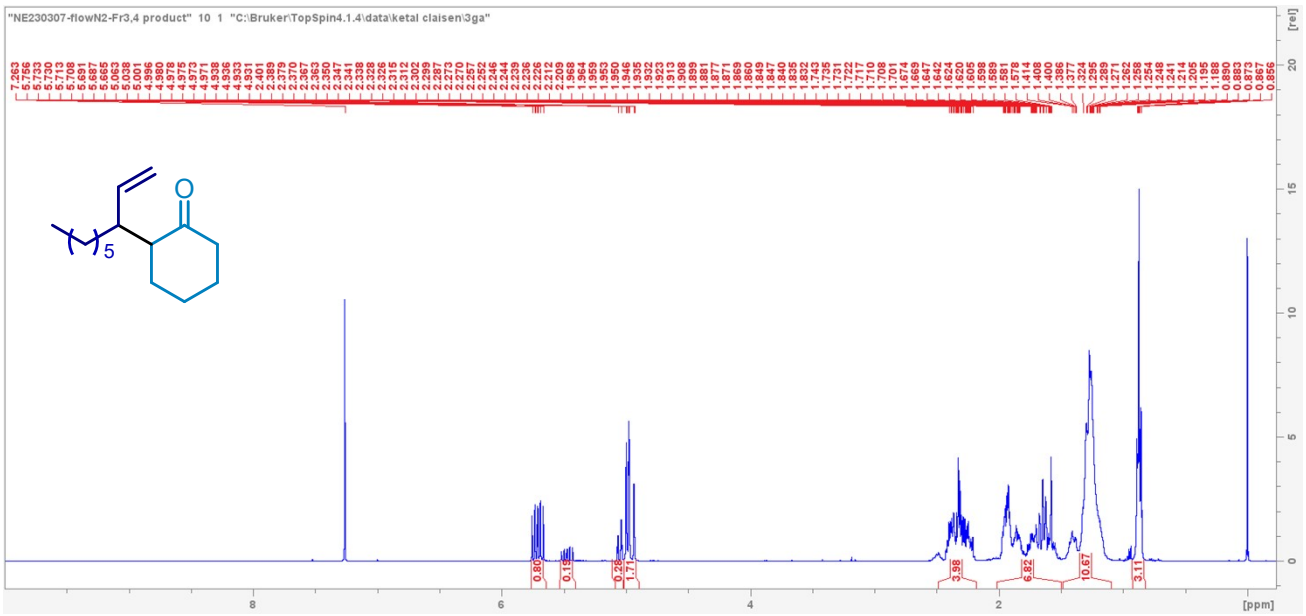
^{1}H NMR of **3fa** ($CDCl_3$, 400 Hz)



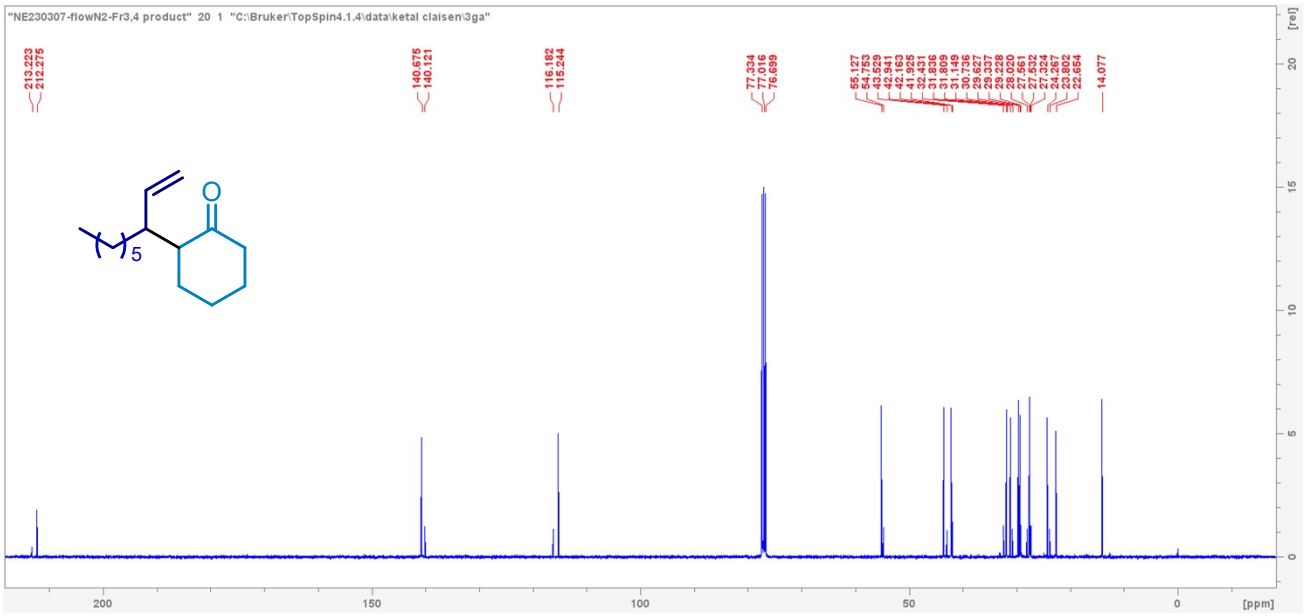
^{13}C NMR of **3fa** ($CDCl_3$, 100 Hz)



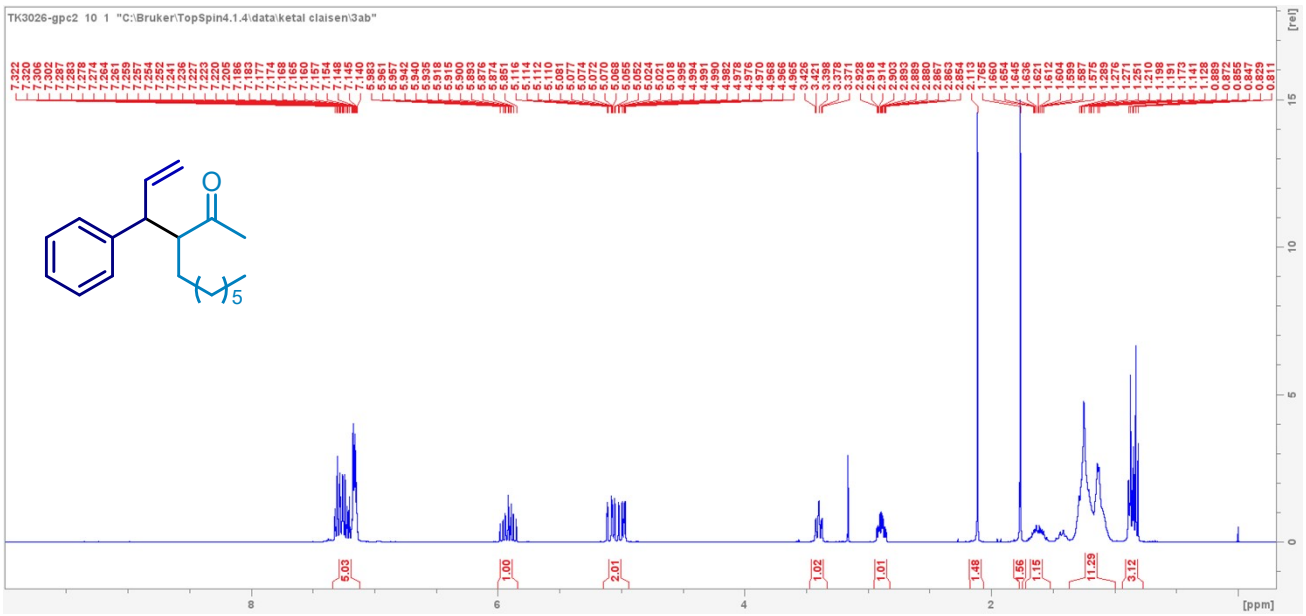
^{1}H NMR of **3ga** ($CDCl_3$, 400 Hz)



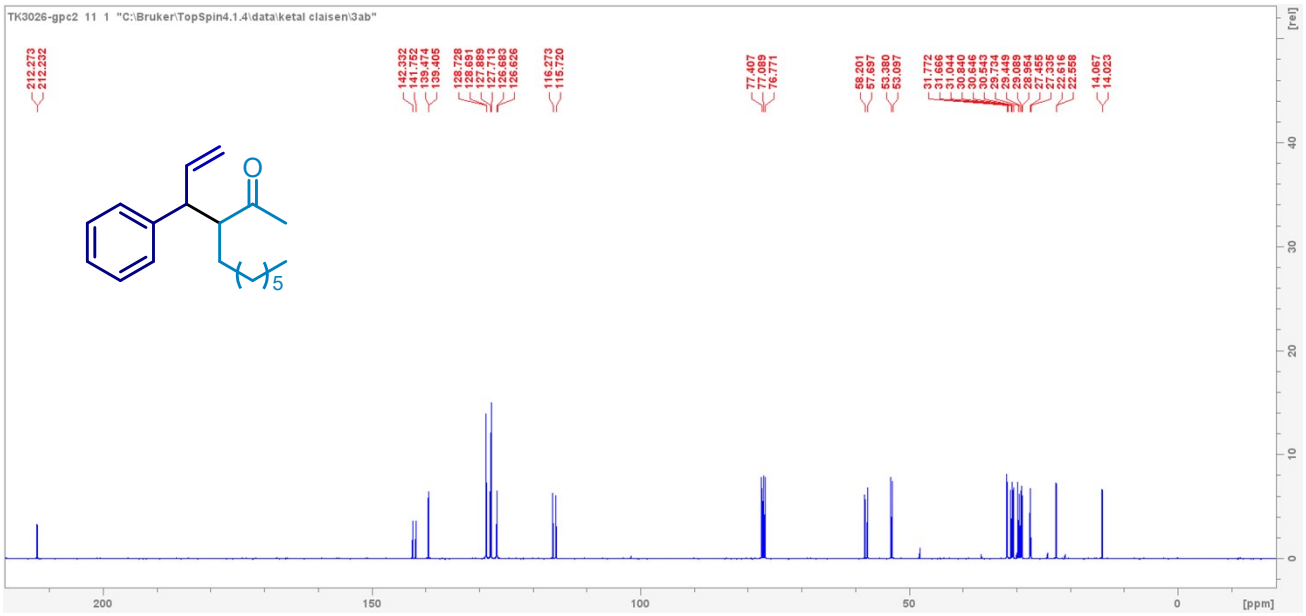
^{13}C NMR of **3ga** ($CDCl_3$, 100 Hz)



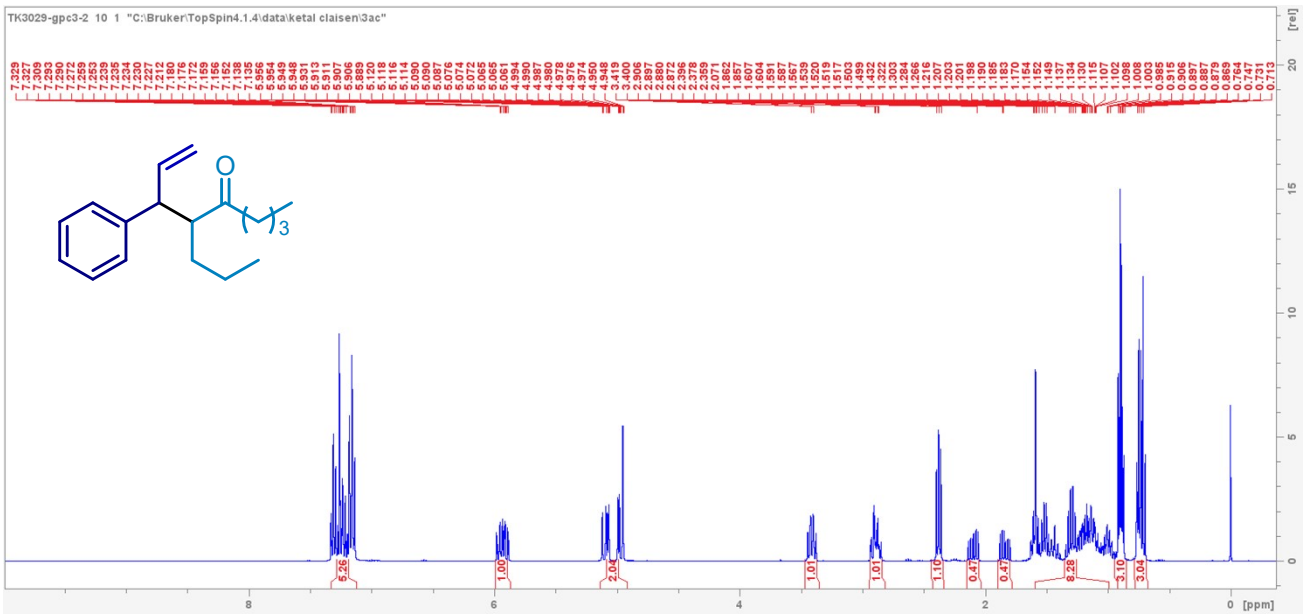
^{1}H NMR of **3ab** ($CDCl_3$, 400 Hz)



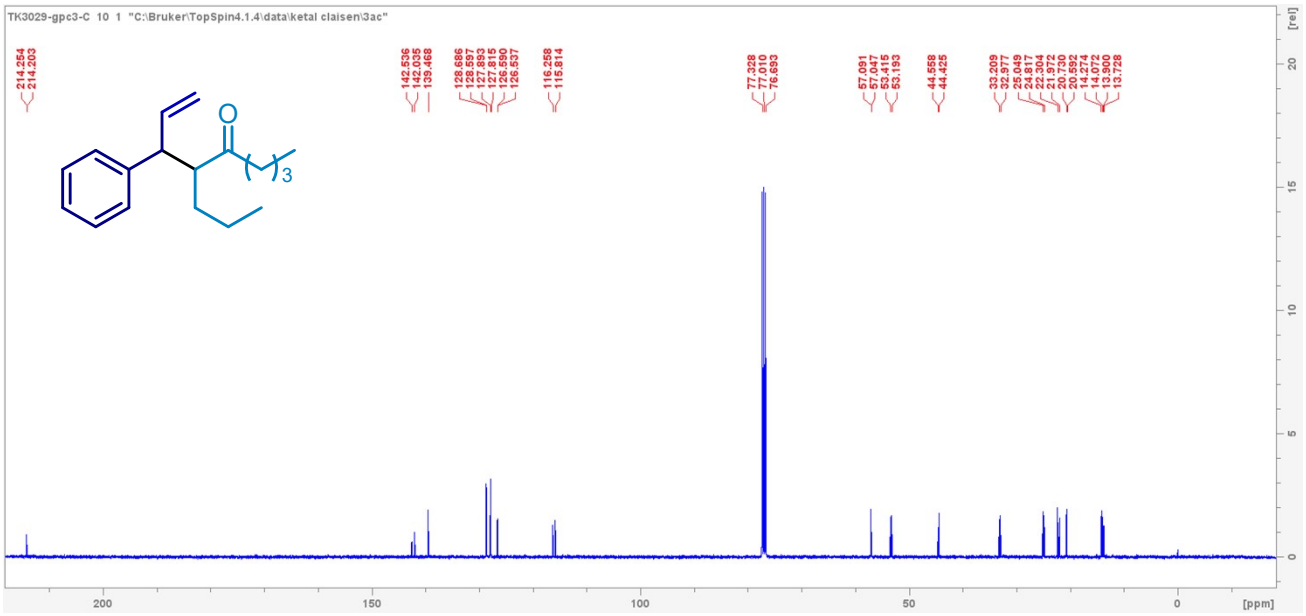
^{13}C NMR of **3ab** ($CDCl_3$, 100 Hz)



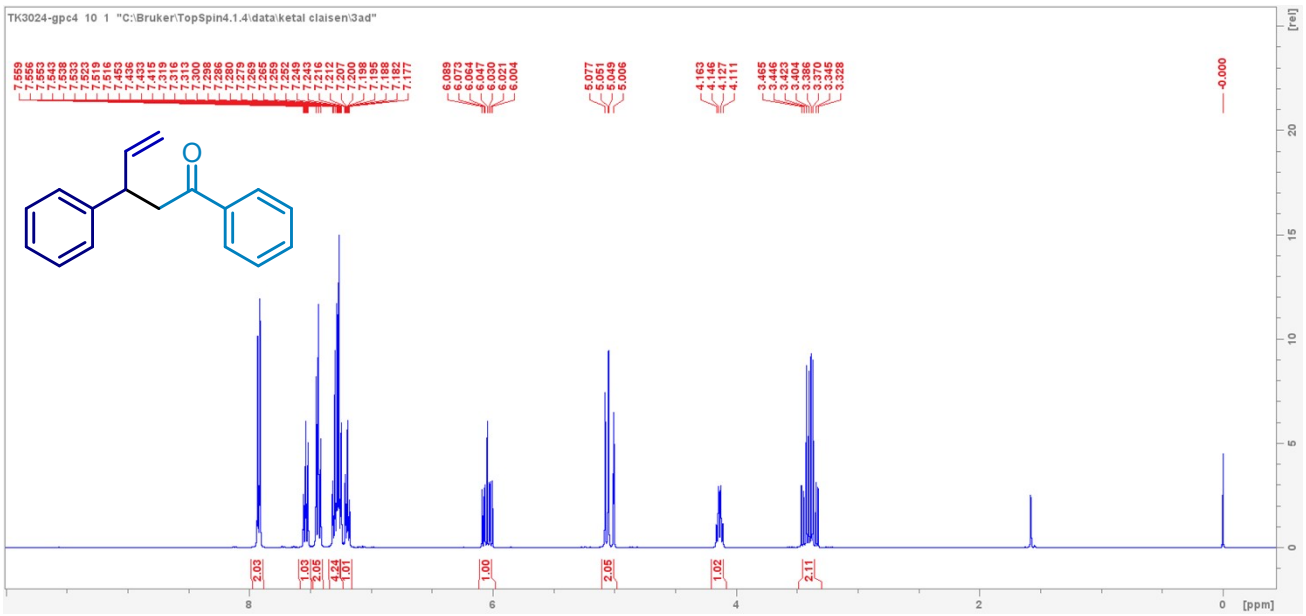
^{1}H NMR of **3ac** ($CDCl_3$, 400 Hz)



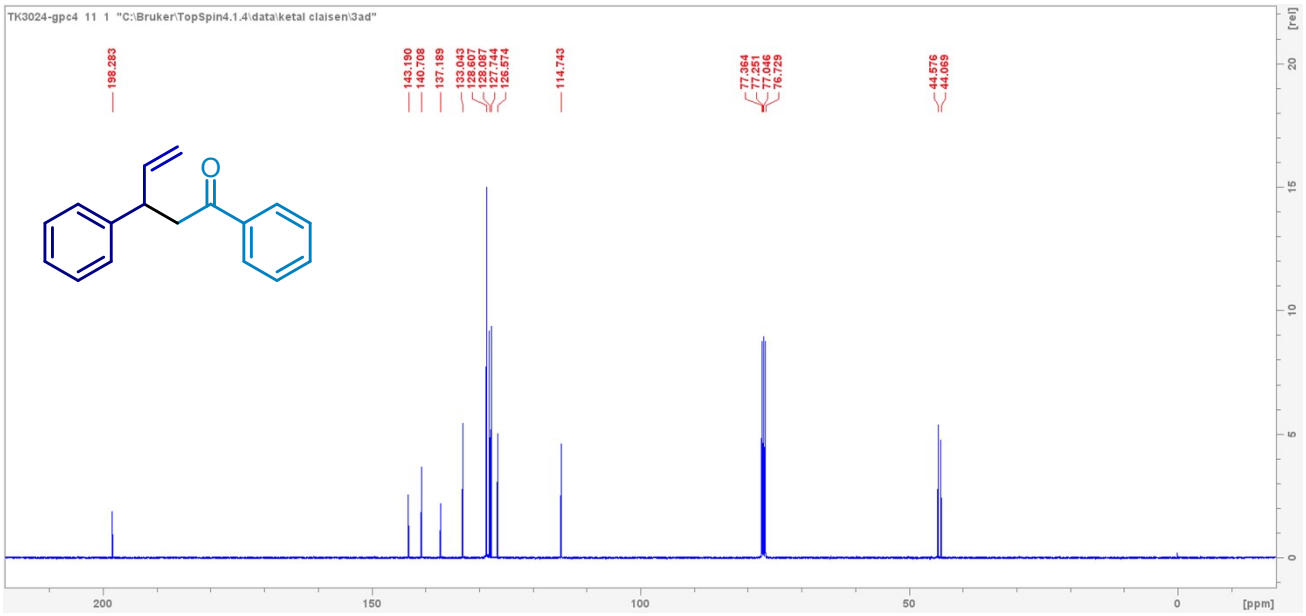
^{13}C NMR of **3ac** ($CDCl_3$, 100 Hz)



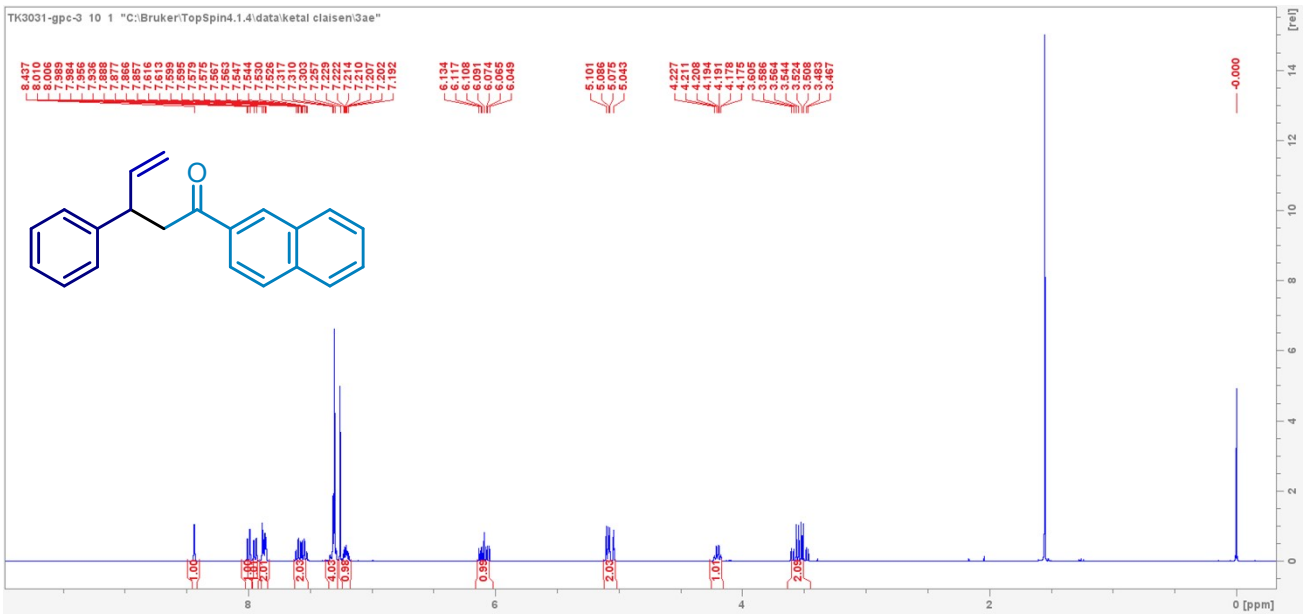
^{1}H NMR of **3ad** ($CDCl_3$, 400 Hz)



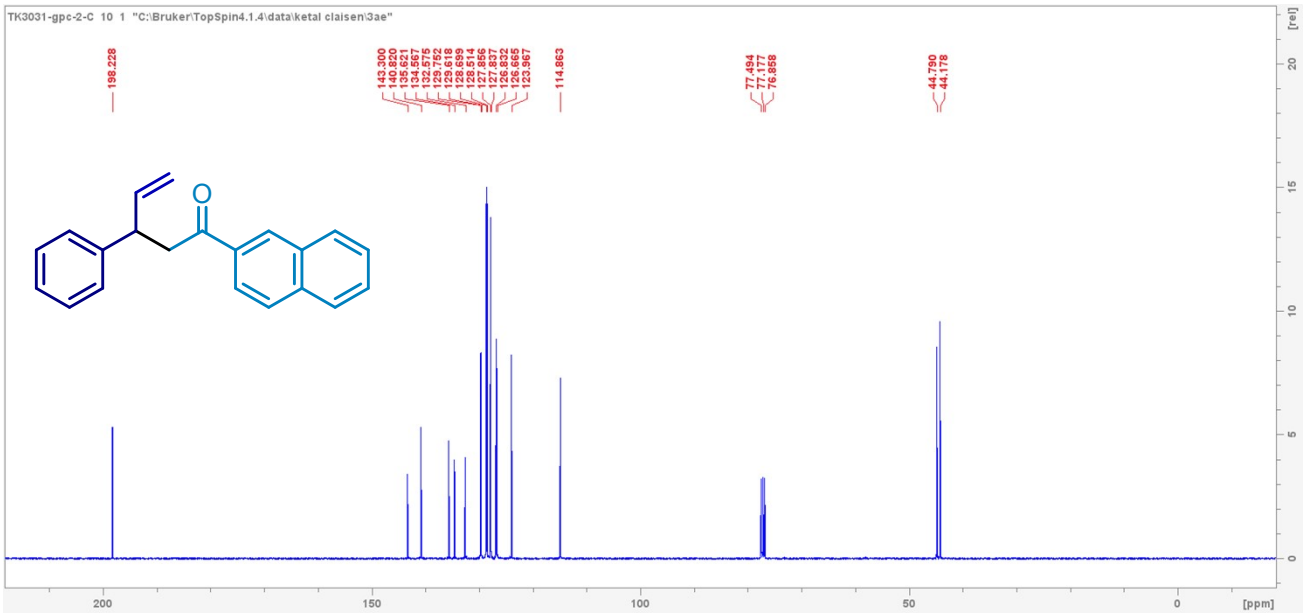
^{13}C NMR of **3ad** ($CDCl_3$, 100 Hz)



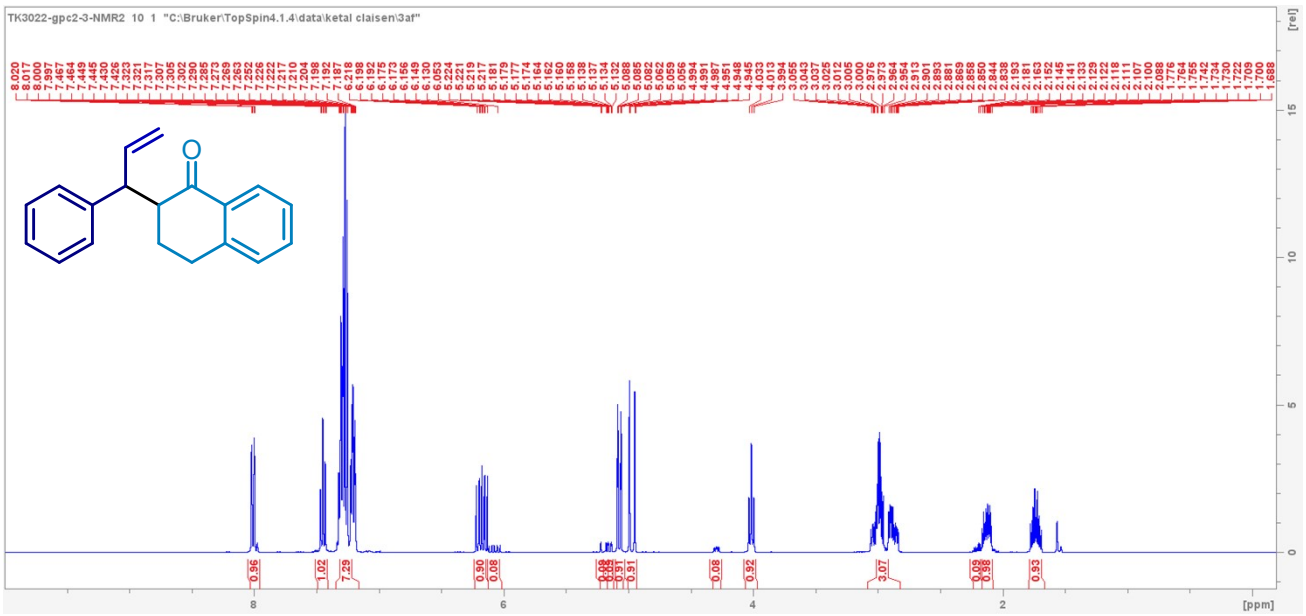
^{1}H NMR of **3ae** ($CDCl_3$, 400 Hz)



^{13}C NMR of **3ae** ($CDCl_3$, 100 Hz)



^{1}H NMR of **3af** ($CDCl_3$, 400 Hz)



^{13}C NMR of **3af** ($CDCl_3$, 100 Hz)