

Supporting Information for

Continuous-flow Dehydrative Amidation between Carboxylic Acids and Amines using Modified Mixed Metal Oxides as Solid Acid Catalysts

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SI-1. General Information

Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECX-600 or ECA-500 spectrometer, operating at 600 MHz or 500 MHz for ^1H , 150 MHz for ^{13}C NMR in CDCl_3 unless otherwise noted. Tetramethylsilane (TMS) served as the internal standard ($\delta = 0$) for ^1H NMR, CDCl_3 ($\delta = 77.0$) was used as the internal standard for ^{13}C NMR. Gas chromatography (GC) was recorded on a Shimadzu GC-2030AF, 100V spectrometer using SH-Rtx-5 Amine column (30 m, 0.25 mmID, 0.25 μm df). Inductively coupled plasma-atomic emission spectrometry (ICP-AES) analysis was performed on a Shimadzu ICPS-7510 equipment. Ammonia-probed temperature-programed desorption measurement was conducted on a BELCAT-II of MicrotracBEL.

For apparatuses for flow systems, a plunger pump (FLOM, UI-22-110P, MP-22-110S), a column heater (Tokyo Rikakikai Co., Ltd., LCR-1300), a back pressure regulator (DFC Co., Ltd., FC-BPV-100) and a stainless column with column ends were used. Preparative thin-layer chromatography (PTLC) was carried out using Wakogel B-5F from Wako Pure Chemical Industries, Ltd. All organic solvents were purchased from FUJIFILM Wako Pure Chemical Co. Ltd. as dried solvents and were used directly or were used after distillation under an argon atmosphere. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ and ammonium molybdate tetrahydrate were purchased from FUJIFILM Wako Pure Chemical Co. Ltd. Deionized water from a MILLIPORE MiLLiQ machine (Gradient A 10) was used as solvent in catalyst preparation without further treatment. Calcination was carried out by using muffle furnace KDF-S80. Chlorobenzene and 3-phenylpropionic acid (**1**) were purchased from FUJIFILM Wako Pure Chemical Co. Ltd. p-toluidine (**2**) and $^n\text{Hexylamine}$ (**4**) were purchased from Tokyo Chemical Industry Co., Ltd (TCI).

SI-2. Experimental Procedures

SI-2-1. General Procedures for Catalyst Preparation

ZrO₂-SnO₂ mixed oxide support and related composite supports were prepared by co-precipitation method using precipitant from a 1:1 molar mixture of metal precursors.^{1,2} In a typical procedure, 2.23 g (10 mmol) of SnCl₂ · 2H₂O was dissolved in 30 mL of deionized water and was added 0.5 mL of conc. HCl (solution A). Separately, 3.22 g of ZrOCl₂ · 8H₂O (10 mmol) was dissolved in 60 mL of deionized water (solution B), and this solution B was added dropwise to the solution A. After addition of solution B, an excess amount of aqueous ammonia (39%) was added to adjust its pH to 9, and the resulting mixture was heated to 115 °C with vigorous stirring for 5 min. A white precipitate was immediately formed. This suspension was then stand for 24 h at room temperature for aging. The solid material was finally filtered and washed with deionized water. This washing step was repeated until chloride ions cannot be detected by addition of aq. AgNO₃ to the filtrate solution. The obtained samples were dried at 120 °C for 16 h. The resulting white solid placed on clean Petri dishes shallowly and calcined at 500 °C (4.2 °C/min of temperature elevation rate) for 6 h in a muffle furnace under air to provide the support ZrO₂-SnO₂ mixed oxide. The ICP-AES analysis indicate to Zr/Sn ratio was 1.0.

The molybdenum species were immobilized by an impregnation method.¹ In a typical procedure for the synthesis of 12 wt% sample, 147.2 mg of ammonium molybdate tetrahydrate (0.12 mmol, corresponds to 0.12 g of MoO₃) was dissolved in 5 mL of deionized water, and few drops of aqueous ammonia (39%) were added to keep the solution pH for 8. The support material (1.0 g) was added to this solution and the mixture was heated at 70 °C for 3 h with stirring. The water was then evaporated under reduced pressure at 45 °C with continuous stirring. The obtained raw catalyst was dried at 110 °C for 12 h and re-calcined at 500 °C (4.2 °C/min of temperature elevation rate) for 5 h to provide the catalyst 12wt%Mo(VI)/ZrO₂-SnO₂. For preparation of the other mixed oxides, aqueous TiCl₄ solution and Si(OEt)₄ were used as precursors of TiO₂ and SiO₂.

SI-2-2. General Procedure for Catalytic Reactions

SI-2-2-1. General Procedure for Batch Reactions

Before conduction the catalytic reactions, catalysts were pre-heated at 100 °C for 1 h under reduced pressure. Twenty-five mg of the pre-treated catalyst in a reaction vessel was charged by 225.3 mg (1.5 mmol) of 3-phenyl propionic acid, 107.2 mg (1.0 mmol) of *p*-toluidine, and 0.5 mL of chlorobenzene, and was equipped with a reflux condenser. This reaction mixture was heated at 125 °C to reflux for 18 h. After cooling to room temperature, solid catalyst was removed by filtration and resulting solid was washed by dichloromethane. This dichloromethane solution was washed by a potassium carbonate solution to remove unreacted carboxylic acid and concentrated to give a sample for ¹H-NMR, and the yield of products and conversion of *p*-anisidine were analyzed by ¹H-NMR using 1,3,5-trimethoxybenzene as an internal standard.

SI-2-2-2. Continuous-flow Dehydrative Amidation Reaction with a Single Pumping System

A pre-heated 5.5 g of catalyst was mixed well with 10 g of celite in a screw vial and was filled in a 10 mm (*id*) x 300 mm (*L*) stainless column with stainless filters on both column ends. The both ends of this column reactor were sealed with an appropriate one-way column cap. One of the end (inlet end) was equipped with 1.0 mm (*id*) PTFE tube with an appropriate fitting tools and connected with a plunger pump, and from the other side of column end (outlet end) a similar tubing was connected to a receiver flask through a back pressure regulator. Before starting the reactions, an appropriate solvent was flowed to immerse its content for at least 1 h, and then, the column heater was turned on to raise its temperature to the desired. From a weight balance between the column soaked with a solvent and the column before feeding a solvent, we can know the inner void volume of the present column reactor to 19.5 mL. After confirming the pressure monitored at the outlet of plunger pimp was raised to 0.2–0.5 MPa, the solvent flow was replaced to the combined substrate solution, and then started the reaction at 0.03 mL/min setting flow rate. As mentioned in the main text, an appropriate incubating period is needed to reach the reaction to steady state, therefore we started to collect samples which used for determination of the yield 12–15 h after starting flow. Details are provided in a later part of this Supporting Information, in most cases of this study, a single sample for yield determination was prepared by collecting outlet solution for 2 hours. When we presented them in graph for the main text, they are plotted as a yield corresponded the midpoint of the sampling period. To isolate the product form outlet solution, preparative TLC was performed for the crude sample.

The following is a typical experimental procedure modeled on the reaction between 3-phenylpropionic acid (**1**) and *p*-toluidine (**2**). 5.5 Gram of the Mo-modified mixed metal oxide catalyst was placed in a screw vial and well mixed with 10 g of Celite. The mixture was packed into 10 mm

(*inner diameter*) x 300 mm (*length*) stainless pipe (column) with stainless filters on both pipe ends. One-way column ends were mounted for pathing through fluids. A 1/16-inch OD (*outer diameter*) stainless tube was attached to one column end using appropriate fittings and ready for preheating. The tube was connected to the outlet of a plunger pump for liquid transfer. The other column end was fitted with 1/16-inch (*od*) PTFE tubing, which was inserted through a back pressure regulator (BPR) into a receiver flask. To this column reactor toluene was flowed to rinse for 1 h at 0.3 mL/min of flow rate, and then the column reactor and the inlet tube were heated at the desired temperature with aluminum heating blocks. A chlorobenzene solution containing 0.1 M of **2** and 0.15 M of **1** was prepared in a reservoir flask, the rinse solvent was replaced to the substrate solution, and then it was flowed by a plunger pump at 0.03 mL/min of flow rate. The BPR was adjusted so that the back pressure measured at the column inlet stabilized in the range of 0.2–0.5 MPa. A void volume of the reactor can be estimated by calculating the weight difference between the reactor filled with a solid material and the column reactor filled with solid and solvent and after sufficient solvent transfer. Based on this void volume, the residence time on the present column reactor was around 11–12 h. Sufficient stabilization time was allowed to approximate plug flow conditions and then the resulting outlet solution was sampled. Specifically, sampling was started after 15–17 hours, which is around 1.5 times the expected residence time. Although sampling periods varies, the plots of figures in the main text or in this SI are represented as average yields during each sampling period. Details of sampling are provided in this SI. The average flow rate during the sampling period can be calculated from the amount of outlet solution obtained by sampling for a predetermined period. If it is significantly different from the set value of 0.03 mL/min, it can be considered that an error has occurred in the pump or flow path. For determination of yield and conversion, the outlet solution was washed with 0.2 M NaHCO₃ aq. and water to remove an unreacted carboxylic acid. After removing organic solvents and volatile materials by evaporation of the resulting reaction mixture, the residue was analyzed by ¹H-NMR or GC, and for an analysis by ¹H-NMR, 1,3,5-trimethoxybenzene was used as an internal standard.

SI-2-2-3. Continuous-flow Dehydrative Amidation Reaction with a Two Pumping System

The following is a typical experimental procedure for several substrate combination, which gave an insoluble salt when mixed in chlorobenzene, modeled on the reaction between 3-phenylpropionic acid (**1**) and morpholine. As following the previous procedure, 5.5 g of the Mo-modified mixed metal oxide catalyst was placed in a screw vial and well mixed with 10 g of Celite. The mixture was packed into 10 mm (*id*) x 300 mm (*l*) stainless column with stainless filters on both pipe ends. One-way column ends were mounted for pathing through fluids. A 1/16-inch OD (*outer diameter*) stainless tube was attached to one column end using appropriate fittings and ready for preheating, and in front of the preheating zone, T-shape mixer was equipped. To the other two ports of the mixer PTFE tubes connected with plunger pumps were inserted. The other column end was fitted with 1/16-inch (*od*)

PTFE tubing, which was inserted through a back pressure regulator (BPR) into a receiver flask. To this column reactor toluene was flowed to rinse from both pumps for 1 h at 0.3 mL/min of combined flow rate, and then the column reactor and the inlet tube were heated at the desired temperature with aluminum heating blocks. A chlorobenzene solution containing 0.1 M of morpholine and predetermined amount of octadecane, an internal standard for determination of actual flow rate of morpholine, a chlorobenzene solution containing 0.15 M of **1** and predetermined amount of hexadecane, an internal standard for determination of actual flow rate of **1**, were independently prepared in reservoir flasks. The rinse solvents were replaced to the substrate solutions, and they were flowed by the plunger pumps at 0.015 mL/min of each flow rate. The BPR was adjusted so that the back pressure measured at the column inlet stabilized in the range of 0.2–0.5 MPa. A void volume of the reactor can be estimated by calculating the weight difference between the reactor filled with a solid material and the column reactor filled with solid and solvent and after sufficient solvent transfer. Based on this void volume, the residence time on the present column reactor was around 12 h. Sufficient stabilization time was allowed to approximate plug flow conditions and then the resulting outlet solution was sampled. Specifically, sampling was started after 17 hours, which is around 1.5 times the expected residence time. As already mentioned in the former, although sampling periods varies, the plots of figures in the main text or in this SI are represented as average yields during each sampling period. Details of sampling are provided in this SI.

The desired stoichiometry is realized when the flow rates of the two substrate solutions were the same. However, it is somewhat difficult to control precisely. Since the yield is greatly affected by the stoichiometry of the carboxylic acid to the amine, in this study, we added an internal standard substance to each of the two substrate solutions, sampled for a certain period, and determined how much they were contained in the outlet solution. Stoichiometry of the acid against the amine are calculated by using these data. Although tables in this SI shows the yield together with the determined stoichiometric ratio, the set value of 1.5 eq. is described in the main text for the sake of simplification.

For determination of yield and conversion, the outlet solution was washed with 0.2 M NaHCO₃ aq. and water to remove an unreacted carboxylic acid. After removing organic solvents and volatile materials by evaporation of the resulting reaction mixture, the residue was analyzed by ¹H-NMR or GC, and for an analysis by ¹H-NMR, 1,3,5-trimethoxybenzene was used as an internal standard.

SI-2-2-4. Continuous-flow Catalytic Amidation between Decanoic Acid (6) and Diethanolamine (5)

Following to the previous standard single-pump flow amidation protocol, continuous-flow amidation was performed using 1.5 eq of diethanolamine (**5**) and the carboxylic acid **6**. Since the product and the amine are water-soluble and emulsify when contained in high concentrations, washing

with aqueous solutions were not performed in work-up processes, and the amine removal using silica gel was utilized as a purification protocol; a 3 mL portion was taken from sample solutions collected in each period, chlorobenzene was evaporated. A 3 g of carboxylic acid-modified silica gel was added, shaken well, and then allowed to stand for overnight. After dilution with ethyl acetate, the solution was filtered and the yield was determined using $^1\text{H-NMR}$ using 1,1,2,2-tetrachloroethylene as an internal standard after solvent removal. This procedure could remove the amine and the crude sample contains only the product amide and the starting carboxylic acid.

SI-3. Physicochemical Evaluation of Mo(VI)/ZrO₂-SnO₂ Catalyst Material

Table S1. Results of ICP-AES elemental analysis and summary of NH₃-probed TPD measurement

ICP-AES		NH ₃ -TPD	
Mo	0.94 mmol/g	Desorption Temp.	210–360 °C
Zr	2.97 mmol/g	Total Acid Amount	0.072 mmol/g
Sn	2.92 mmol/g		
Zr/Sn	1.0		

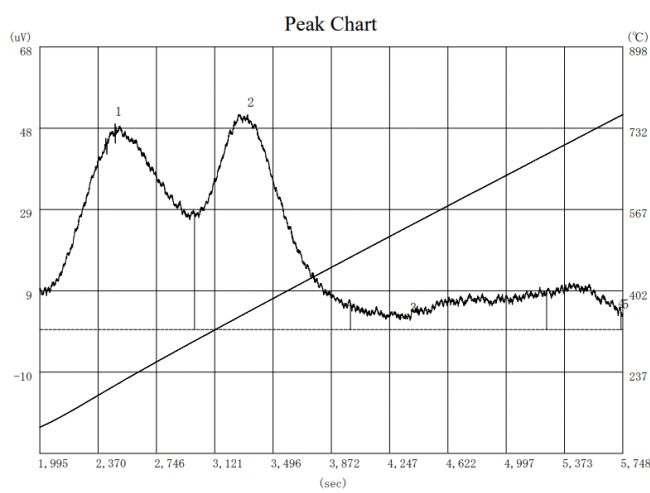


Figure S1. NH₃-TPD profile of 12wt%Mo(VI)/ZrO₂-SnO₂

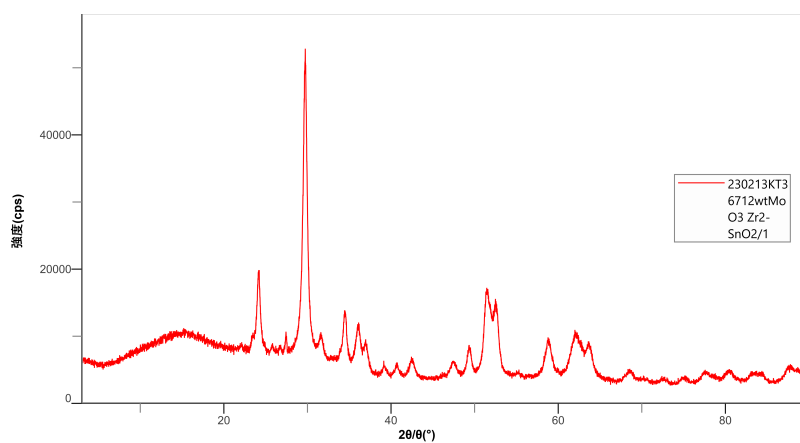


Figure S2. XRD pattern of 12wt%Mo(VI)/ZrO₂-SnO₂

Additional information on total acid amount for the other catalysts

Table S2. Total acid amount of the selected catalysts

Catalyst	Total Acid Amount
6wt% Mo(VI)/ZrO ₂ -SnO ₂	0.068 mmol/g
12wt% Mo(VI)/ZrO ₂ -SnO ₂	0.072 mmol/g
25wt% Mo(VI)/ZrO ₂ -SnO ₂	0.129 mmol/g
25wt% Mo(VI)/TiO ₂ -SiO ₂	0.376 mmol/g

The total acid amount for Mo(VI)/ZrO₂-SnO₂ seemed to be corresponded to the amount of Mo loading; however, it should be noted that the difference in quantity seen here is hardly reflected in the difference in activity. In addition, although the amount of 25wt%Mo(VI)/TiO₂-SiO₂ was sufficiently large, its activity was almost the lowest among tested (Table 1 in the main text). It seemed to be difficult to conclude the amount of total acid site was responsible for the catalytic performance.

In the following sections, regarding the presentation of additional information, experimental results those can be seen in the main text are indicated in italics, and the locations that can be confirmed in the main text are specified.

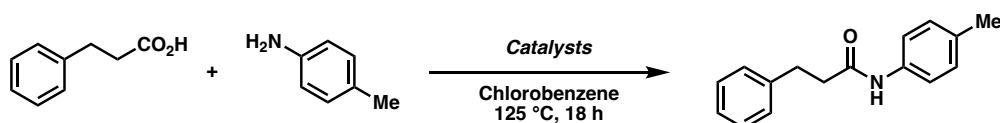
SI-4. Catalyst Evaluation under Batch Conditions

SI-4-1. General Scope of the Catalysis for Batch Amidation Conditions

SI-4-1-1. Survey of Reaction Conditions in Batch Amidation Reaction of 3-Phenylpropionic acid and *p*-Toluidine

After finding potential catalysis of Mo-modified mixed metal oxide composite for dehydrative amidation between 3-phenylpropionic acid and *p*-anisidine as shown in Table 1 of the main text (entries 1–4), we started deep investigations in its catalysis for the amidation reaction in batch system before moving to continuous-flow examination.

Table S3. Investigation in catalytic activities of Mo-modified mixed metal oxides

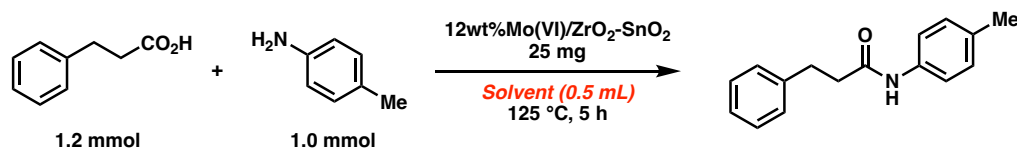


Entry	Corresponding Entry in Table 1 ^a	Catalyst		Amine Conc. [M]	Acid Conc [equiv.]	Yield [%] ^b
			Usage [mg/mmol]			
<i>SI</i> ^c	<i>Entry 4</i>	25wt%Mo(VI)/TiO ₂ -ZrO ₂	50	1.00	1.05	37
S2		25wt%Mo(VI)/TiO ₂ -ZrO ₂	50	1.00	1.05	72
S3		12wt%Mo(VI)/TiO ₂ -ZrO ₂	50	1.00	1.05	74
S4		6wt%Mo(VI)/TiO ₂ -ZrO ₂	50	1.00	1.05	69
S5		25wt%Mo(VI)/TiO ₂ -ZrO ₂	50	0.25	1.05	37
S6		25wt%Mo(VI)/TiO ₂ -ZrO ₂	50	0.50	1.05	65
S7		25wt%Mo(VI)/TiO ₂ -ZrO ₂	50	2.00	1.05	86
S8		25wt%Mo(VI)/TiO ₂ -ZrO ₂	25	0.50	1.05	33
S9		25wt%Mo(VI)/TiO ₂ -ZrO ₂	25	1.00	1.05	63
<i>SI10</i>	<i>Entry 5</i>	25wt%Mo(VI)/TiO ₂ -ZrO ₂	25	2.00	1.05	73
<i>SI11</i>	<i>Entry 6</i>	25wt%Mo(VI)/TiO ₂ -ZrO ₂	25	2.00	1.20	90
<i>SI12</i>	<i>Entry 7</i>	25wt%Mo(VI)/TiO ₂ -SiO ₂	25	2.00	1.20	72
<i>SI13</i>	<i>Entry 8</i>	25wt%Mo(VI)/TiO ₂ -SnO ₂	25	2.00	1.20	81
<i>SI14</i>	<i>Entry 9</i>	25wt%Mo(VI)/ZrO ₂ -SiO ₂	25	2.00	1.20	90
<i>SI15</i>	<i>Entry 10</i>	25wt%Mo(VI)/ZrO ₂ -SnO ₂	25	2.00	1.20	91
<i>SI16</i>	<i>Entry 11</i>	25wt%Mo(VI)/SiO ₂ -SnO ₂	25	2.00	1.20	87
<i>SI17</i>	<i>Entry 12</i>	12wt%Mo(VI)/ZrO ₂ -SnO ₂	25	2.00	1.20	93
<i>SI18</i>	<i>Entry 12</i>	12wt%Mo(VI)/ZrO ₂ -SnO ₂	25	2.00	1.50	99
<i>SI19</i>	<i>Entry 13</i>	6wt%Mo(VI)/ZrO ₂ -SnO ₂	25	2.00	1.20	84

^a The corresponding entry in Table 1 of the main text. ^b Determined by ¹H-NMR analysis. ^c The reaction was performed for 6 h.

SI-4-1-2. Investigation into Solvent Effects

Table S4. Effect of Solvents^a



Entry	Solvent	Yield [%] ^b
S20	Chlorobenzene	49
S21	1,2-Dichlorobenzene	52
S22	1,1,2,2-Tetrachloroethane	34
S23	Sulfolane	13
S24	<i>N</i> -Methylpyrrolidone	6
S25	<i>N,N</i> -Dimethylformamide	13
S26	<i>N,N</i> -Diethylacetoamide	11
S27	Acetophenone	13
S28	Acetylacetone	Trace
S29	1,4-Dioxane	24
S30	Diglyme ^c	24
S31	<i>p</i> -Xylene	46
S32	Chlorocyclohexane	39
S33	Acetonitrile	54
S34	Acetonitrile ^d	7
S35	Propionitrile	63
S36	Phenylacetonitrile	30
S37	Benzonitrile	39
S38	Isobutyronitrile	72
S39	Isobutyronitrile ^e	36

^a All reaction were performed in an oil bath heated at 125 °C equipped with a reflux condenser. ^b Determined by ¹H-NMR analysis. ^c The reaction was performed for 18 h. ^d The reaction was performed at 80 °C. ^e The reaction was performed at 105 °C.

In this study we mainly used chlorobenzene as a standard solvent for the amidation reaction. We additionally noticed *p*-xylene can be another option for solvent (Entry S31). Isobutyronitrile was also able to use for the reaction (Entry S38); in this case, we confirmed formation of the corresponding isobutylamide.

SI-4-1-3. Control Experiments and Related Information for Catalyst Evaluation

To confirm actual contribution of the present catalysis in amide formation reactions, we performed several control experiments for reactions between aliphatic carboxylic acid such as **1** and aliphatic amines. Regarding the reaction between **1** and *p*-anisidine, we have come to recognize that the effect of the catalyst in the reaction is remarkable from the results shown in Figure 2 of the main text.

Table S5. Difference in Yields between With or Without Catalyst

Entry	Amine	Catalyst	Temperature [°C]	Yield [%] ^a
S40		wo	150	68
S41		25 mg	150	79
S42		wo	130	34
S43	Pyrrolidine	25 mg	130	75
S44		wo	150	73
S45		25 mg	150	95
S46		wo	130	17
S47	"Hexylamine (4)"	25 mg	130	82

^a Determined by ¹H-NMR analysis.

Although clear differences between with or without using the catalyst could be observed in both cases when the reactions performed at 150 °C in chlorobenzene, the 10–20% difference in yields are not satisfactory and we aware the amidation reactions with aliphatic amines should be done at lower temperature. Fortunately, the reaction at 130 °C exhibited larger differences in yield, thus we decided to set 130 °C is the standard reaction temperature for reactions with aliphatic amines.

Table S6. Poisoning Effect of Basic Additives

Entry	Additive	Yield [%] ^a	Comment
S17	No	93	Appear in Table S2
S48	Pyridine	71	
	Pyridine	70–75	Approximate Value form Graph in ref. 3
S49	Triethylamine	80	
	Triethylamine	70–75	Approximate Value form Graph in ref. 3

^a Determined by ¹H-NMR analysis.

We also tested poisoning effects of strongly basic additives in this reaction system. The current acid-catalytic system requires tolerance toward basic substances because the reactions must be performed under the presence of large amount of amine substrate. Shimizu et al. indicated that their niobium solid acid possessed high base tolerance from poisoning experiments with several basic additives.³ Following this, we also tested the reaction under the conditions that 0.5 eq. of pyridine or triethylamine were added to the standard reaction medium to confirm to what extent our catalysts have similar functions. Although the yields are significantly dropped as comparing with those in the absence

of such additives, we could confirm that compatibility of the present catalyst is comparable to Nb_2O_3 and possessed much higher base-resistance than homogeneous Lewis acid ZrCl_4 .

We here provide information on the interaction of carboxylic acids (Lewis base) with catalysts (solid acid). Shimizu et al. disclosed that the high catalytic activity was reflected in the lower wavenumber shift of the C=O frequency³; however, our measurement by the usual IR of the mixture of the catalyst and the carboxylic acid, no significant shift was observed; 1709.5 cm^{-1} for n-caprylic acid and 1705.2 cm^{-1} for the acid-adsorbed 12wt%Mo(VI)/ ZrO_2 - SnO_2 . Unlike the Shimizu's research, it should be taken into account that our measurement was not conducted under mimicking the reaction conditions by employing in situ measurement manner. It also should be considered the reaction we should discuss was the liquid-phase continuous-flow reaction in the presence of large amount of strong base amines. This matter continues to be investigated in our laboratory.

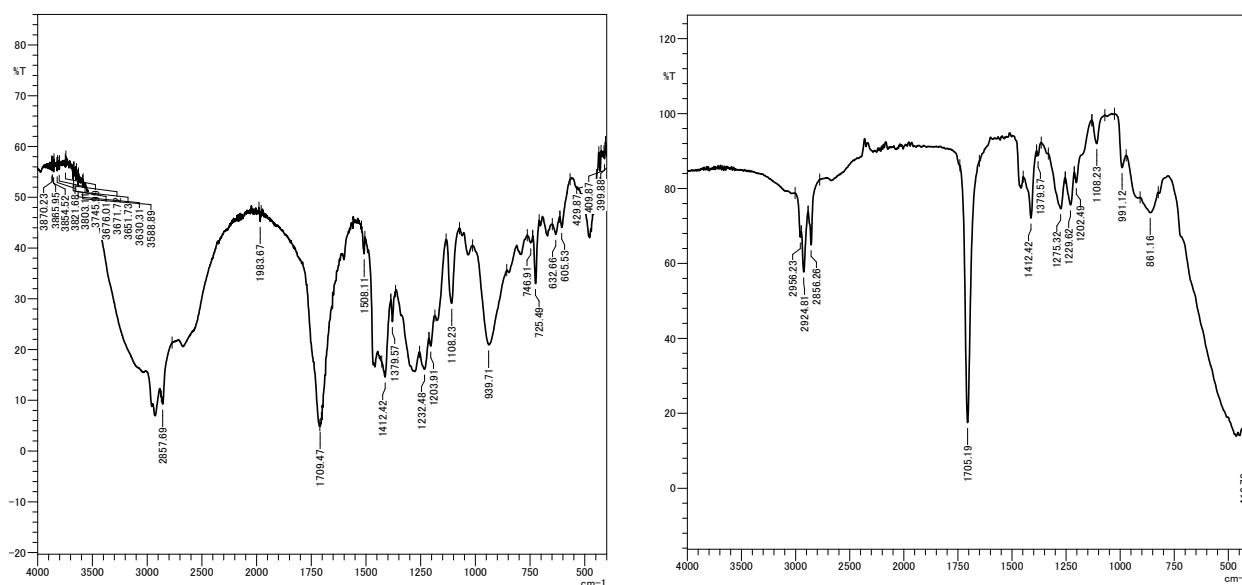


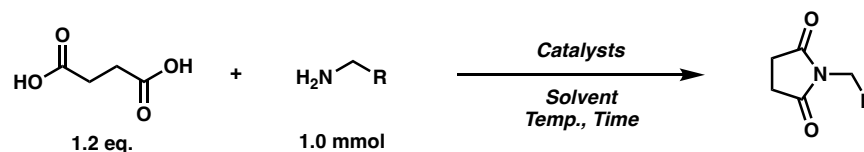
Figure S3. IR spectra of n-caprylic acid (neat) and the acid-adsorbed catalyst.

The acid-adsorbed catalyst sample was prepared by addition of 129.6 mg of n-caprylic acid to 220.2 mg of 12wt%Mo(VI)/ ZrO_2 - SnO_2 . Before the measurement, the mixture was well-mixed under argon atmosphere.

SI-4-2. General Scope of the Catalysis for Batch Cyclic Imide Formation Reactions

SI-4-2-1. Initial Investigations for Cyclic Imide Formation Reactions

Table S7. Succinimide Formation in the presence of Nb₂O₃ or the Mo-based Catalyst



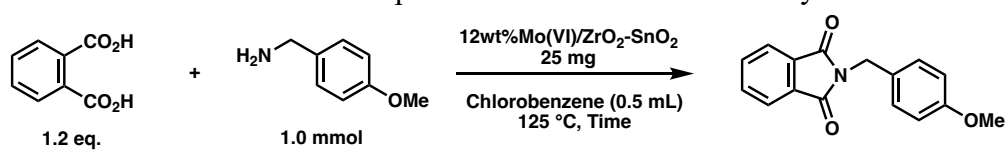
Entry	Catalyst	R in Amine	Solvent	Temp. [°C]	Time [h]	Yield [%] ^a
S50 ^b	Nb ₂ O ₅ ^c , 50 mg	ⁿ C ₇ H ₁₅	Hexane	70	10	NR
S51	12wt%Mo(VI)/ZrO ₂ -SnO ₂ , 25 mg	ⁿ C ₇ H ₁₅	Hexane	70	10	NR
S52	12wt%Mo(VI)/ZrO ₂ -SnO ₂ , 25 mg	ⁿ C ₇ H ₁₅	Chlorobenzene	125	10	78
S53	12wt%Mo(VI)/ZrO ₂ -SnO ₂ , 25 mg	Ph	Chlorobenzene	125	7	77
S54	12wt%Mo(VI)/ZrO ₂ -SnO ₂ , 25 mg	Ph	Chlorobenzene	125	12	91
S55	12wt%Mo(VI)/ZrO ₂ -SnO ₂ , 25 mg	2-Furfuryl	Chlorobenzene	125	7	75
S56	12wt%Mo(VI)/ZrO ₂ -SnO ₂ , 25 mg	2-Furfuryl	Chlorobenzene	125	12	60

^a Determined by ¹H-NMR analysis. ^b Following the literature (ref. yy), the reaction was performed using 1.0 eq. of succinic acid. ^c JRC-NBO2 calcinated at 500 °C for 5 h was used.

Following the previous literature protocol,⁴ we first tested succinimide formation with an aliphatic primary amine using hexane as a solvent under refluxing conditions (Table S5); however, we could not reproduce the literature result by our hand. Not only the acid but also amine did not dissolve in hexane at all, and no corresponding imide formation was observed. It was also observed that reagents including the catalyst separate from the solvent and adhere to the walls of the reaction vessel, and not participate in the reaction. This situation did not change when the reaction was performed at higher temperature, and just resulted in complete evaporation of hexane. Using chlorobenzene drastically improved the situation and the corresponding imide was obtained in 78% yield. Benzylamine and 2-furfuryl amine also gave the corresponding imide in good to high yield.

Cyclic imide formation with phthalic acid and benzylamine derivative also proceeded to give the corresponding phthalimide in high yield using chlorobenzene as a solvent (Table S6)

Table S8. Phthalimide Formation in the presence of the Mo-based Catalyst



Entry	Time [h]	Yield [%] ^a
S57	6	90
S58	12	90
S59	18	89
S60	24	88 ^b

^a Determined by ¹H-NMR analysis. ^b Isolated yield.

SI-5. Additional Information for Continuous-flow Investigation on Dehydrative Amidation

SI-5-1. Investigations on Dehydrative Amidation between Acid 1 and Amine 2

SI-5-1-1. Initial Investigations on Composite Catalyst Preparation

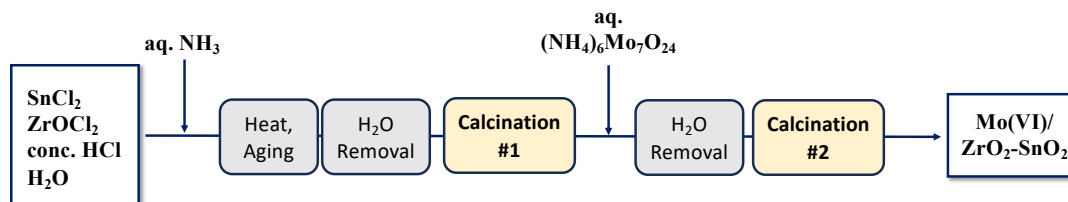


Figure S4. Outlook of preparation protocol for Mo(VI)-modified mixed metal oxides

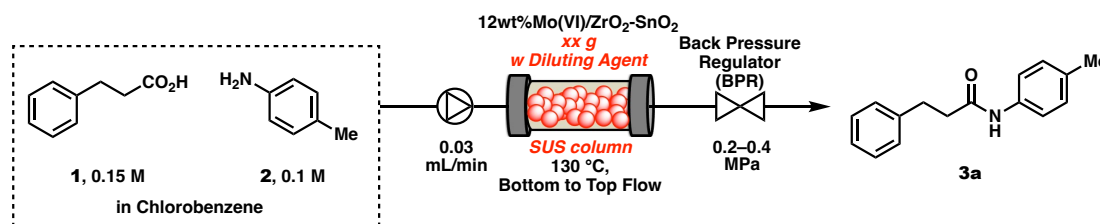
As described in *SI-2*, the present catalysts are prepared through two-times calcination steps (Figure S3). Our previous studies on these solid acids disclosed their catalytic abilities were greatly depended on preparation protocol, especially on calcination temperature of support materials, therefore we first checked effects of calcination temperature of both support preparation and impregnation steps.

Table S9. Effect of calcination temperature

Entry	Calcination Temperature ^a		v_1 [mL/min]	t_R^b [min]	WHSV ^c $\times 10^{-3}$ [h ⁻¹]	Yield [%] ^d
	#1	#2				
S57	400	400	0.027	482	12.9	17
S58	400	500	0.028	464	12.2	33
S59 ^e	500	500	0.030	433	13.1	31
S60	700	500	0.027	482	12.9	17

^a See Figure S4. ^b Residence time; obtained from actual flow rate v_1 and the void volume of the reactor column 13 mL. ^c Weight-hourly-space-velocity based on the product **3a**. ^d Yield of the sample collected 12 h after starting. Determined by ¹H-NMR analysis. ^e The reaction was performed at 145 °C.

Based on the results shown in Table S7, we decided to use the catalyst prepared as following Entry 59's condition for following investigations. We also performed several optimization studies for the flow system as shown in Table S8. Although the yield of S64 was lower than those of S63 and S65, we decided to perform following investigation at 150 °C to keep reproducibility.

Table S10. Effects of catalyst dosage, diluting agent, and column size.

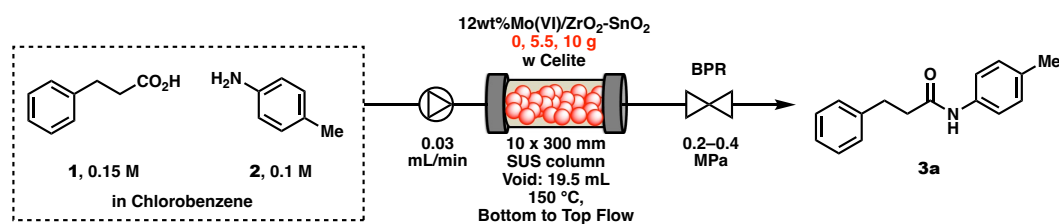
Entry	Reactor (Void [mL])	Catalyst Dosage [g]	Diluting Agent	t_R^a [min]	WHSV ^b x 10 ⁻³ [h ⁻¹]	F/V ^c [mmol/h dL]	Yield [%] ^d
S61	10 x 200 (13.0)	3.0	Celite	433	14.4	1.15	31
S62	10 x 200 (13.0)	5.5	Celite	433	7.8	1.15	46
S63	10 x 300 (19.5)	5.5	Celite	650	7.8	0.76	63
S64 ^e	10 x 300 (19.5)	5.5	Celite	650	7.8	0.76	58
S65 ^f	10 x 300 (19.5)	5.5	Celite	650	7.8	0.76	65
S66	10 x 300 (19.5)	5.5	MS 3A	650	7.8	0.76	11
S67	10 x 300 (19.5)	5.5	MgSO ₄	650	7.8	0.76	30

^a Residence time; obtained from actual flow rate v_1 and the void volume of the reactor column. ^b Weight-hourly-space-velocity based on the product **3a**. ^c Molar flow/reactor volume. ^d Yield of the sample collected 12 h after starting for entries S61 and S62. In the cases of entries S63–S67, samples for determination of their yields were collected after 16 h. Yields were determined by ¹H-NMR analysis. ^e The reaction was performed at 150 °C. ^f The reaction was performed at 170 °C.

SI-5-1-2. Details of the Continuous-flow Experiments for Synthesis of **3a**

In this section we disclosed details of the flow experiments shown in Figure 2 in the main text. Flow rate for these experiments were set to 0.03 mL/min and could be confirmed to be within the range of ± 0.005 even if there is some margin. As also mentioned in the main text, an appropriate incubating period is needed to reach the reaction to steady state, therefore we started to collect samples which used for determination of the yield 12–15 h after starting flow. In most cases of this study, a single sample for yield determination was prepared by collecting outlet solution for 2 hours. When we presented them in graph for the main text, they are plotted as a yield corresponded the midpoint of the sampling period.

Table S11. Details of data for Figure 2 of the main text



Entry	Catalyst Dosage [g]	Sampling Time [h]	Actual Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield [%] ^c
<i>S68-1^d</i>	0	17–19	0.030	–	0.76	7
<i>S68-2^d</i>	0	19–22	0.030	–	0.76	8
<i>S68-3^d</i>	0	26–28	0.030	–	0.76	7
<i>S69-1^e</i>	5.5	12–14	0.035	9.1	0.89	46
<i>S69-2^e</i>	5.5	14–16	0.035	9.1	0.89	43
<i>S69-3^e</i>	5.5	16–18	0.035	9.1	0.89	41
<i>S69-4^e</i>	5.5	18–20	0.035	9.1	0.89	40
<i>S69-5^e</i>	5.5	20–22	0.035	9.1	0.89	39
<i>S69-6^e</i>	5.5	22–34	0.035	9.1	0.89	37
<i>S69-7^e</i>	5.5	34–36	0.033	8.6	0.84	33
<i>S69-8^e</i>	5.5	36–38	0.033	8.6	0.84	33
<i>S69-9^e</i>	5.5	38–40	0.033	8.6	0.84	31
<i>S69-10^e</i>	5.5	40–42	0.033	8.6	0.84	33
<i>S69-11^e</i>	5.5	42–44	0.033	8.6	0.84	33
<i>S69-12^e</i>	5.5	44–46	0.033	8.6	0.84	33
<i>S69-13^e</i>	5.5	46–62	0.033	8.6	0.84	32
<i>S69-14^e</i>	5.5	62–64	0.033	8.6	0.84	38
<i>S69-15^e</i>	5.5	64–66	0.033	8.6	0.84	31
<i>S69-16^e</i>	5.5	66–68	0.033	8.6	0.84	29
<i>S69-17^e</i>	5.5	68–86	0.033	8.6	0.84	24
<i>S69-18^e</i>	5.5	86–90	0.033	8.6	0.84	25
<i>S69-19^e</i>	5.5	90–107	0.033	8.6	0.84	23
<i>S69-20^e</i>	5.5	107–111	0.033	8.6	0.84	22
<i>S69-21^e</i>	5.5	111–115	0.033	8.6	0.84	22
<i>S70-1^f</i>	10.0	14–16	0.031	4.5	0.79	57
<i>S70-2^f</i>	10.0	16–18	0.031	4.5	0.79	64
<i>S70-3^f</i>	10.0	18–20	0.031	4.5	0.79	63
<i>S70-4^f</i>	10.0	20–22	0.031	4.5	0.79	61
<i>S70-5^f</i>	10.0	22–24	0.031	4.5	0.79	61(58 ^g)

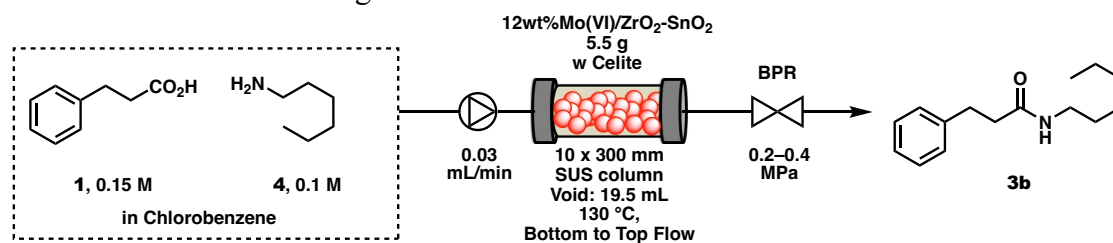
^a Weight-hourly-space-velocity based on the product **3a**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d Details of the blue plots in Figure 2 of the main text. ^e Details of the yellow plots in Figure 2 of the main text. ^f Details of the red plots in Figure 2 of the main text. ^g Isolated yield.

SI-5-2. Investigations on Dehydrative Amidation between Acid 1 and Amine 4

SI-5-2-1. Details of the Continuous-flow Experiments for Synthesis of 3b

In this section we disclosed details of the flow experiments shown in Figure 3 in the main text. Flow rate for these experiments were set to 0.03 mL/min and could be confirmed to be within the range of 0.031–0.033 mL/min. In most cases of this study, a single sample for yield determination was prepared by collecting outlet solution for 2 hours. When we presented them in graph for the main text, they are plotted as a yield corresponded the midpoint of the sampling period.

Table S12. Details of data for Figure 3 of the main text^a



Entry	Sampling Time [h]	Actual Flow Rate [mL/min]	Yield [%] ^b	TON ^c	Estimated Total Amount of 3b [g]
S71-1	17–18	0.031	53	0.25	0.02
S71-2	18–19	0.031	56	0.51	0.05
S71-3	19–20	0.031	59	0.78	0.07
S71-4	20–24	0.033	62	1.94	0.17
S71-5 ^d	24–36	0.033	75	6.19	0.56
S71-6	36–48	0.033	82	11.18	1.00
S71-7 ^e	48–60	0.033	84	15.90	1.43
S71-8	60–66	0.033	83	18.22	1.64
S71-9	66–72	0.033	83	20.54	1.85
S71-10	72–84	0.033	84	25.26	2.27
S71-11	82–90	0.033	82	27.57	2.48
S71-12	90–96	0.033	83	29.89	2.69
S71-13 ^f	96–108	0.033	84 (81 ^g)	34.60	3.11
S71-14	108–114	0.033	82	36.89	3.31
S71-15	114–120	0.033	81	39.17	3.52

^a WHSV based on the product 3b, 7.9–8.4 x 10⁻³ h⁻¹; F/V index, molar flow/reactor volume, 0.82 mmol/h dL. ^b Determined by ¹H-NMR analysis. ^c Based on the estimated total acid amount, 0.072 mmol/g shown in SI-2. ^d Same as the data shown in Entry 1-1 in Table 2 of the main text. ^e Same as the data shown in Entry 1-2 in Table 2 of the main text. ^f Same as the data shown in Entry 1-3 in Table 2 of the main text. ^g Isolated yield.

SI-5-2-2. Effects of Concentration for Flow Synthesis of 3b

To shorten an incubating time to reach steady state of yielding the desired amide, we tuned flow rate of the reaction from 0.03 mL/min to 0.06 mL/min for the first 12 h. The results obtained were shown as Entries 2–5 in Table 2 of the main text, and here the details are shown to compare the results in Table S10. In Table S10, the flow rate was constant 0.03 mL/min, and it can be seen from Figure S4 and Table S11 that the time to reach >80% yield was reduced from 36–48 hours to 24–36 hours.

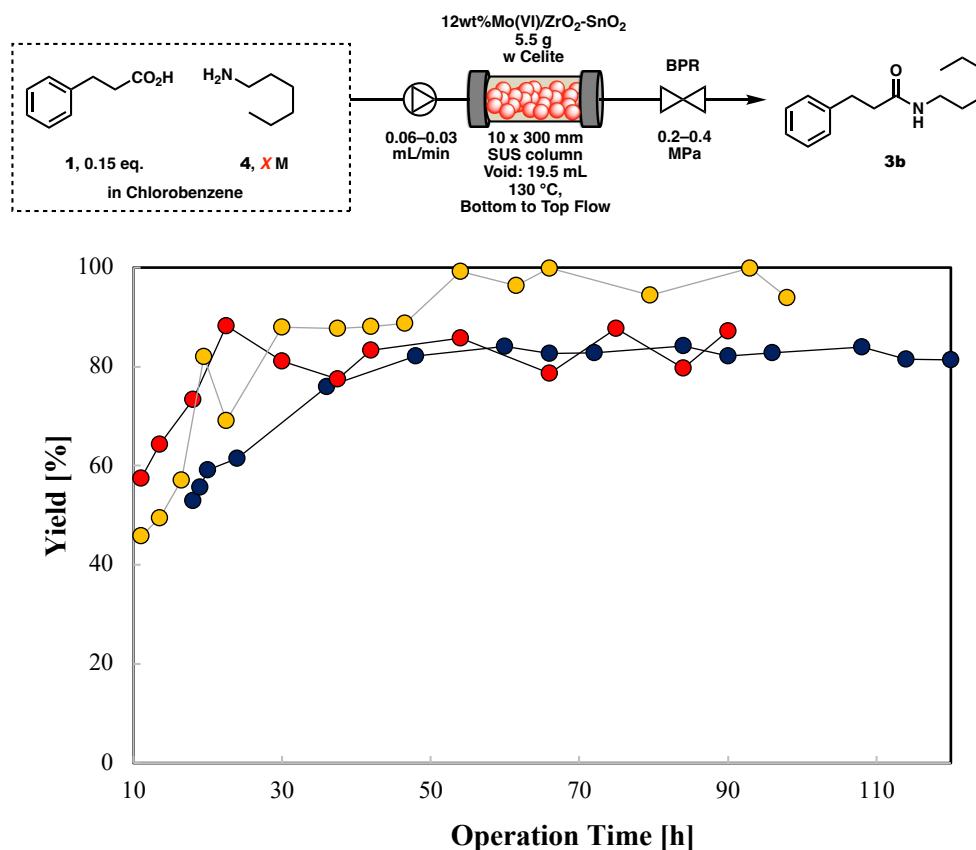


Figure S5. Continuous-flow reaction between acid **1** and amine **4**

Conditions are shown in the above scheme.

Dark blue, use of 0.1 M mother solution, flow rate was constant to 0.03 mL/min, the same data as Table S12 and Figure 2 of the main text, Entry S71.

Red, use of 0.1 M mother solution, flow rate of the initial 12 h was 0.06 mL/min, and then reduced to 0.03 mL/min, Entry S72.

Yellow, use of 0.05 M mother solution, flow rate of the initial 12 h was 0.06 mL/min, and then reduced to 0.03 mL/min, Entry S73.

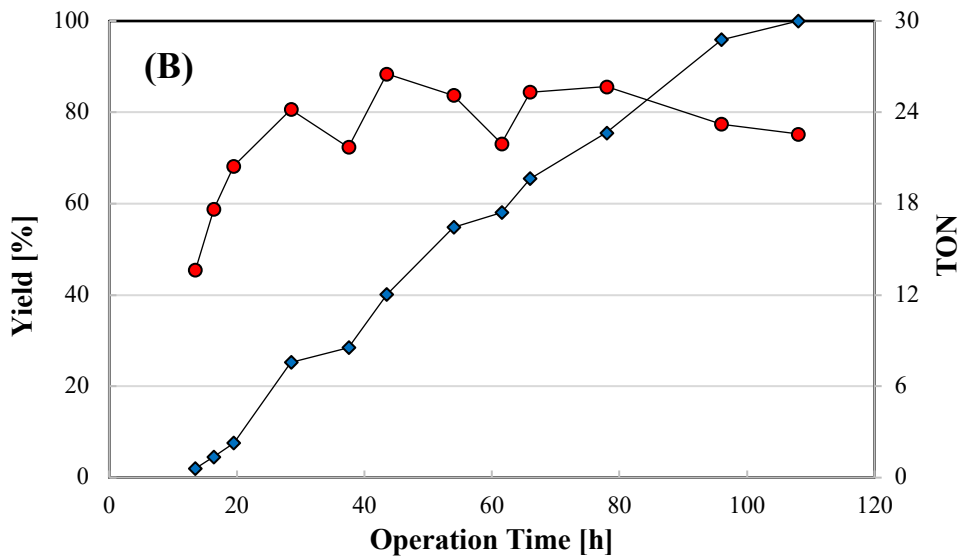
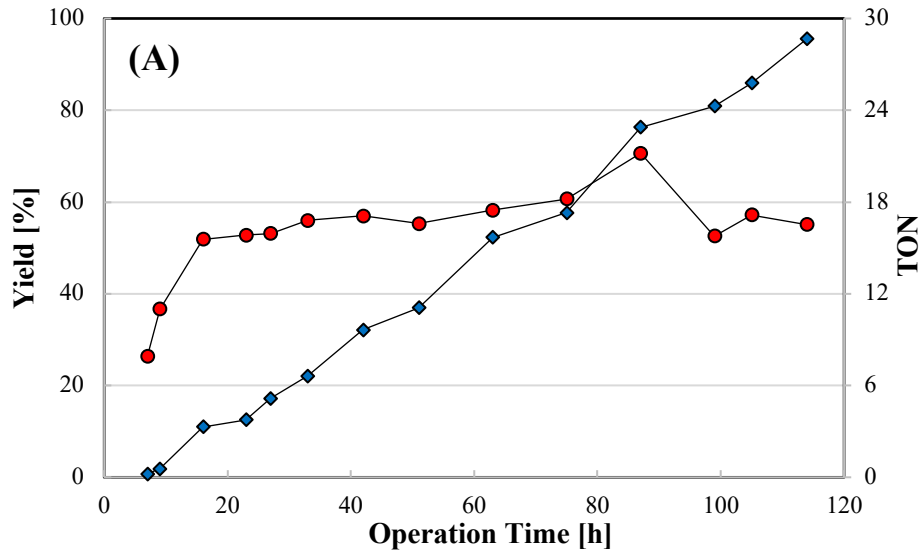
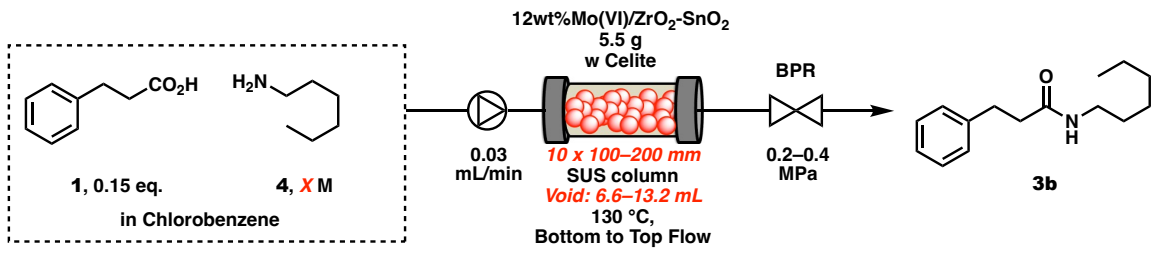
Table S13. Details of Continuous-flow reaction between acid **1** and amine **4**^a

Entry	Corresponding Entry in Table 2 ^b	Sampling Time [h]	Actual Flow Rate [mL/min]	Yield [%] ^c	TON ^d	Estimated Total Amount of 3b [g]
S72-1		10–12	0.060	57	1.82	0.17
S72-2		12–15	0.032	64	3.27	0.30
S72-3		15–21	0.032	73	6.18	0.57
S72-4		21–24	0.032	88	7.64	0.71
S72-5	<i>Entry 2-1</i>	24–36	0.032	81	13.45	1.24
S72-6		36–39	0.032	77	14.90	1.38
S72-7		39–45	0.032	83	17.82	1.65
S72-8		45–63	0.032	86	26.55	2.45
S72-9		63–69	0.032	79	29.45	2.72
S72-10		69–81	0.032	88	35.27	3.26
S72-11	<i>Entry 2-2</i>	81–87	0.032	80	38.18	3.53
S72-12		87–93	0.032	87	41.09	3.80
S73-1		10–12	0.060	46	0.91	0.08
S73-2		12–15	0.030	49	1.59	0.15
S73-3		15–18	0.030	57	2.27	0.21
S73-4		18–21	0.030	82	2.95	0.27
S73-5		21–24	0.030	69	3.64	0.34
S73-6	<i>Entry 3-1</i>	24–36	0.030	88	6.36	0.59
S73-7		36–39	0.030	88	7.05	0.65
S73-8		39–45	0.030	88	8.41	0.78
S73-9		45–48	0.030	89	9.09	0.84
S73-10		48–60	0.030	99	11.82	1.09
S73-11		60–63	0.030	96	12.50	1.16
S73-12		63–69	0.030	99	13.86	1.28
S73-13	<i>Entry 3-2</i>	69–90	0.030	94	18.64	1.72
S73-14		90–96	0.030	99	20.00	1.85
S73-15		96–100	0.030	94	20.91	1.93

^a Entry S72: **4**, 0.1 M; WHSV based on the product **3b**, $8.1 \times 10^{-3} \text{ h}^{-1}$; F/V index, molar flow/reactor volume, 0.82 mmol/h dL. Entry S73: **4**, 0.05 M; WHSV based on the product **3b**, $3.8 \times 10^{-3} \text{ h}^{-1}$; F/V index, molar flow/reactor volume, 0.38 mmol/h dL. ^b The corresponding entry in Table 2 of the main text. ^c Determined by ¹H-NMR analysis. ^d Based on the estimated total acid amount; 0.072 mmol/g shown in *SI-2*.

SI-5-2-3. Effects of Reactor Column Size for Flow Synthesis of 3b

In this section we disclosed details of the flow experiments shown in Table 2, entries 6–8 in the main text. Flow rate for these experiments were constant 0.03 mL/min and could be confirmed to be within the range of 0.026–0.029 mL/min. Flow experiments with smaller reactor columns containing 5.5 g of the catalyst were carried out using substrate solutions of 0.1 M or 0.4 M of amine **4**.



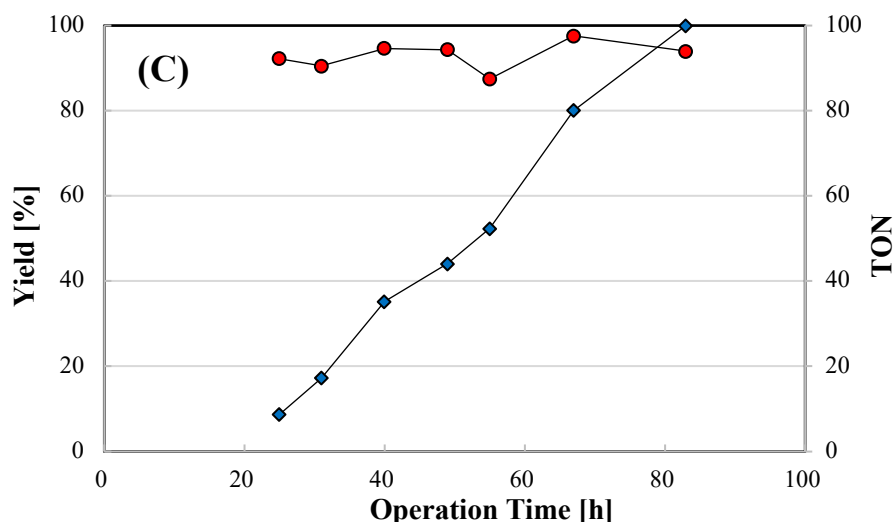


Figure S6. Continuous-flow reaction between acid **1** and amine **4** with different reactors. (A) 10 x 100 mm column reactor and 0.1 M solution of **1** was utilized, Entry S74. (B) 10 x 200 mm column reactor and 0.1 M solution of **1** was utilized, Entry S75. (C) 10 x 200 mm column reactor and 0.4 M solution of **1** was utilized, Entry S76. The other conditions are shown in the above scheme.

Red, Yield of **4**. Blue, TON based on the estimated acid amount of the catalyst.

Table S14. Details of Continuous-flow reaction between acid **1** and amine **4** shown in Figure S6^a

Entry	Corresponding Entry in Table 2 ^b	Sampling Time [h]	Yield [%] ^c	TON ^d	Estimated Total Amount of 3b [g]
S74-1		6–8	26	0.23	0.02
S74-2		8–10	37	0.55	0.05
S74-3		10–22	52	3.29	0.30
S74-4		22–24	53	3.75	0.35
S74-5		24–30	53	5.15	0.48
S74-6		30–36	56	6.63	0.61
S74-7	Entry 7-1	36–48	57	9.63	0.89
S74-8		48–54	55	11.09	1.02
S74-9		54–72	58	15.69	1.45
S74-10		72–78	61	17.29	1.60
S74-11		78–86	71	22.88	2.11
S74-12		96–102	53	24.27	2.24
S74-13		102–108	57	25.77	2.38
S74-14	Entry 7-1	108–120	55	28.68	2.65
S75-1		12–15	45	0.60	0.06
S75-2		15–18	59	1.37	0.13
S75-4		18–21	68	2.27	0.21
S75-5		21–36	81	7.59	0.70
S75-6		36–39	72	8.54	0.79
S75-7		39–48	88	12.04	1.11
S75-8	Entry 6-1	48–60	84	16.45	1.52

S75-9		60–63	73	17.42	1.61
S75-10		63–69	84	19.64	1.81
S75-11		69–87	86	22.65	2.09
S75-12		87–105	77	28.78	2.66
S75-13		105–111	75	30.00	2.84
S76-1		22–28	92	8.72	0.81
S76-2		28–34	91	17.28	1.60
S76-3		34–46	95	35.17	3.25
S76-4	Entry 8-1	46–52	94	44.09	4.07
S76-5		52–58	87	52.36	4.84
S76-6		58–76	98	80.04	7.40
S76-7	Entry 8-2	76–90	94	100.76	9.31

^a Entry S74: 10 mm (*id*) x 100 mm (*L*) stainless column was used. **4**, 0.1 M; Flow Rate, 0.029 mL/min; WHSV based on the product **3b**, $7.4 \times 10^{-3} \text{ h}^{-1}$; F/V index, molar flow/reactor volume, 2.22 mmol/h dL. Entry S75: 10 mm (*id*) x 200 mm (*L*) stainless column was used. **4**, 0.1 M; Flow Rate, 0.029 mL/min; WHSV based on the product **3b**, $7.4 \times 10^{-3} \text{ h}^{-1}$. F/V index, molar flow/reactor volume, 1.11 mmol/h dL. Entry S76: 10 mm (*id*) x 200 mm (*L*) stainless column was used. **4**, 0.4 M; Flow Rate, 0.026 mL/min; WHSV based on the product **3b**, $26.5 \times 10^{-3} \text{ h}^{-1}$. F/V index, molar flow/reactor volume, 3.97 mmol/h dL. ^b The corresponding entry in Table 2 of the main text. ^c Determined by ¹H-NMR analysis. ^d Based on the estimated total acid amount; 0.072 mmol/g shown in *SI-2*.

Although there was some variation, the use of the 10 x 200 reactor whose volume is 15.7 mL also achieved an average yield of 80%, which was almost the same as that of the larger 10 x 300 mm reactor. The residence time when using the 10 x 200 mm reactor was 440 min, which is significantly shorter than that of the 10 x 300 mm reactor, but it was confirmed that sufficient conversion of substrates to the product amide was taking place. Subsequent substrate scope study was performed by using the larger reactor, but the fact that the 10 x 200 mm reactor can be used comparably provides important information for scale-up production. High yields are also obtained when high concentration solutions are used. Although the use of a high-concentration solution imposes a heavy burden on the catalyst, it can be considered that the increased frequency of contact between substrates superior to this. By using a 0.4 M substrate solution and using the 10 x 200 mm reactor, this system could be implemented with a F/V index of 3.97 mmol/h dL and a WHSV of 0.03 h^{-1} , which gave the maximum 3.7 mmol/h dL of mole-based STY and 0.9 g/h dL for the amide **2b**.

SI-5-3. Details of Substrate Scope Studies

In this section we disclosed details of the flow experiments shown in Table 3, which displayed substrate scope of the present catalysis. Flow rate for these experiments were constant 0.03 mL/min, 10 x 300 mm reactor columns containing 5.5 g of the catalyst were used for these experiments. Substrate solutions of 0.1 M amines were generally utilized.

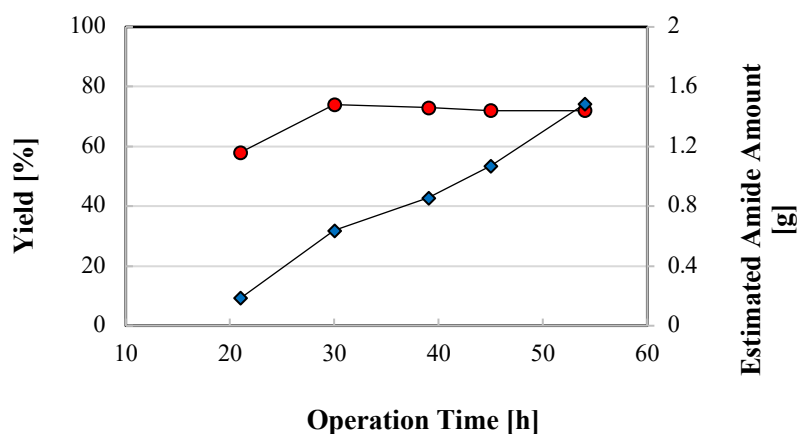
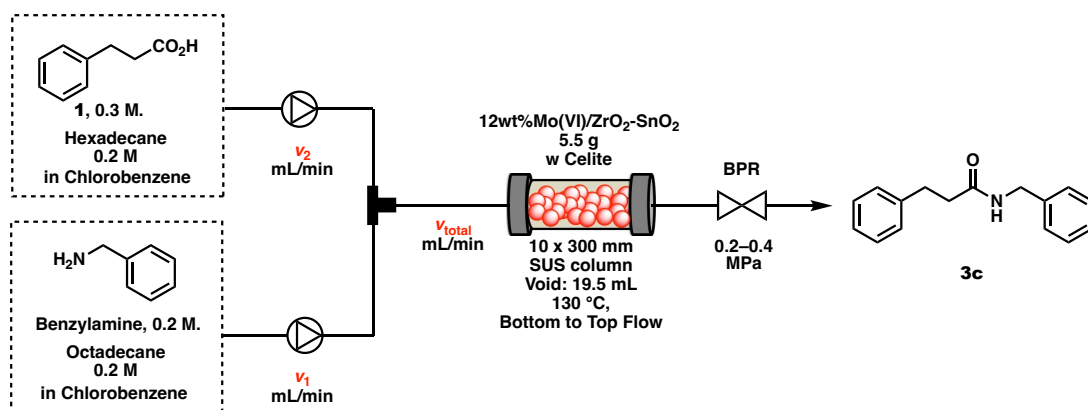


Figure S7. Continuous-flow synthesis of **3c**

Conditions are shown in the upper scheme. Details are described in Table S15

Red, Yield of **3c**. Blue, Estimated total amide amount produced.

Table S15. Details of Continuous-flow reaction shown in Figure S7

Entry	Sampling Time [h]	Flow Rate [mL/min]		Acid /Amine	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
		v_1	v_{Total}					
S77-1	18-24	0.0185	0.032	1.1	9.6	0.94	58	0.18
S77-2	24-36	0.0178	0.032	1.2	9.3	0.91	74 ^d	0.64
S77-3	36-42	0.0174	0.030	1.1	9.0	0.88	73	0.86
S77-4	42-48	0.0173	0.030	1.1	9.0	0.88	72(70 ^e)	1.07
S77-5	48-60	0.0166	0.030	1.2	8.7	0.85	72	1.48

^a Weight-hourly-space-velocity based on the product **3c**. ^b Molar flow/reactor volume. ^c Determined by GC analysis. ^d Suggesting 0.160 g/h dL of STY. ^e Isolated yield and suggesting 0.152 g/h dL of STY. The same results to that appear in Table 3 of the main text.

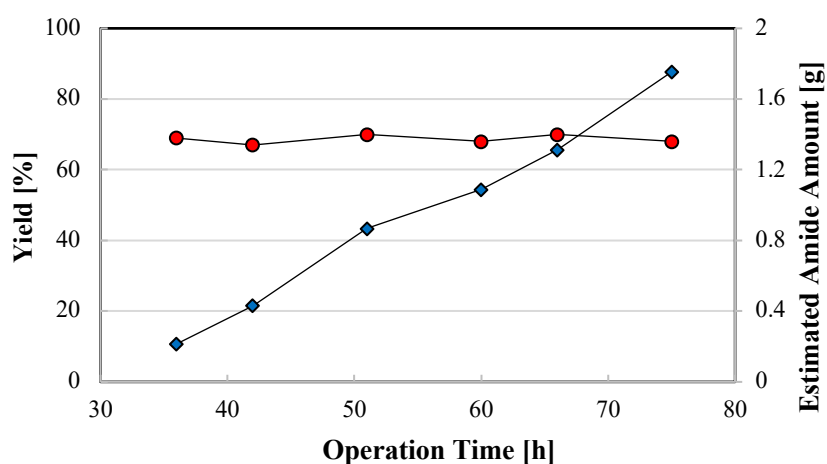
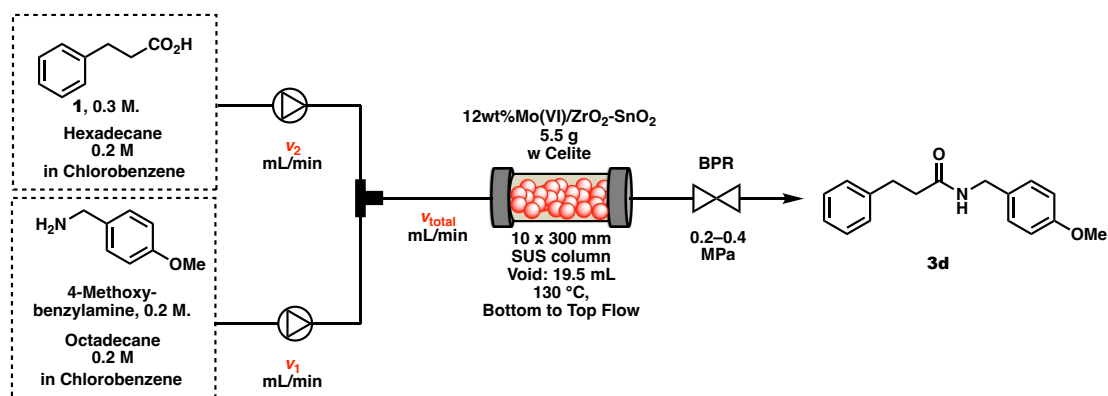


Figure S8. Continuous-flow synthesis of **3d**

Conditions are shown in the upper scheme. Details are described in Table S16

Red, Yield of **3d**. Blue, Estimated total amide amount produced.

Table S16. Details of Continuous-flow reaction shown in Figure S8

Entry	Sampling Time [h]	Flow Rate [mL/min]		Acid /Amine	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
		v_1	v_{Total}					
S78-1	33-39	0.0161	0.030	1.3	9.4	0.82	69	0.22
S78-2	39-45	0.0167	0.030	1.2	9.8	0.85	67	0.43
S78-3	45-57	0.0161	0.030	1.3	9.4	0.82	70	0.87
S78-4	57-63	0.0167	0.030	1.2	9.8	0.85	68	1.09
S78-5	63-69	0.0167	0.030	1.2	9.8	0.85	70(68 ^d)	1.31
S78-6	69-81	0.0167	0.030	1.2	9.8	0.85	68	1.75

^a Weight-hourly-space-velocity based on the product **3d**. ^b Molar flow/reactor volume. ^c Determined by GC analysis. ^d Isolated yield and suggesting 0.155 g/h dL of STY. The same results to that appear in Table 3 of the main text.

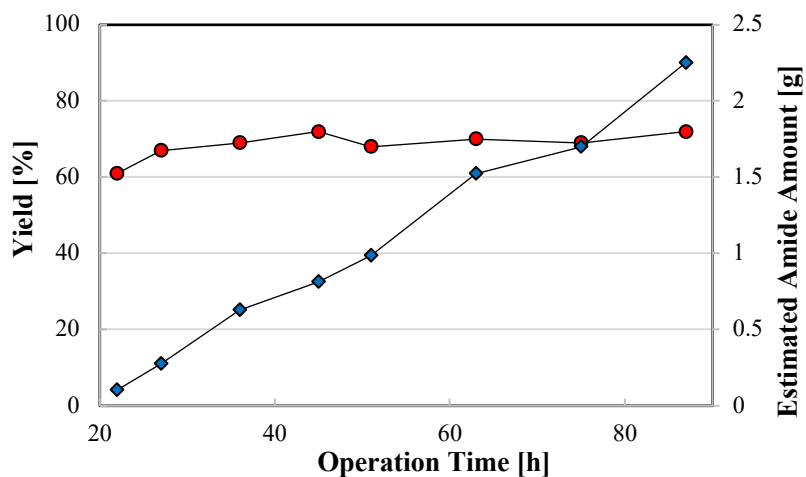
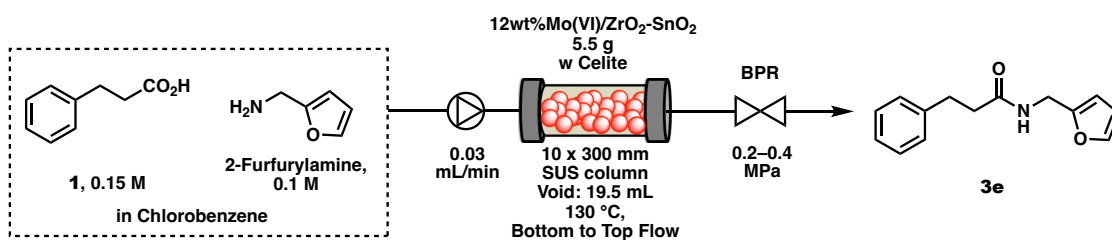


Figure S9. Continuous-flow synthesis of **3e**

Conditions are shown in the upper scheme. Details are described in Table S17

Red, Yield of **3e**. Blue, Estimated total amide amount produced.

Table S17. Details of Continuous-flow reaction shown in Figure S9

Entry	Sampling Time [h]	Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S79-1	20–24	0.031	7.8	0.79	61	0.10
S79-2	24–30	0.031	7.8	0.79	67	0.28
S79-3	30–42	0.031	7.8	0.79	69	0.63
S79-4	42–48	0.031	7.8	0.79	72 ^d	0.81
S79-5	48–54	0.031	7.8	0.79	68	0.99
S79-6	54–72	0.031	7.8	0.79	70(69 ^e)	1.52
S79-7	72–78	0.031	7.8	0.79	69	1.70
S79-8	78–96	0.031	7.8	0.79	72	2.25

^a Weight-hourly-space-velocity based on the product **3e**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d Suggesting 0.130 g/h dL of STY. ^e Isolated yield and suggesting 0.127 g/h dL of STY. The same results to that appear in Table 3 of the main text.

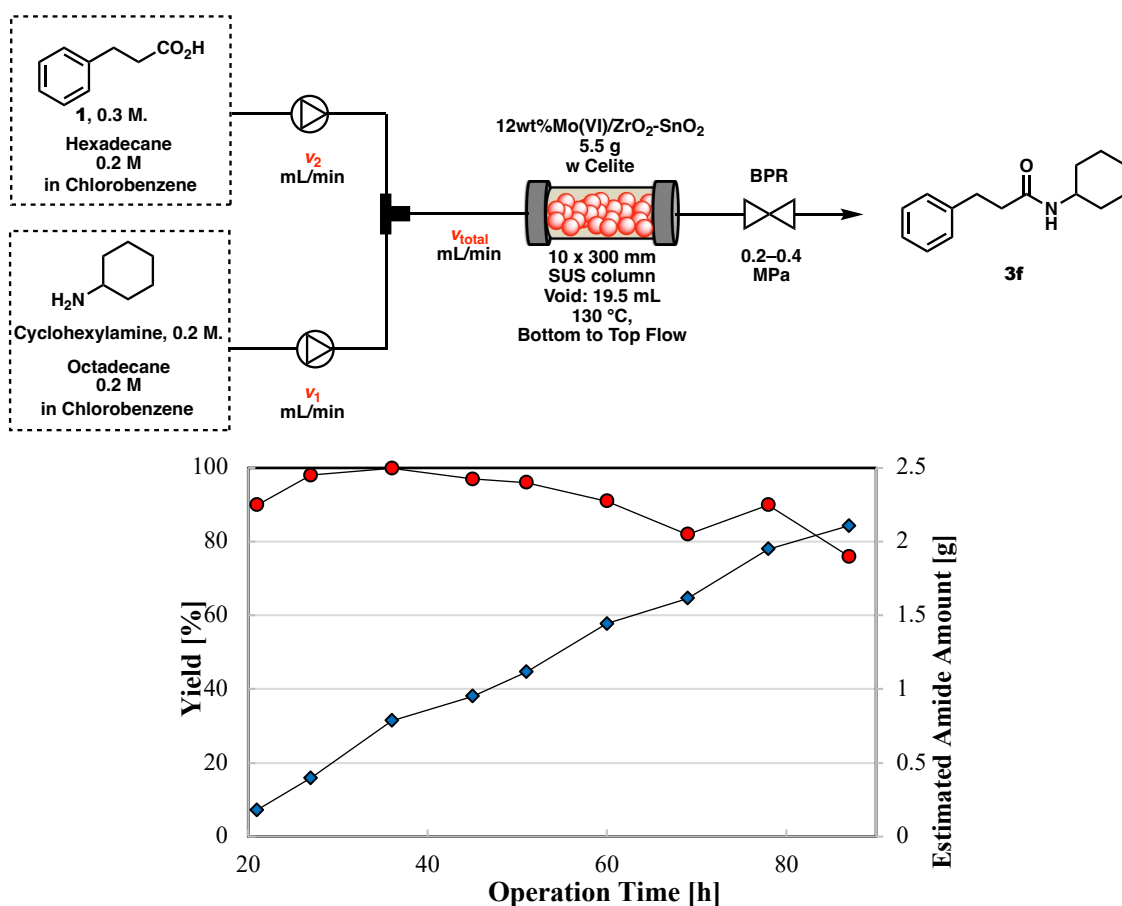


Figure S10. Continuous-flow synthesis of **3f**

Conditions are shown in the upper scheme. Details are described in Table S18
 Red, Yield of **3f**. Blue, Estimated total amide amount produced.

Table S18. Details of Continuous-flow reaction shown in Figure S10

Entry	Sampling Time [h]	Flow Rate [mL/min]		Acid /Amine	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
		v_1	v_{Total}					
S80-1	18–24	0.0121	0.029	2.1	6.1	0.62	90	0.14
S80-2	24–30	0.0133	0.031	2.0	6.7	0.68	98	0.51
S80-3	30–42	0.0116	0.031	2.5	5.9	0.59	>99 ^d	0.58
S80-4	42–48	0.0103	0.026	2.3	5.2	0.52	97	0.69
S80-5	48–54	0.0103	0.026	2.3	5.2	0.52	96	0.81
S80-6	54–66	0.0108	0.026	2.1	5.5	0.55	91	1.06
S80-7	66–72	0.0126	0.026	1.6	6.4	0.64	82(81 ^e)	1.20
S80-8	72–84	0.0111	0.026	2.0	5.6	0.57	90	1.45
S80-9	84–90	0.0126	0.026	1.6	6.4	0.64	76	1.60

^a Weight-hourly-space-velocity based on the product **3f**. ^b Molar flow/reactor volume. ^c Determined by GC analysis. ^d Suggesting 0.137 g/h dL of STY. ^e Isolated yield and suggesting 0.121 g/h dL of STY. The same results to that appear in Table 3 of the main text.

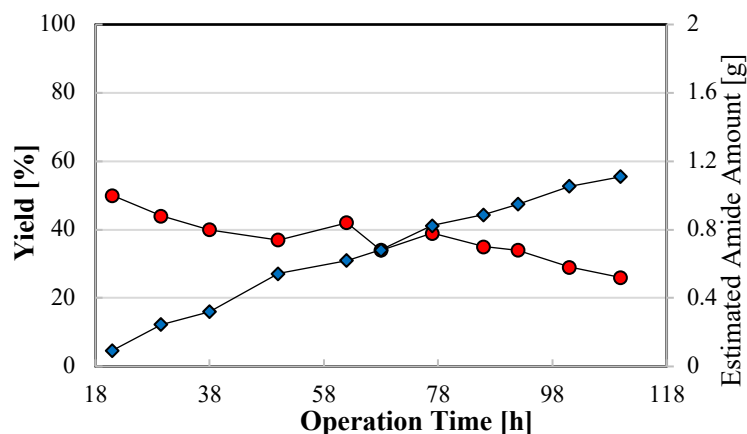
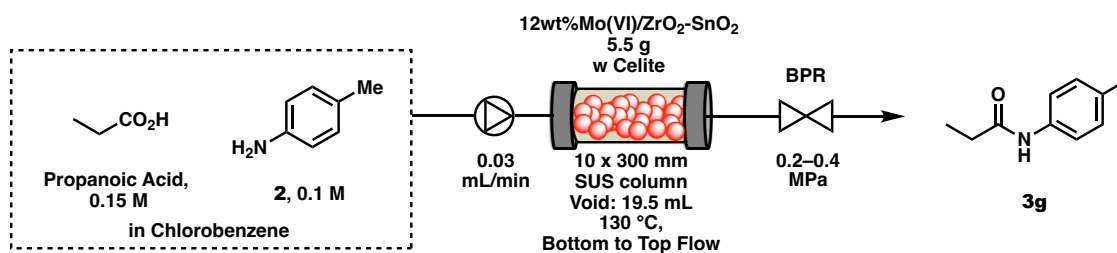


Figure S11. Continuous-flow synthesis of **3g**

Conditions are shown in the upper scheme. Details are described in Table S19

Red, Yield of **3g**. Blue, Estimated total amide amount produced.

Table S19. Details of Continuous-flow reaction shown in Figure S11

Entry	Sampling Time [h]	Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S81-1	18–24	0.032	5.7	0.82	50 ^d	0.09
S81-2	24–35	0.032	5.7	0.82	44	0.25
S81-3	35–41	0.032	5.7	0.82	40	0.32
S81-4	41–59	0.034	6.1	0.87	37	0.54
S81-5	59–65	0.031	5.5	0.79	42	0.62
S81-6	65–71	0.031	5.5	0.79	34	0.68
S81-7	71–83	0.031	5.5	0.79	39	0.82
S81-8	83–89	0.031	5.5	0.79	35	0.87
S81-9	89–95	0.031	5.5	0.79	34	0.95
S81-10	95–107	0.031	5.5	0.79	29(27 ^e)	1.05
S81-11	107–113	0.036	6.4	0.92	26	1.11

^a Weight-hourly-space-velocity based on the product **3g**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d Suggesting 0.067 g/h dL of STY. ^e Isolated yield and suggesting 0.037 g/h dL of STY. The same results to that appear in Table 3 of the main text.

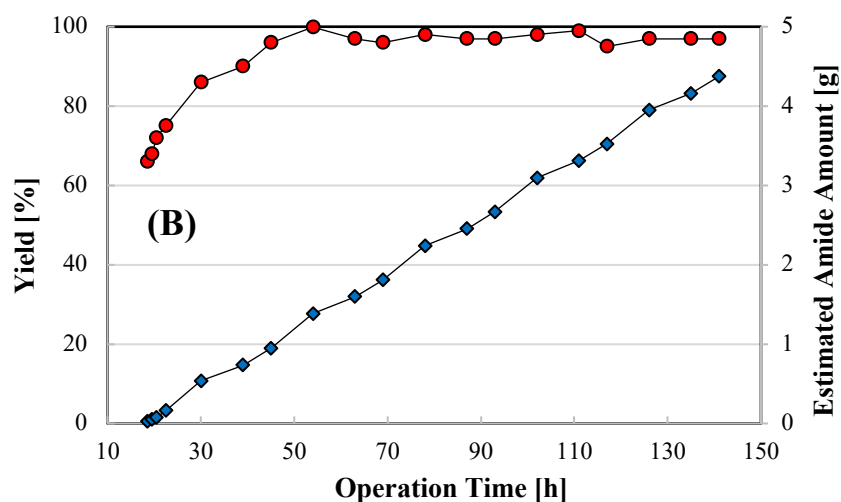
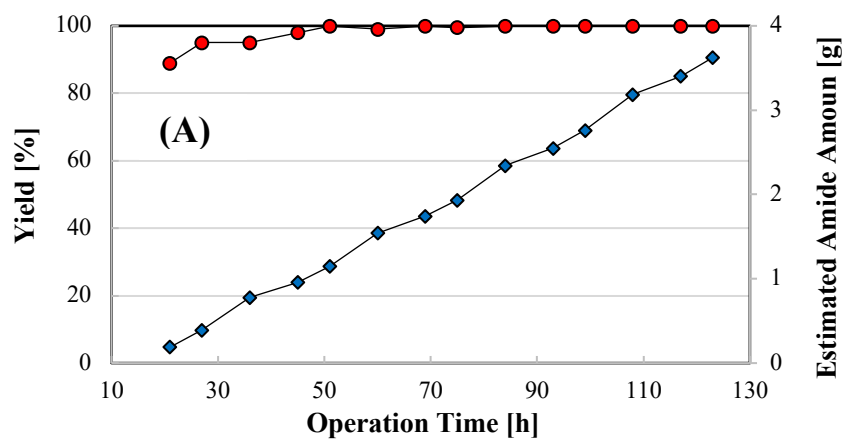
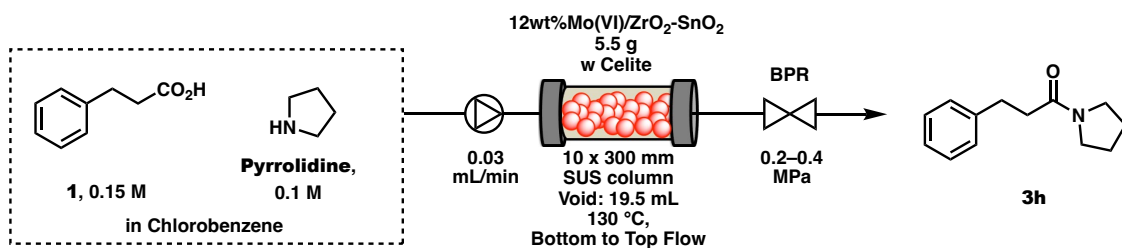


Figure S12. Continuous-flow synthesis of **3h**

Conditions are shown in the upper scheme. Details are described in Table S20

Red, Yield of **3h**. Blue, Estimated total amide amount produced.

(A): Performed at 150 °C, Entry S82. (B): Performed at 130 °C, Entry S83.

Table S20. Details of Continuous-flow reaction shown in Figure S12

Entry	Sampling Time [h]	Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S82-1	18-24	0.029	6.4	0.74	89	0.19
S82-2	24-30	0.029	6.4	0.74	95	0.39
S82-3	30-42	0.028	6.2	0.71	95	0.78
S82-4	42-48	0.025	5.5	0.64	98	0.96
S82-5	48-54	0.026	5.8	0.66	>99	1.15
S82-6	54-66	0.027	6.0	0.69	99	1.54
S82-7	66-72	0.028	6.2	0.71	>99	1.75
S82-8	72-78	0.026	5.8	0.66	>99	1.93

S82-9	78–90	0.028	6.2	0.71	>99	2.34
S82-10	90–96	0.028	6.2	0.71	>99	2.55
S82-11	96–102	0.029	6.4	0.74	>99	2.76
S82-12	102–114	0.029	6.4	0.74	>99	3.18
S82-13	114–120	0.030	6.7	0.76	>99	3.40
S82-14	120–126	0.030	6.7	0.76	>99	3.62
S83-1	18–19	0.031	6.9	0.79	66	0.02
S83-2	19–20	0.031	6.9	0.79	68	0.05
S83-3	20–21	0.031	6.9	0.79	72	0.08
S83-4	21–24	0.030	6.7	0.76	75	0.16
S83-5	24–36	0.030	6.7	0.76	86	0.54
S83-6	36–42	0.030	6.7	0.76	90	0.74
S83-7	42–48	0.030	6.7	0.76	96	0.95
S83-8	48–60	0.030	6.7	0.76	>99	1.38
S83-9	60–66	0.030	6.7	0.76	97	1.60
S83-10	66–72	0.030	6.7	0.76	96(94 ^d)	1.81
S83-11	72–84	0.030	6.7	0.76	98	2.24
S83-12	84–90	0.030	6.7	0.76	97	2.45
S83-13	90–96	0.030	6.7	0.76	97	2.66
S83-14	96–108	0.030	6.7	0.76	98	3.10
S83-15	108–114	0.030	6.7	0.76	99 ^e	3.31
S83-16	114–120	0.030	6.7	0.76	95	3.52
S83-17	120–132	0.030	6.7	0.76	97	3.95
S83-18	132–138	0.030	6.7	0.76	97	4.16
S83-19	138–144	0.030	6.7	0.76	97	4.37

S82: Performed at 150 °C. S83: Performed at 130 °C

^a Weight-hourly-space-velocity based on the product **3g**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d Isolated yield and suggesting 0.149 g/h dL of STY. The same results to that appear in Table 3 of the main text. ^e Suggesting 0.154 g/h dL of STY.

Although yields of entry 82 are all high, we have confirmed this type of amidation reaction between aliphatic acid and aliphatic amine gave the corresponding product in significant yield as shown in **SI-4-1-3**, therefore we considered that the results obtained in this experiment were judged to be strongly affected by the background reaction.

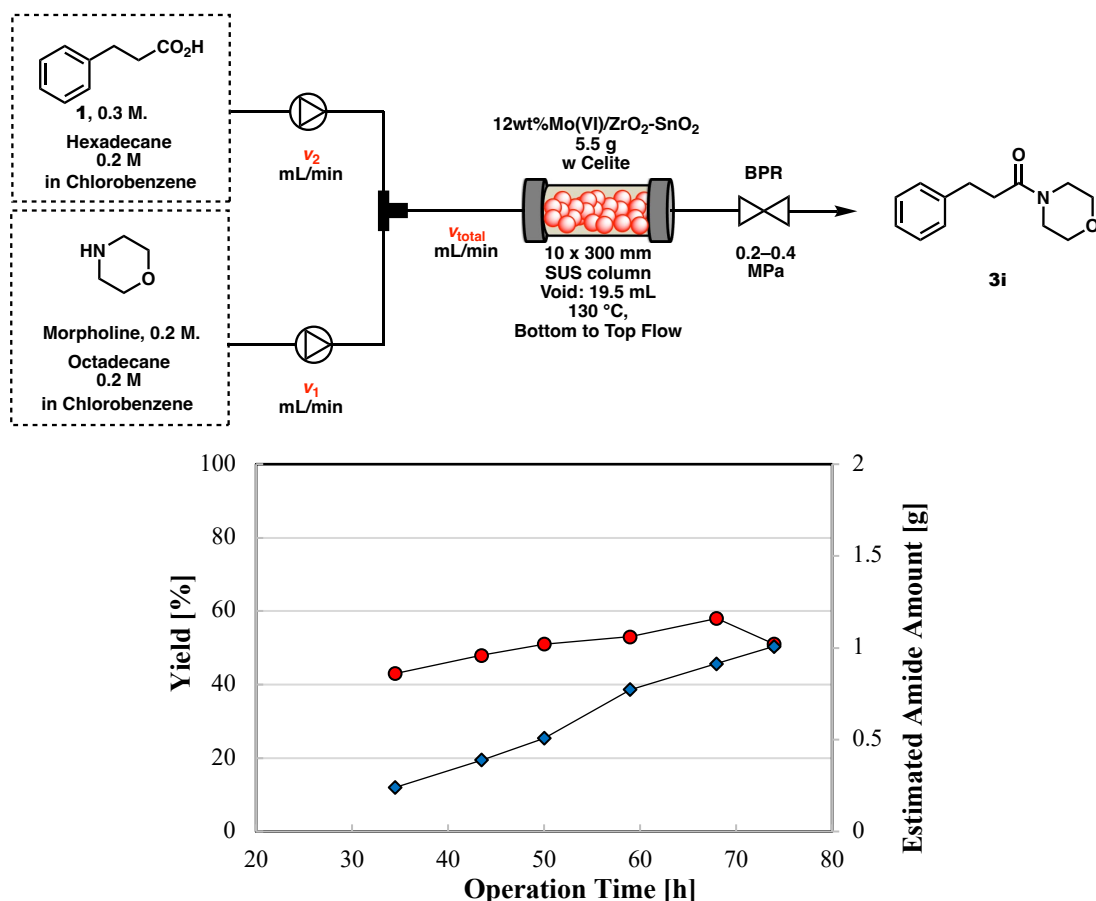


Figure S13. Continuous-flow synthesis of **3i**

Conditions are shown in the upper scheme. Details are described in Table S21

Red, Yield of **3i**. Blue, Estimated total amide amount produced.

(A): Performed at 150°C. (B): Performed at 130 °C

Table S21. Details of Continuous-flow reaction shown in Figure S13

Entry	Sampling Time [h]	Flow Rate [mL/min]		Acid /Amine	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
		v_1	v_{Total}					
S84-1	29–40	0.0193	0.036	1.3	9.2	0.98	43	0.24
S84-2	40–47	0.0170	0.034	1.5	8.1	0.87	48	0.39
S84-3	47–53	0.0145	0.030	1.6	6.9	0.74	51(51 ^d)	0.51
S84-4	53–65	0.0158	0.036	1.9	7.6	0.81	53	0.77
S84-5	65–71	0.0155	0.034	1.8	7.4	0.79	58 ^c	0.91
S84-6	71–77	0.0117	0.025	1.7	5.6	0.60	51	1.01

^a Weight-hourly-space-velocity based on the product **3i**. ^b Molar flow/reactor volume. ^c Determined by GC analysis. ^d Isolated yield and suggesting 0.085 g/h dL of STY. The same results to that appear in Table 3 of the main text. ^e Suggesting 0.10 g/h dL of STY.

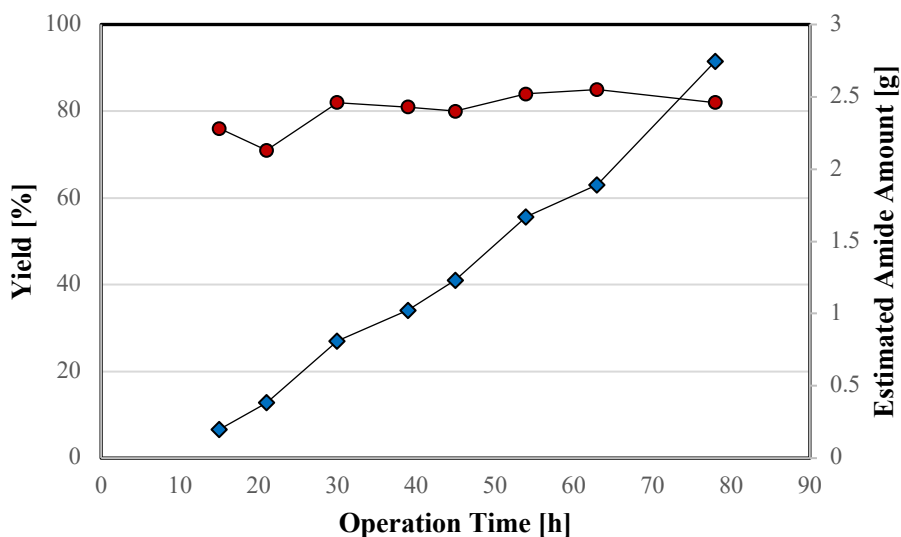
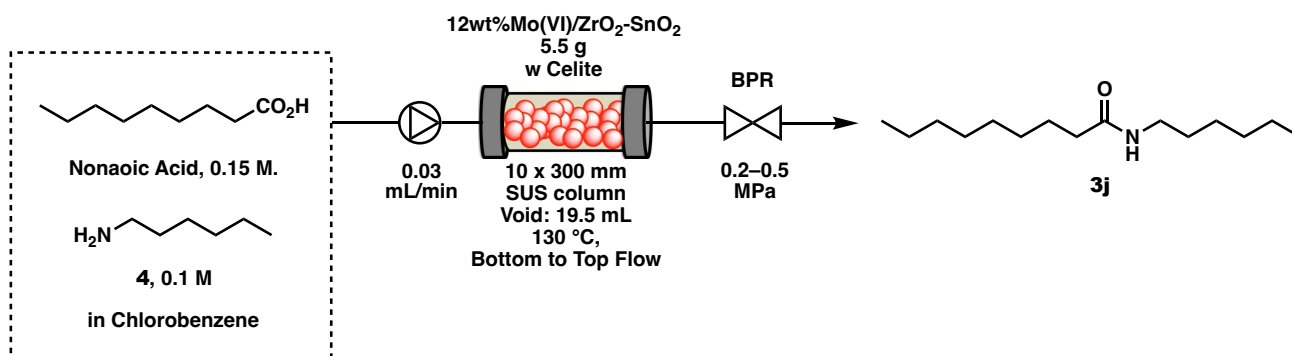


Figure S14. Continuous-flow synthesis of **3j**

Conditions are shown in the upper scheme. Details are described in Table S22
Red, Yield of **3j**. Blue, Estimated total amide amount produced.

Table S22. Details of Continuous-flow reaction shown in Figure S14

Entry	Sampling Time [h]	Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S85-1	12–18	0.03	1.7	0.77	76	0.20
S85-2	18–24	0.03	1.7	0.77	71	0.38
S85-3	24–36	0.03	1.7	0.77	82	0.81
S85-4	36–42	0.03	1.7	0.77	81	1.02
S85-5	42–48	0.03	1.7	0.77	80	1.23
S85-6	48–60	0.03	1.7	0.77	84 ^d	1.67
S85-7	60–66	0.03	1.7	0.77	85	1.89
S85-8	66–90	0.03	1.7	0.77	82(80)	2.75

^a Weight-hourly-space-velocity based on the product **3j**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d Suggesting 0.156 g/h dL of STY. ^e Isolated yield and suggesting 0.149 g/h dL of STY. The same results to that appear in Table 3 of the main text.

SI-5-4. Studies on Diethanolamide Synthesis

In synthesizing diethanolamide, the effect of concentration was first examined, and it was found that the higher the concentration gave higher yield of the desired amide (Figure S15 and Table S23). From these results, we assumed that the background reaction was expected when highly nucleophilic diethanolamine was used, and thus reactions in the presence or absence of the catalyst were verified in two types of column reactors. These results are shown below (Figures S15 and S16).

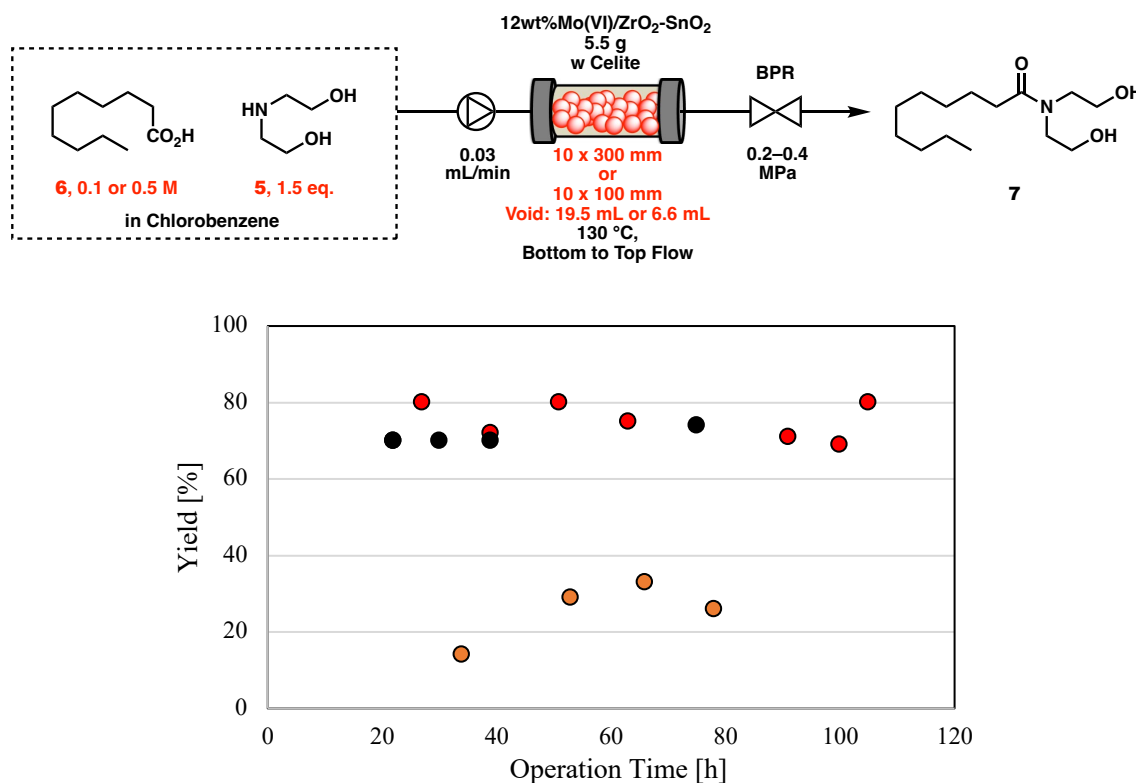


Figure S15. Continuous-flow synthesis of diethanolamide 7

Conditions are shown in the upper scheme. Details are described in Table S23

Orange, With catalyst, 0.1 M solution of 6, 10 x 300 mm column reactor, Entry S86.

Red, With catalyst, 0.5 M solution of 6, 10 x 300 mm column reactor, Entry S87.

Black, Without catalyst, 0.5 M solution of 6, 10 x 300 mm column reactor, Entry S88.

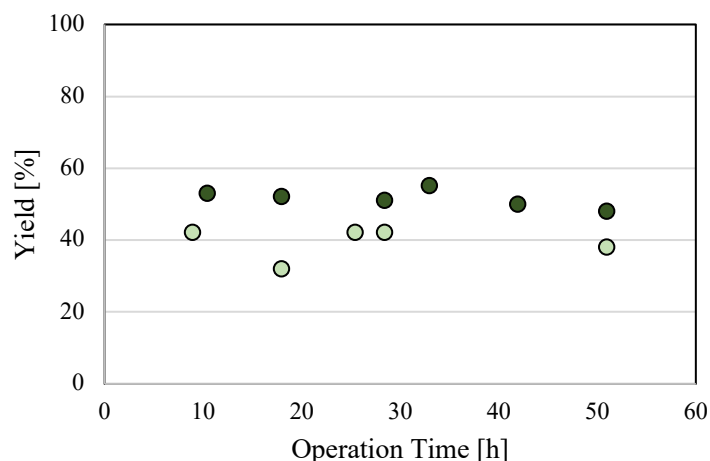


Figure S16. Continuous-flow synthesis of diethanolamide **7** (2)

Conditions are shown in the upper scheme. Details are described in Table S23

Dark Green, With catalyst, 0.5 M solution of **6**, 10 x 100 mm column reactor, Entry S89.

Pale Green, Without catalyst, 0.5 M solution of **6**, 10 x 100 mm column reactor, Entry S90.

Table S23. Details of Continuous-flow reaction shown in Figures S15 and S16

Entry	Conc. 6 , [M]	Reactor Size [mL]	Sampling Time [h]	Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S86-1	0.1	23.55	22–46	0.030	8.5	0.76	14	0.16
S86-2			46–60	0.030	8.5	0.76	29	0.35
S86-3			60–72	0.030	8.5	0.76	33	0.53
S86-4			72–84	0.030	8.5	0.76	26	0.68
							26 (Av.)	
S87-1 ^d	0.5	23.55	20–24	0.029	41.0	3.69	70	0.63
S87-2 ^d			24–30	0.029	41.0	3.69	80	1.71
S87-3 ^d			30–48	0.029	41.0	3.69	72	4.64
S87-4 ^d			48–54	0.029	41.0	3.69	80	5.72
S87-5 ^d			54–72	0.029	41.0	3.69	75	8.77
S87-6 ^d			84–98	0.029	41.0	3.69	71	11.01
S87-7 ^d			98–102	0.029	41.0	3.69	69	11.63
S87-8 ^d			102–108	0.029	41.0	3.69	80	12.72
							75 (Av.)	
S88-1	0.5	23.55	20–24	0.030	–	3.82	70	0.65
S88-2			24–36	0.030	–	3.82	70	2.61
S88-3			36–42	0.030	–	3.82	70	3.60
S88-4			66–86	0.030	–	3.82	74	6.70
							71 (Av.)	
S89-1	0.5	7.85	9–12	0.029	41.0	11.08	53	0.36
S89-2			12–24	0.029	41.0	11.08	52	1.77
S89-3			27–30	0.029	41.0	11.08	51	2.11
S89-4			30–36	0.029	41.0	11.08	55	2.86
S89-5			36–48	0.029	41.0	11.08	50 (42 ^e)	4.21
S89-6			48–54	0.029	41.0	11.08	48	4.86
							51(Av.)	
S90-1	0.5	7.85	8–10	0.030	–	11.47	42	2.45
S90-2			12–24	0.030	–	11.47	32	2.66
S90-3			24–27	0.030	–	11.47	42	3.10
S90-4			27–30	0.030	–	11.47	42	3.31

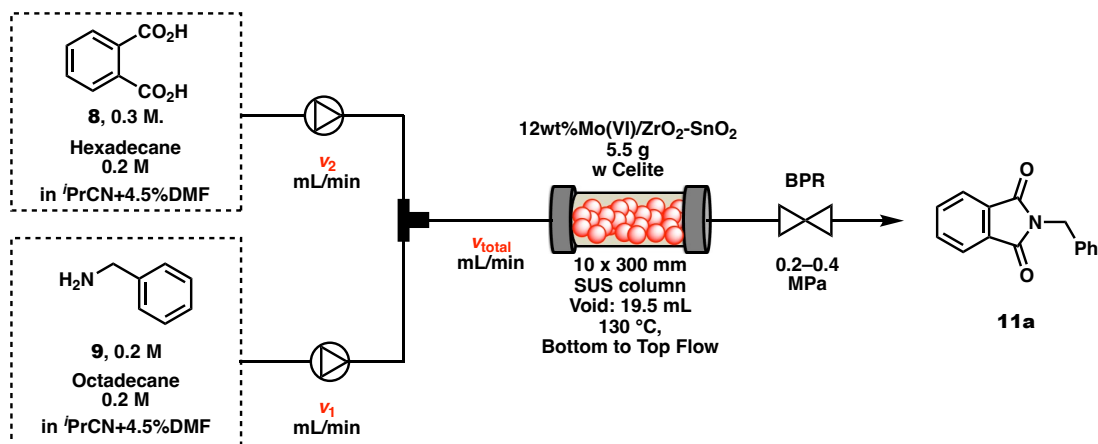
S90-5	48-54	0.030	–	11.47	38	3.52
						39(Av.)

^a Weight-hourly-space-velocity based on the product **7**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d The same results to that appear in Figure 4 of the main text. ^e Isolated yield.

SI-5-5. Studies on Cyclic Imide Synthesis

In the following Table S24 and S25, we described details of results composed Figure 5 of the mail text.

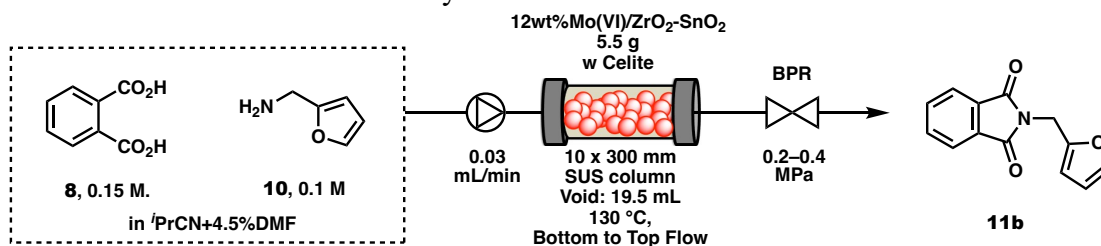
Table S24. Details of continuous-flow synthesis of imide **11a**



Entry	Sampling Time [h]	Flow Rate [mL/min]	Acid /Amine	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S91-1	24–36	0.0159	1.7	8.3	0.81	93	0.51
S91-2	36–42	0.0146	1.9	7.5	0.74	95 ^d	0.74
S91-3	42–48	0.0155	1.6	8.0	0.79	88(84 ^e)	0.98

^a Weight-hourly-space-velocity based on the product **11a**. ^b Molar flow/reactor volume. ^c Determined by GC analysis. ^d Suggesting 0.16 g/h dL of STY. ^e Isolated yield.

Table S25. Details of continuous-flow synthesis of imide **11b**

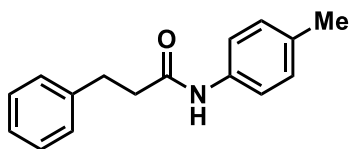


Entry	Sampling Time [h]	Flow Rate [mL/min]	WHSV ^a x 10 ⁻³ [h ⁻¹]	F/V ^b [mmol/h dL]	Yield ^c [%]	Estimated Total Amount [g]
S92-1	18–24	0.029	7.2	0.74	>99	0.24
S92-2	24–36	0.029	7.2	0.74	>99	0.71
S92-3	30–42	0.029	7.2	0.74	>99	0.95
S92-4	42–48	0.029	7.2	0.74	>99 ^d (97 ^e)	1.19
S92-5	48–54	0.029	7.2	0.74	>99	1.42

^a Weight-hourly-space-velocity based on the product **11b**. ^b Molar flow/reactor volume. ^c Determined by ¹H-NMR analysis. ^d Suggesting 0.17 g/h dL of STY. ^e Isolated yield.

SI-9. Spectroscopic Data

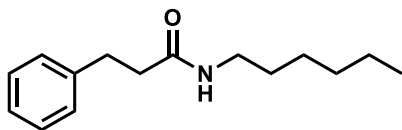
N-(4-Methylphenyl)-3-phenylpropanamide (**3a**)⁵



While conducting the experiment denoted Entry S70, 5.0 mL of sample solution was taken from the outlet solution collected during 20–24 h. After usual work-up procedures including washing with 0.2 M K_2CO_3 aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 4/1) to give 69.3 mg (58%) of **3a**.

1H NMR ($CDCl_3$, 600 MHz): δ = 2.30 (s, 3H), 2.65 (t, J = 7.6 Hz, 3H), 3.05 (t, J = 7.6 Hz, 3H), 6.96 (bs, 1H), 7.10 (d, J = 7.6 Hz, 2H), 7.21-7.31 (m, 7H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 20.8, 31.6, 39.2, 120.1, 126.3, 128.3, 128.5, 129.3, 133.9, 135.1, 140.6, 170.4.

N-Hexylbenzenepropanamide (**3b**)⁶

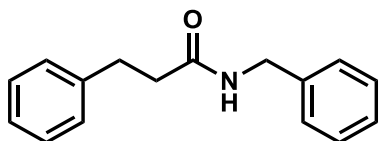


While conducting the experiment denoted Entry S71, 5.0 mL of sample solution was taken from the outlet solution collected during 96–108 h (Entry S71-13). After usual work-up procedures including washing with 0.2 M K_2CO_3 aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 4/1) to give 94.0 mg (81%) of **3b**.

1H NMR ($CDCl_3$, 600 MHz): δ = 0.87 (t, J = 7.2 Hz, 3H), 1.22-1.29 (m, 6H), 1.38-1.43 (m, 2H), 2.46 (t, J = 7.9 Hz, 2H), 2.95 (t, J = 7.6 Hz, 2H), 3.17-3.20 (m, 2H), 5.72 (bs, 1H), 7.18-7.19 (m, 3H), 7.25-7.28 (m, 2H);

^{13}C NMR ($CDCl_3$, 150 MHz): δ = 13.9, 22.4, 26.4, 29.4, 31.4, 31.7, 38.3, 39.4, 126.1, 128.2, 128.3, 140.8, 172.0

N-(Phenylmethyl)benzenepropanamide (**3c**)⁷

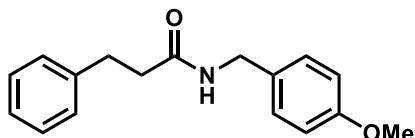


While conducting the experiment denoted Entry S77, 5.0 mL of sample solution was taken from the outlet solution collected during 42–48 h (Entry S77-4). After usual work-up procedures including

washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 4/1) to give 117.8 mg (70%) of **3c**.

¹H NMR (CDCl₃, 600 MHz): δ = 2.51 (t, *J* = 7.6 Hz, 2H), 2.99 (t, *J* = 7.6 Hz, 2H), 4.39 (d, *J* = 5.5 Hz, 2H), 5.68 (bs, 1H), 7.13-7.30 (m, 10H); ¹³C NMR (CDCl₃, 150 MHz): δ = 31.7, 38.5, 43.5, 126.2, 127.4, 127.7, 128.4, 128.5, 128.6, 138.1, 140.7, 171.8.

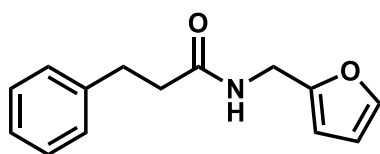
N-[(4-Methoxyphenyl)methyl]benzenepropanamide (**3d**)⁸



While conducting the experiment denoted Entry S78, 5.0 mL of sample solution was taken from the outlet solution collected during 63–69 h (Entry S78-5). After usual work-up procedures including washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 4/1) to give 128.4 mg (68%) of **3d**.

¹H NMR (CDCl₃, 600 MHz): δ = 2.49 (t, *J* = 7.6 Hz, 2H), 2.99 (t, *J* = 7.6 Hz, 2H), 3.79 (s, 3H), 4.32 (d, *J* = 5.5 Hz, 2H), 5.58 (bs, 1H), 6.82 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 7.18-7.29 (m, 5H); ¹³C NMR (CDCl₃, 126 MHz): δ = 31.6, 38.3, 42.9, 55.2, 113.9, 126.1, 128.3, 128.4, 129.0, 130.1, 140.7, 158.9, 171.8.

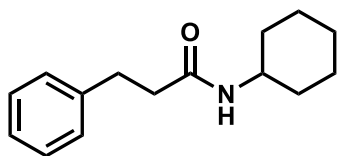
N-(2-Furanylmethyl)benzenepropanamide (**3e**)⁹



While conducting the experiment denoted Entry S79, 5.0 mL of sample solution was taken from the outlet solution collected during 54–72 h (Entry S79-6). After usual work-up procedures including washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 2/1) to give 79.0 mg (69%) of **3e**.

¹H NMR (CDCl₃, 600 MHz): δ = 2.41 (t, *J* = 7.6 Hz, 2H), 2.88 (t, *J* = 7.6 Hz, 2H), 4.31 (d, *J* = 4.8 Hz, 2H), 5.79 (bs, 1H), 6.06 (d, *J* = 2.8 Hz, 1H), 6.21 (s, 1H), 7.09-.24 (m, 6H); ¹³C NMR (CDCl₃, 126 MHz): δ = 31.5, 36.4, 38.2, 107.4, 110.4, 126.2, 128.3, 128.5, 140.7, 142.1, 151.2, 171.9.

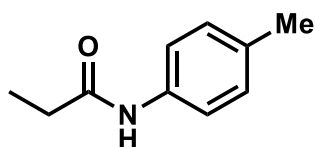
N-Cyclohexylbenzenepropanamide (**3f**)⁹



While conducting the experiment denoted Entry S80, 5.0 mL of sample solution was taken from the outlet solution collected during 54–72 h (Entry S80-7). After usual work-up procedures including washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 2/1) to give 93.5 mg (81%) of **3f**.

¹H NMR (CDCl₃, 600 MHz): δ = 0.92-1.07 (m, 3H), 1.20-1.27 (m, 2H), 1.49-1.58 (m, 3H), 1.73-1.76 (m, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 2.87 (t, *J* = 7.6 Hz, 2H), 3.62-3.68 (m, 1H), 5.44 (s, 1H), 7.11-7.20 (m, 5H); ¹³C NMR (CDCl₃, 126 MHz): δ = 24.7, 25.4, 31.8, 33.0, 38.7, 48.0, 126.1, 128.3, 128.4, 140.9, 171.0.

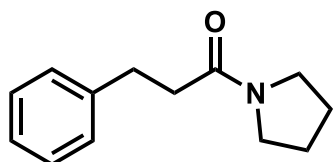
N-(4-Methylphenyl)propanamide (**3g**)¹⁰



While conducting the experiment denoted Entry S81, 5.0 mL of sample solution was taken from the outlet solution collected during 95–107 h (Entry S81-10). After usual work-up procedures including washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 4/1) to give 21.9 mg (27%) of **3g**.

¹H NMR (CDCl₃, 600 MHz): δ = 1.21 (t, *J* = 7.2 Hz, 3H), 2.29 (s, 3H), 2.35 (q, *J* = 7.6 Hz, 2H), 7.09 (d, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.59 (bs, 1H); ¹³C NMR (CDCl₃, 126 MHz): δ = 9.7, 20.8, 30.5, 120.0, 129.3, 133.6, 135.4, 172.2.

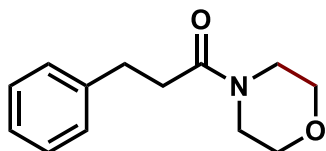
3-Phenyl-1-(1-pyrrolidinyl)-1-propane (**3h**)⁹



While conducting the experiment denoted Entry S83, 5.0 mL of sample solution was taken from the outlet solution collected during 66–72 h (Entry S83-10). After usual work-up procedures including washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 4/1) to give 95.3 mg (94%) of **3h**.

^1H NMR (CDCl_3 , 600 MHz): δ = 1.80-1.90 (m, 4H), 2.55-2.58 (m, 2H), 2.97-3.00 (m, 2H), 3.29 (t, J = 6.5 Hz, 2H), 3.46 (t, J = 8.2 Hz, 2H), 7.18-7.30 (m, 5H); ^{13}C NMR (CDCl_3 , 126 MHz): δ = 24.3, 26.0, 31.2, 36.7, 45.6, 46.5, 126.0, 128.37, 128.39, 141.5, 170.7.

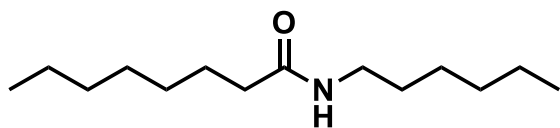
1-(4-Morpholinyl)-3-phenyl-1-propanone (**3i**)¹¹



While conducting the experiment denoted Entry S84, 5.0 mL of sample solution was taken from the outlet solution collected during 47–53 h (Entry S84-3). After usual work-up procedures including washing with 0.2 M K_2CO_3 aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 1/2) to give 52.3 mg (51%) of **3i**.

^1H NMR (CDCl_3 , 600 MHz): δ = 2.61 (t, J = 7.6 Hz, 2H), 2.98 (t, J = 7.9 Hz, 2H), 3.35 (t, J = 4.8 Hz, 2H), 3.50 (t, J = 4.8 Hz, 2H), 3.62 (bs, 4H), 7.19-7.30 (m, 5H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 31.4, 34.7, 41.8, 45.9, 66.4, 66.7, 126.2, 128.3, 128.4, 140.9, 170.8.

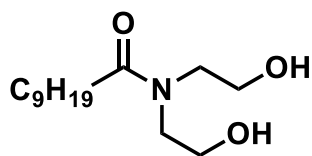
N-Hexylnonanamide (**3j**)¹²



While conducting the experiment denoted Entry S85, 5.0 mL of sample solution was taken from the outlet solution collected during 66–90 h (Entry S85-8). After usual work-up procedures including washing with 0.2 M K_2CO_3 aqueous solution, the product was isolated by column chromatography (hexane/toluene/triethylamine = 20/5/1) to give 91.3 mg (80%) of **3j**.

^1H NMR (CDCl_3 , 600 MHz): δ = 0.86-0.90 (m, 6H), 1.27-1.29 (m, 14H), 1.49 (qn, J = 7.2 Hz, 2H), 1.62 (qn, J = 7.0 Hz, 2H), 2.15 (t, J = 7.6 Hz, 2H), 3.24 (dd, J = 6.9, 6.2 Hz, 2H), 5.44 (bs, 1H); ^{13}C NMR (CDCl_3 , 150 MHz): δ = 13.88, 13.93, 22.45, 22.50, 25.6, 26.5, 28.9, 29.2, 29.5, 31.4, 31.6, 36.8, 39.4, 173.1.

N,N-Bis(2-hydroxyethyl)decanamide (7)

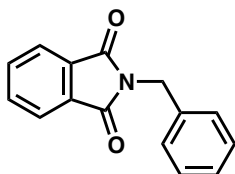


While conducting the experiment denoted Entry S88, 5.0 mL of sample solution was taken from the outlet solution collected during 36–48 h (Entry S88-5). After removal of the solvent by evaporation, carboxylic acid-functionalized silica gel (Fuji Silysia, COOH) was added to the resulting mixture and stand for overnight. Liquid was filtered and concentrated to give the crude sample without non-reacted diethanolamine. The desired product was isolated by column chromatography (hexane/EtOAc/EtOH = 2/4/1) to give 271.1 mg (42%) of **7**.

HRMS (DART): Calcd for $C_{14}H_{29}O_3N[M]^+$ 259.2147, Found as $[M+H]^+$, 260.2234

FTIR (cm^{-1}) (DCM solution): 721, 860, 1052, 1212, 1364, 1422, 1468, 1620($\nu_{amide-c=O}$), 2853, 2923, 3368(ν_{OH}); 1H NMR ($CDCl_3$, 600 MHz): δ =0.88 (t, J = 7.2 Hz, 6H), 1.26-1.30 (m, 13H), 1.59-1.64 (m, 2H), 2.38 (t, J = 7.9 Hz, 2H), 3.49-3.54 (m, 4H), 3.76-3.82 (m, 4H), 4.21 (bs, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 14.0, 22.6, 25.3, 29.2, 29.40, 29.42, 29.44, 31.8, 33.6, 50.5, 52.2, 60.7, 61.3, 175.7.

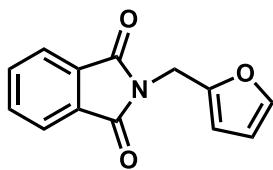
2-Benzylisoindoline-1,3-dione (**11a**)¹³



While conducting the experiment denoted Entry S90, 5.0 mL of sample solution was taken from the outlet solution collected during 42–48 h (Entry S90-3). After usual work-up procedures including washing with 0.2 M K_2CO_3 aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 1/2) to give 99.1 mg (84%) of **11a**.

1H NMR ($CDCl_3$, 600 MHz): δ = 4.85 (s, 2H), 7.25-7.44 (mdd, 5H), 7.70-7.84 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 41.6, 123.3, 127.8, 128.58, 128.65, 132.1, 134.0, 136.3, 168.0.

2-(2-Furanylmethyl)-1*H*-isoindole-1,3(2*H*)-dione (11b)¹⁴

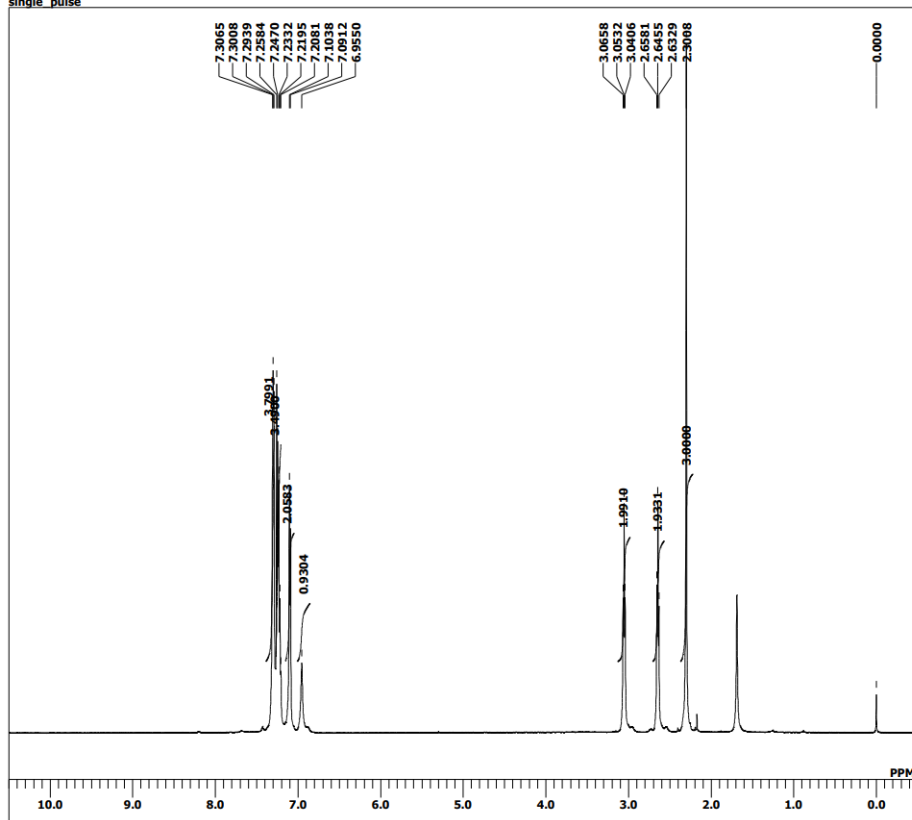


While conducting the experiment denoted Entry S91, 5.0 mL of sample solution was taken from the outlet solution collected during 42–48 h (Entry S91-4). After usual work-up procedures including washing with 0.2 M K₂CO₃ aqueous solution, the product was isolated by PTLC (hexane/EtOAc = 2/1) to give 110.4 mg (97%) of **11b**.

¹H NMR (CDCl₃, 600 MHz): δ = 4.86 (s, 2H), 6.30 (dd, *J* = 2.1, 2.0 Hz, 1H), 6.37 (d, *J* = 2.8 Hz, 1H), 7.33 (br, 1H), 7.71 (dd, *J* = 2.8, 3.4 Hz, 2H), 7.86 (dd, *J* = 2.8, 3.4 Hz, 2H); ¹³C NMR (CDCl₃, 150 MHz): δ = 34.2, 108.7, 110.4, 123.4, 132.0, 134.0, 142.4, 149.2, 167.6.

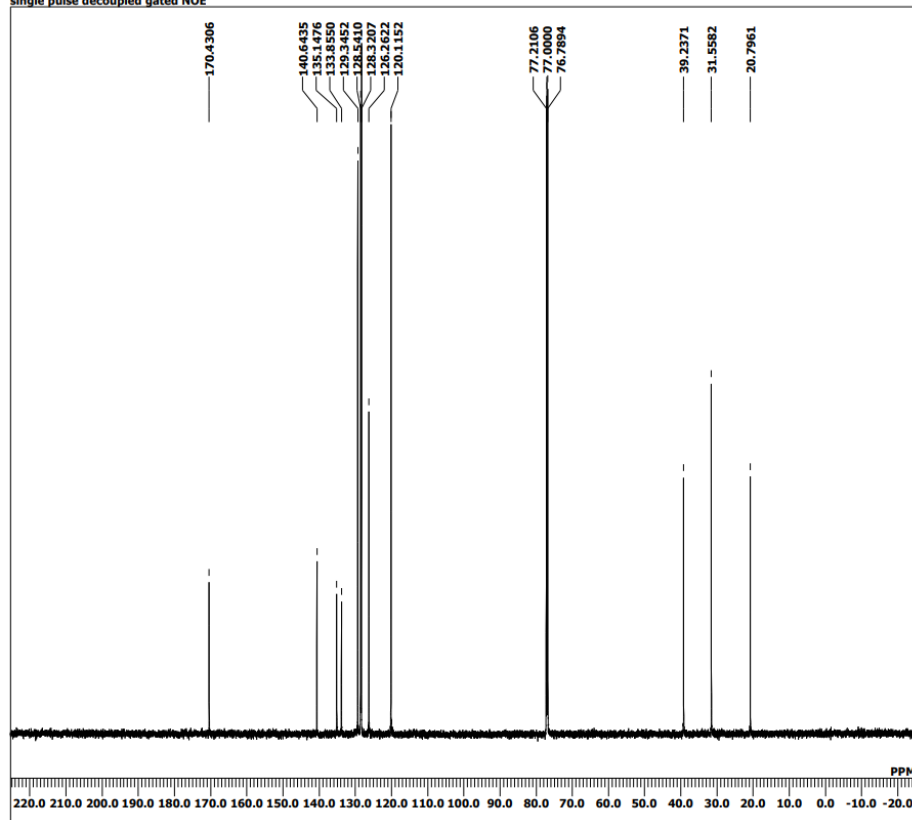
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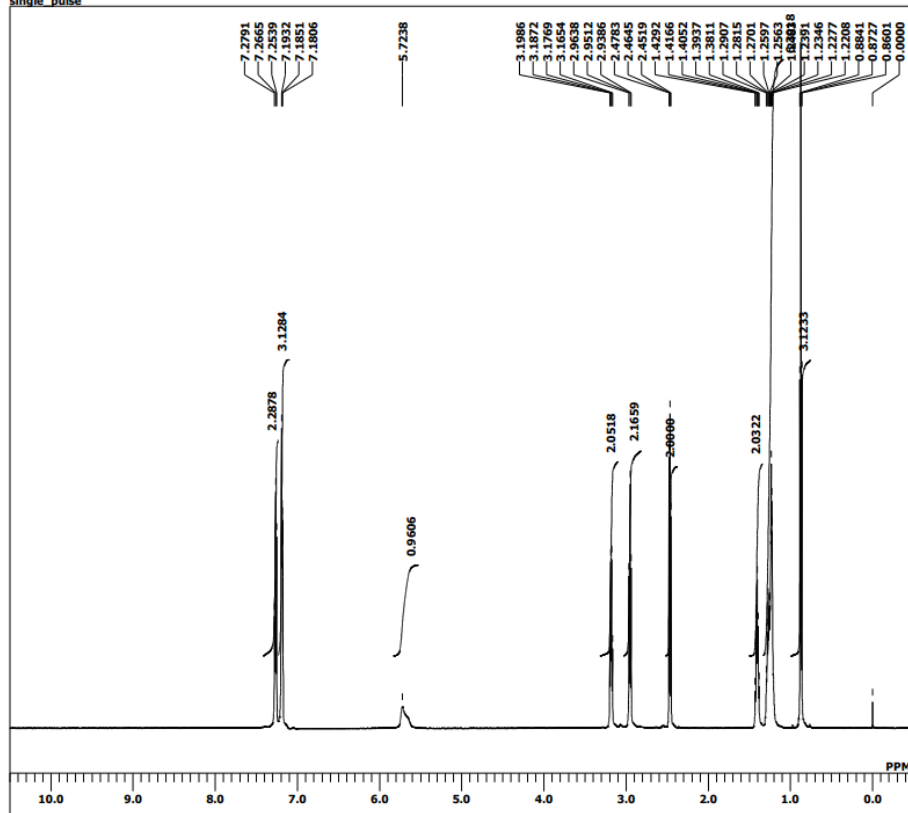
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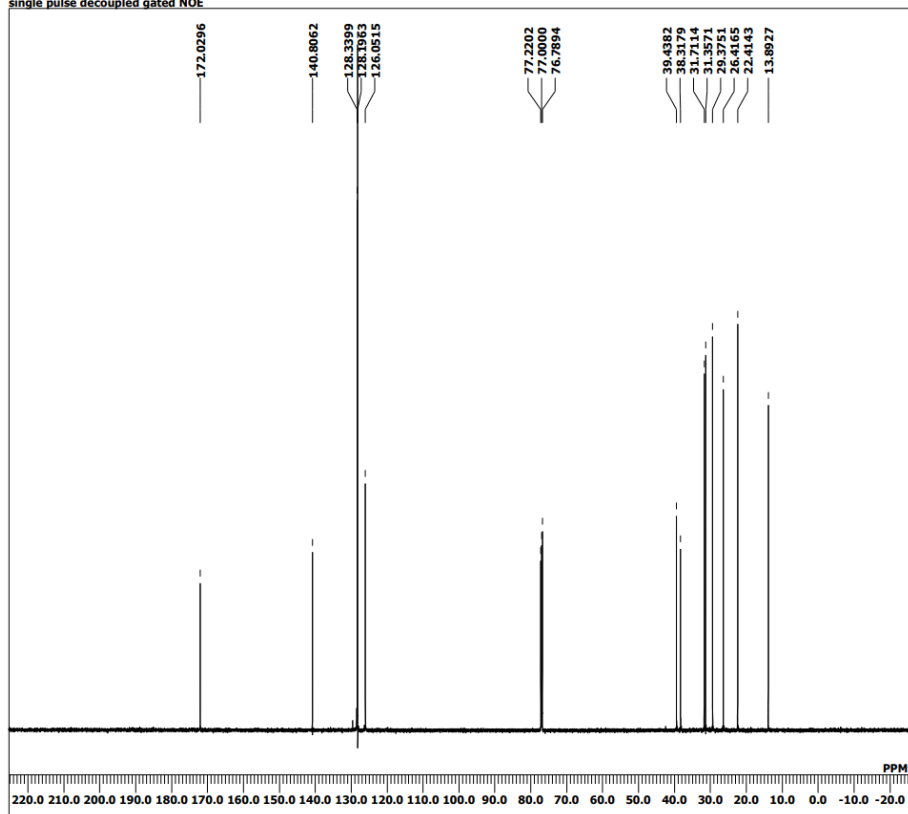
N-Hexylbenzenepropanamide (3b)

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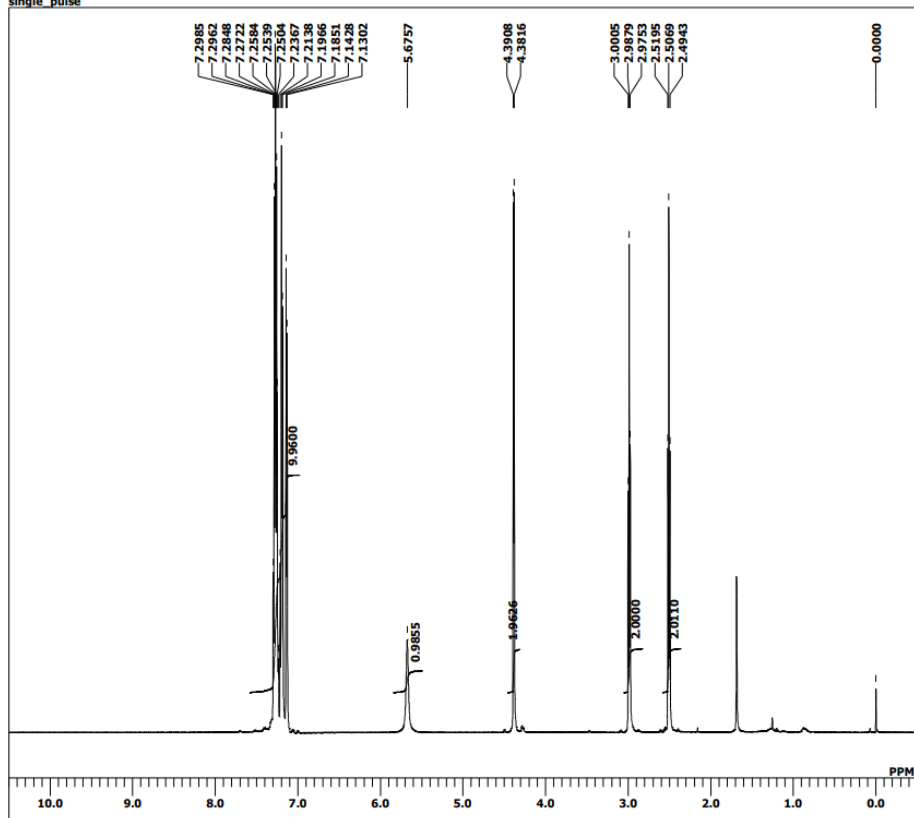
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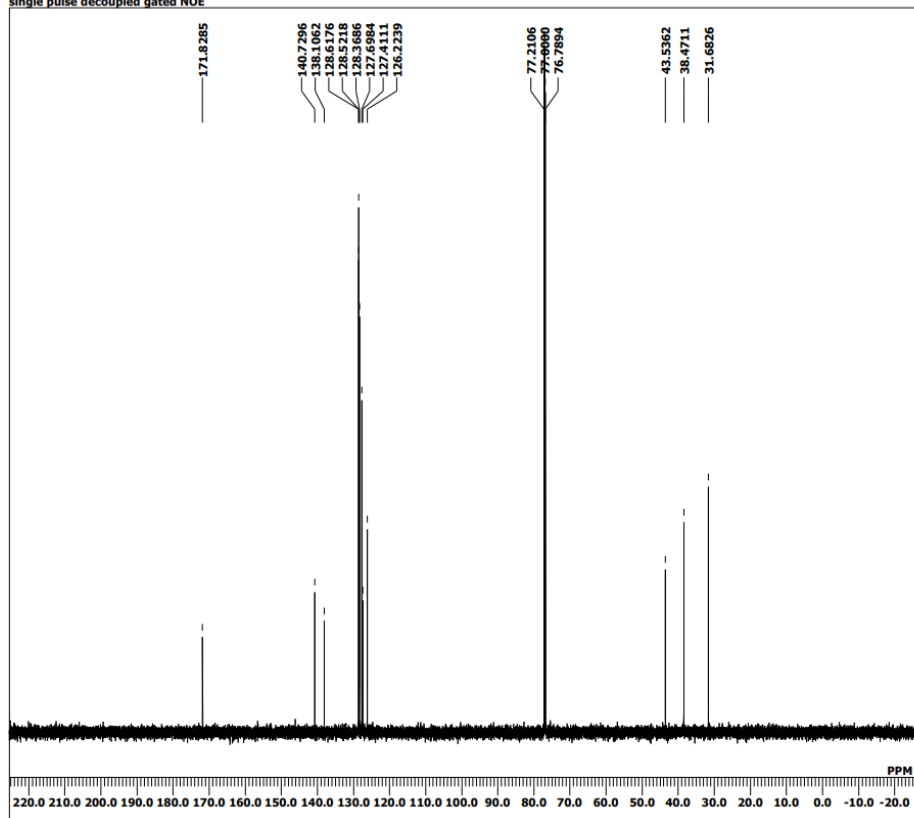
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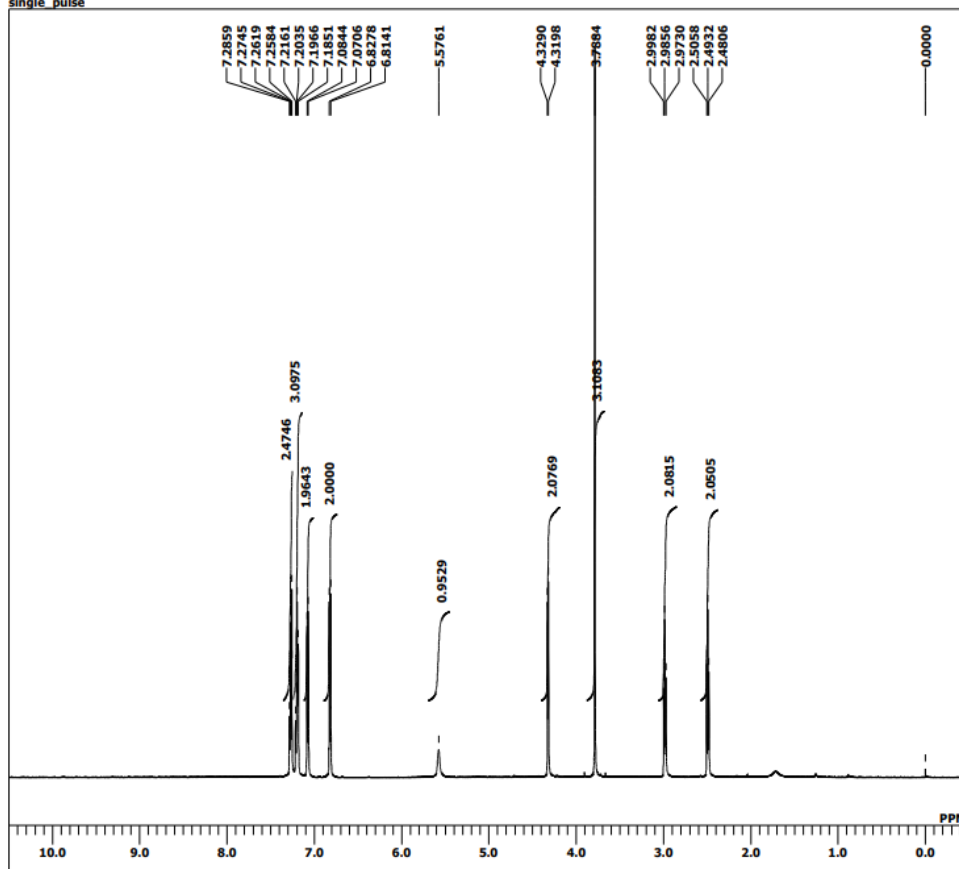
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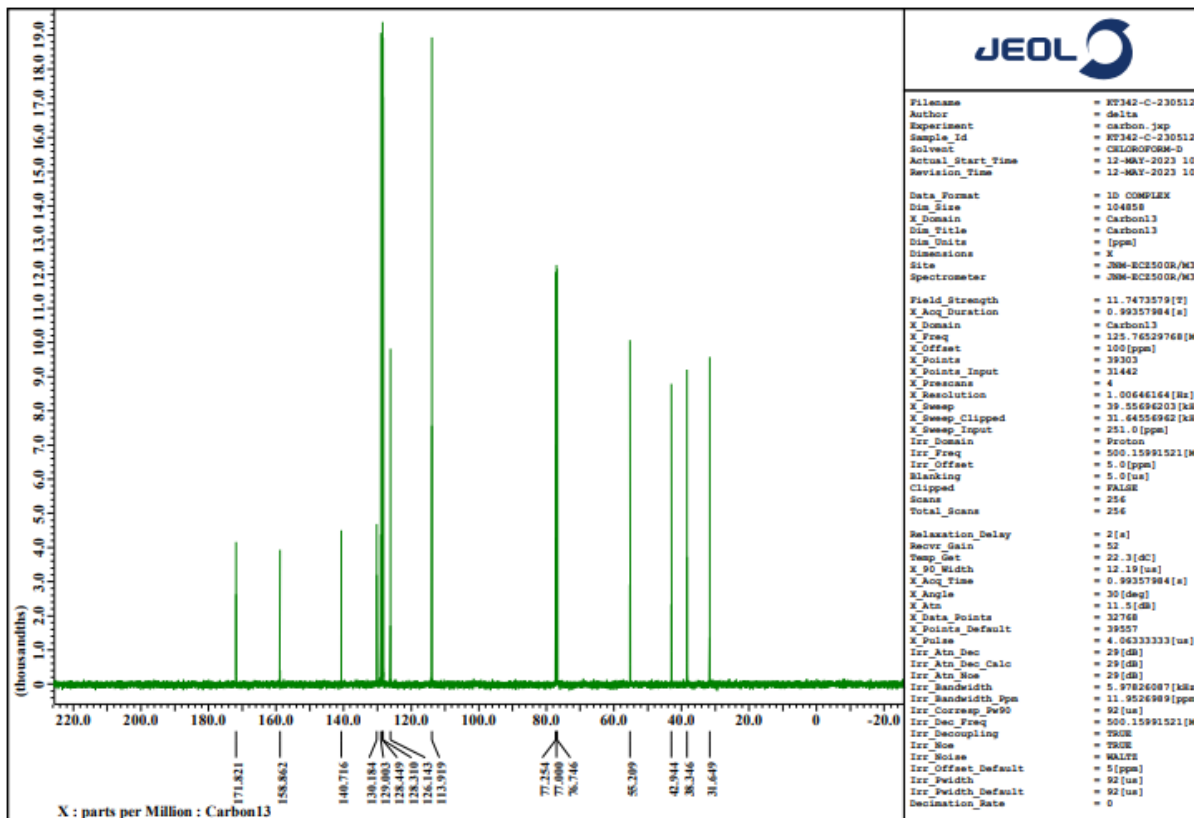
N-[(4-Methoxyphenyl)methyl]benzenepropanamide (3d)

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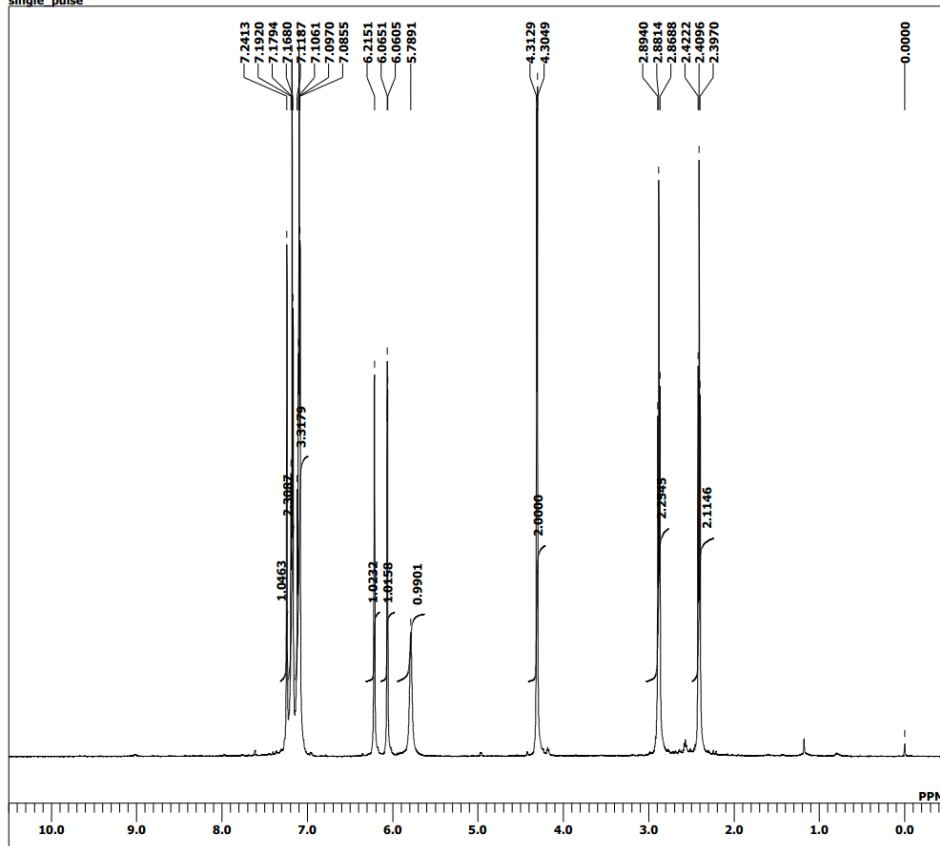
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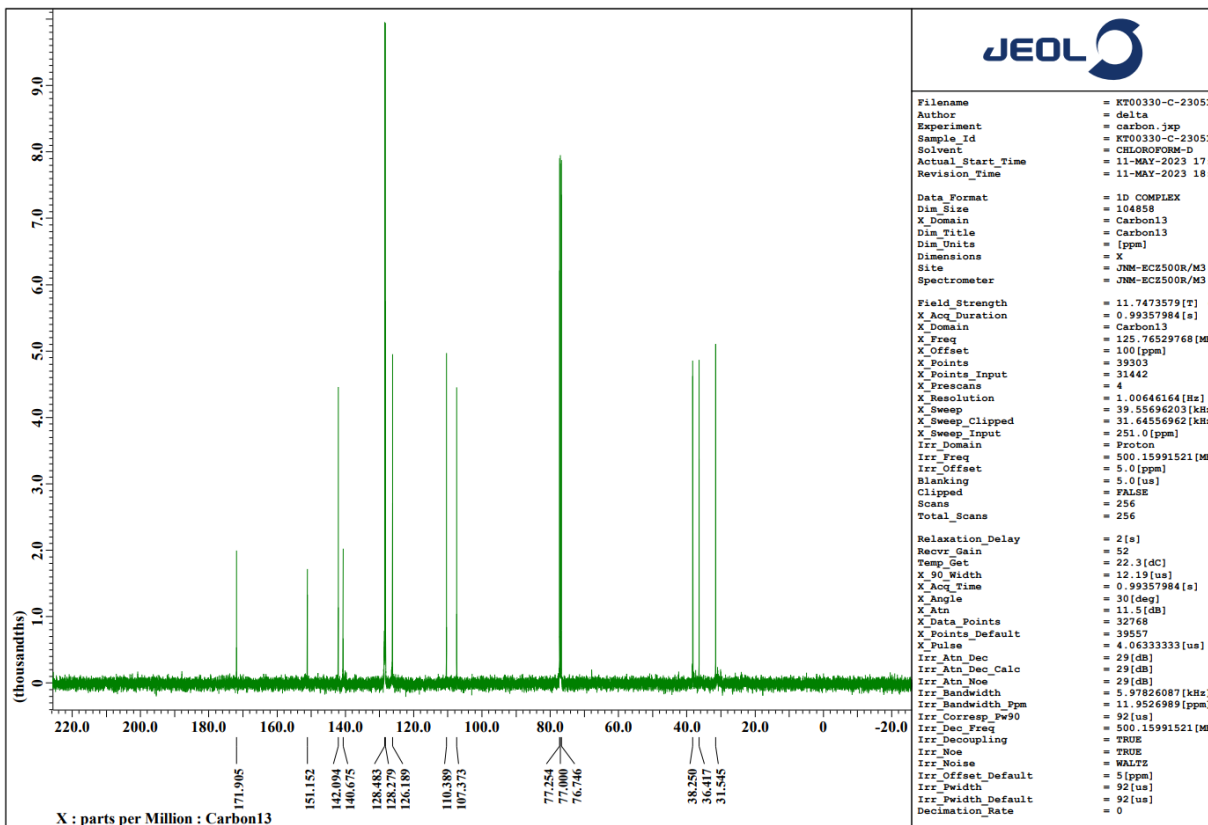
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N-(2-Furanylmethyl)benzenepropanamide (3e)

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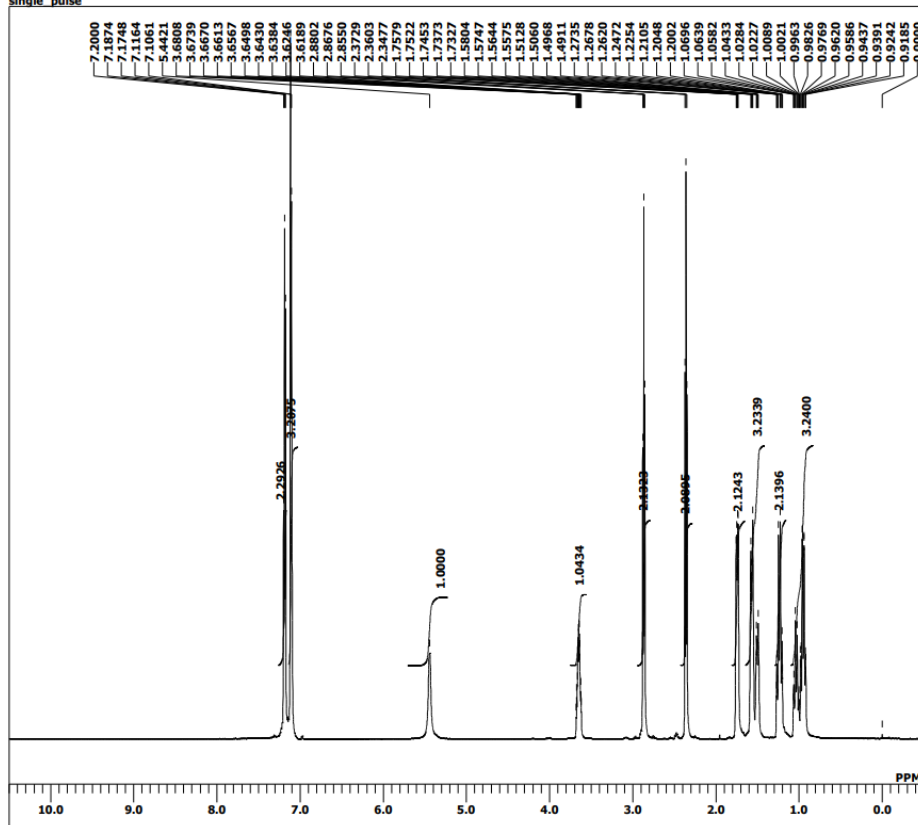


JEOL

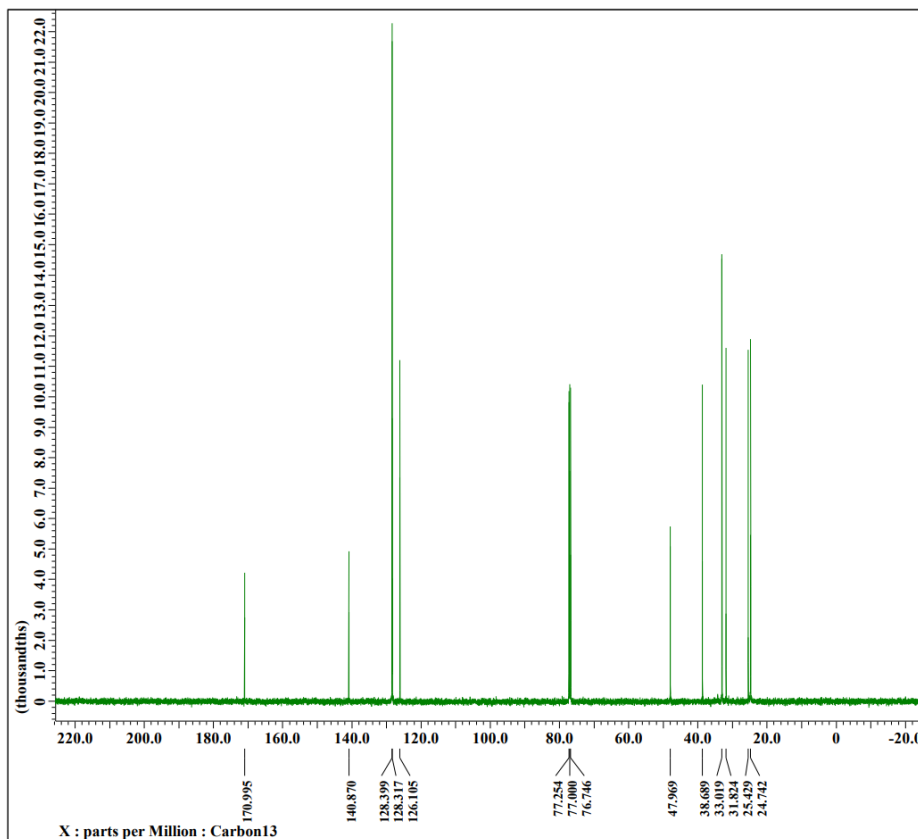
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X_Resolution = 1.00646164 [Hz]
X_Sweep = 39.55696203 [kHz]
X_Sweep_Clipped = 31.64556962 [kHz]
X_Sweep_Input = 251.0 [ppm]
Irr_Domain = Proton
Irr_Freq = 500.15991521 [MHz]
Irr_Offset = 5.0 [ppm]
Blanking = FALSE
Clipped = 256
Total_Scans = 256
Relaxation_Delay = 2 [s]
Recpr_Gain = 52
Temp_Get = 22.3 [dC]
X_90_Width = 12.19 [us]
X_Acq_Time = 0.99357984 [s]
X_Angle = 30 [deg]
X_Atn = 11.5 [dB]
X_Data_Points = 32768
X_Points_Default = 39557
X_Pulse = 4.06333333 [us]
Irr_Atn_Dec = 29 [dB]
Irr_Atn_Dec_Calc = 29 [dB]
Irr_Atn_No = 29 [dB]
Irr_Bandwidth = 5.97826087 [kHz]
Irr_Bandwidth_Ppm = 11.9526989 [ppm]
Irr_Corresp_Pw90 = 92 [us]
Irr_Dec_Freq = 500.15991521 [MHz]
Irr_Decoupling = TRUE
Irr_No = TRUE
Irr_Noise = WALTZ
Irr_Offset_Default = 5 [ppm]
Irr_Fwidth = 92 [us]
Irr_Fwidth_Default = 92 [us]
Decimation_Rate = 0

N-Cyclohexylbenzenepropanamide (3f)

WEca\data\Takeda\KT00346-H-221119-1.als
single_pulse



DATIM 19-11-2022 02:22:59
 DFILC WEca\data\Takeda\KT00346-H-221119-1
 OBNUC 1H
 EXMOD single_pulse.ex2
 OBFRQ 600.17 MHz
 OBSET 5.30 KHz
 OBFIN 5.47 Hz
 POINT 13107
 FREQU 9008.87 Hz
 SCANS 8
 ACQTM 1.4549 sec
 PD 5.0000 sec
 PW1 6.88 usec
 IRATN 0
 CTEMP 23.0 c
 SLVNF CDCL3
 EXREF 0.00 ppm
 BF 1.20 Hz
 RGAIN 48

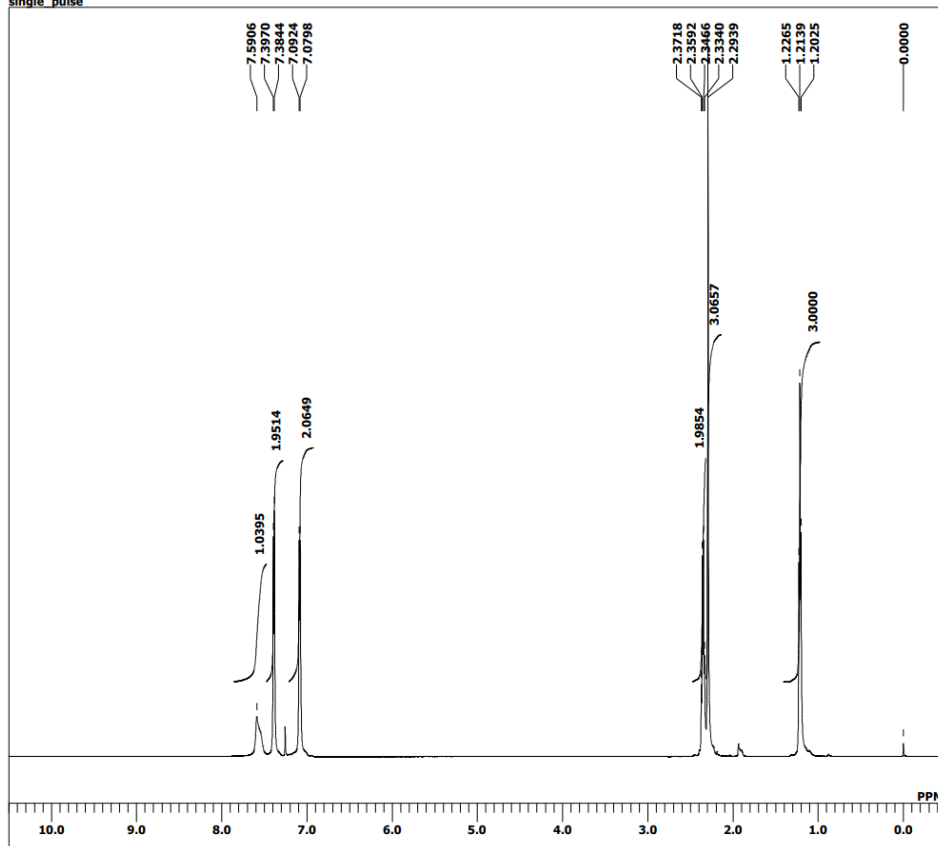


JEOL

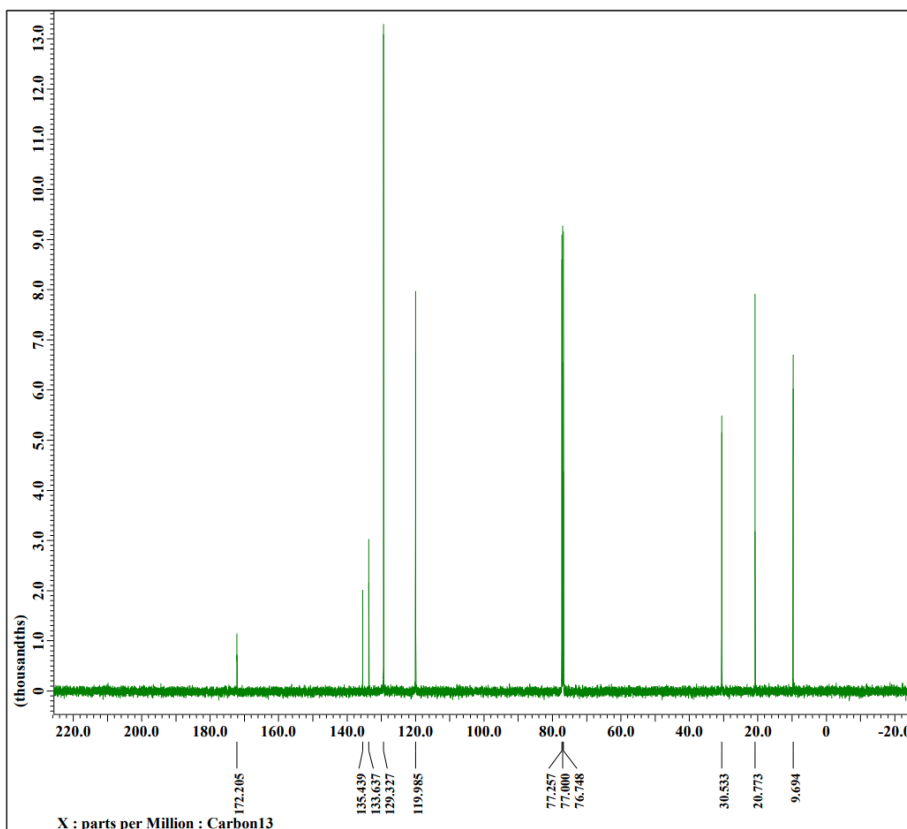
Filename = KT00346-C-23051
 Author = delta
 Experiment = carbon_jmp
 Sample_Id = KT00346-C-23051
 Solvent = CHLOROFORM-D
 Actual_Start_Time = 11-MAY-2023 18:
 Revision_Time = 11-MAY-2023 18:
 Data_Format = 1D COMPLEX
 Dim_Size = 104858
 X_Domain = Carbon13
 Dim_File = Carbon13
 Dim_Units = [ppm]
 Dimensions = X
 Site = JNM-ECZ500R/M3
 Spectrometer = JNM-ECZ500R/M3
 Field_Strength = 11.7473579 [T]
 X_Acq_Duration = 0.9937984 [s]
 X_Domain = Carbon13
 X_Freq = 125.76529768 [MHz]
 X_Offset = 100 [ppm]
 X_Points = 39303
 X_Points_Input = 31442
 X_Prescans = 4
 X_Resolution = 1.00646164 [Hz]
 X_Sweep = 39.55696203 [kHz]
 X_Sweep_Clipped = 31.64556962 [kHz]
 X_Sweep_Input = 251.0 [ppm]
 Irr_Domain = Proton
 Irr_Freq = 500.15991521 [MHz]
 Irr_Offset = 5.0 [ppm]
 Blanking = 5.0 [us]
 Clipped = FALSE
 Scans = 256
 Total_Scans = 256
 Relaxation_Delay = 2 [s]
 Recvr_Gain = 52
 Temp_Gst = 22.3 [dC]
 X_90_Width = 12.19 [us]
 X_Acq_Time = 0.9937984 [s]
 X_Angle = 30 [deg]
 X_Atn = 11.5 [dB]
 X_Data_Points = 32768
 X_Points_Default = 39557
 X_Pulse = 4.06333333 [us]
 Irr_Atn_Dec = 29 [dB]
 Irr_Atn_Dec_Calc = 29 [dB]
 Irr_Atn_Noise = 29 [dB]
 Irr_Bandwidth = 5.97826087 [kHz]
 Irr_Bandwidth_Ppm = 11.9526989 [ppm]
 Irr_Corresp_Fw90 = 92 [us]
 Irr_Dec_Freq = 500.15991521 [MHz]
 Irr_Decoupling = TRUE
 Irr_Noise = TRUE
 Irr_Noise = WALTZ
 Irr_Offset_Default = 5 [ppm]
 Irr_Pwidth = 92 [us]
 Irr_Pwidth_Default = 92 [us]
 Decimation_Rate = 0

N-(4-Methylphenyl)propenamide (3g)

WEca\data\Takeno\KT00297-H-230512-1.als
single_pulse



DATIM 11-05-2023 22:34:45
DFILE WEca\data\Takeno\KT00297-H-230512-1
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
OBSET 5.30 KHz
OBFIN 5.47 Hz
POINT 13107
FREQU 9008.87 Hz
SCANS 8
ACQTM 1.4549 sec
PD 5.0000 sec
PW1 6.88 usec
IRATN 0
CTEMP 22.8 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.20 Hz
RGAIN 38



JEOL

Filename = KE297-C-230512_1
Author = delta
Experiment = carbon.jpg
Sample_Id = KE297-C-230512_1
Solvent = CHLOROFORM-D
Actual_Start_Time = 12-MAY-2023 11:15:11
Revision_Time = 12-MAY-2023 15:11:11

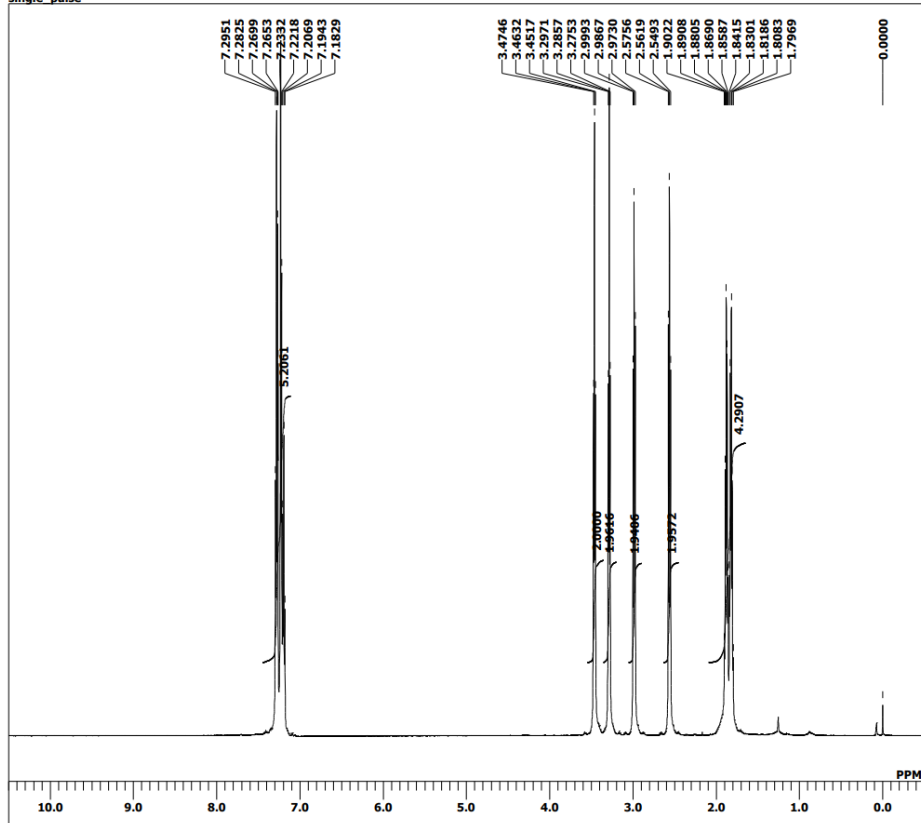
Data_Format = 1D_COMPLEX
Dim_Size = 104858
X_Domain = Carbon13
Dim_Title = Carbon13
Dim_Units = [ppm]
Dimensions = X
Site = JNM-ECE500R/M3
Spectrometer = JNM-ECE500R/M3

Field_Strength = 11.7473579 [T]
X_Acq_Duration = 0.99357984 [s]
X_Domain = Carbon13
X_Freq = 125.76529768 [MHz]
X_Offset = 100 [ppm]
X_Points = 39303
X_Points_Input = 31442
X_Prescans = 4
X_Resolution = 1.00646164 [Hz]
X_Sweep = 39.55696203 [kHz]
X_Sweep_Clipped = 31.64559962 [kHz]
X_Sweep_Input = 251.0 [ppm]
Irr_Domain = Proton
Irr_Freq = 500.15991521 [MHz]
Irr_Offset = 5.0 [ppm]
Blanking = 5.0 [us]
Clipped = FALSE
Scans = 256
Total_Scans = 256

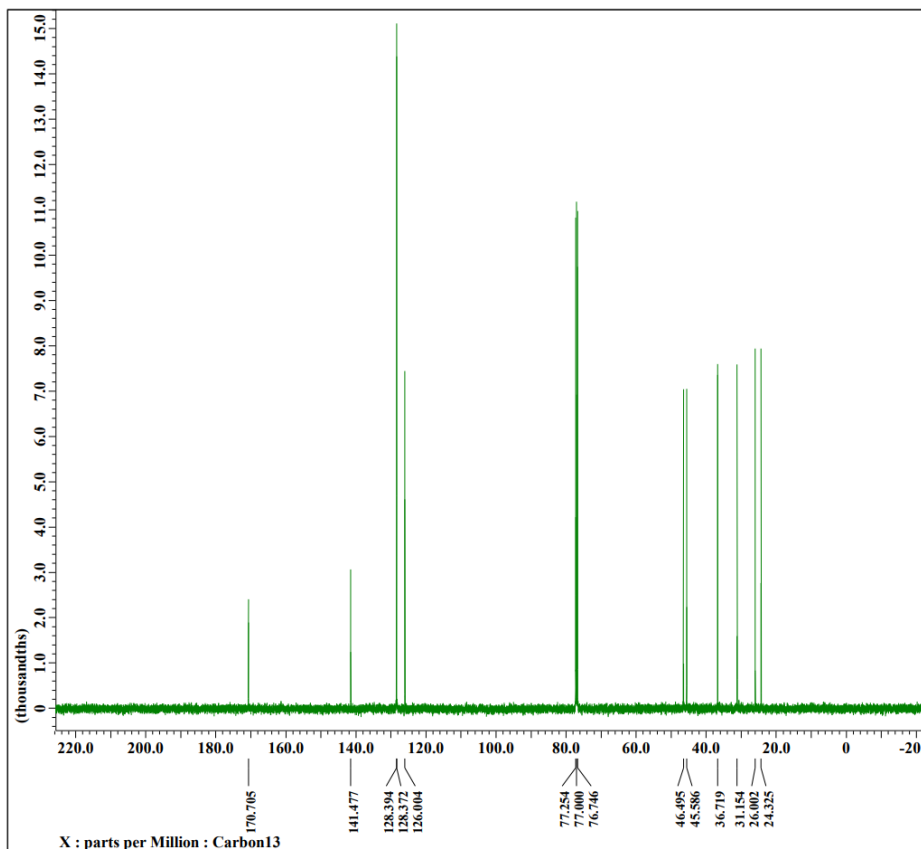
Relaxation_Delay = 2 [s]
Recvr_Gain = 52
Temp_Get = 22.3 [dC]
X_90_Width = 12.19 [us]
X_Acq_Time = 0.99357984 [s]
X_Angle = 30 [deg]
X_Atn = 11.5 [dB]
X_Data_Points = 32768
X_Points_Default = 39557
X_Pulse = 4.06333333 [us]
Irr_Atn_Dec = 29 [dB]
Irr_Atn_Dec_Calc = 29 [dB]
Irr_Atn_Noise = 29 [dB]
Irr_Bandwidth = 5.97826087 [kHz]
Irr_Bandwidth_Ppm = 11.9526989 [ppm]
Irr_Corresp_Pw90 = 92 [us]
Irr_Dec_Freq = 500.15991521 [MHz]
Irr_Decoupling = TRUE
Irr_Noise = TRUE
Irr_Noise = WALTZ
Irr_Offset_Default = 5 [ppm]
Irr_Pwidth = 92 [us]
Irr_Pwidth_Default = 92 [us]
Decimation_Rate = 0

3-Phenyl-1-(1-pyrrolidiny)-1-propane (3h)

W\Eca\data\Takeno\KT00302-H-221122-1.als
single_pulse



```
DATIM 22-11-2022 02:23:05
DFILE W\Eca\data\Takeno\KT00302-H-221122-1
OBNUC 1H
EXMOD single_pulse.ex2
OBSFQ 600.17 MHz
OBSET 5.30 KHz
OBFIN 5.47 Hz
POINT 13107
FREQU 9008.87 Hz
SCANS 8
ACQTM 1.4549 sec
PD 5.0000 sec
PW1 6.88 usec
IRATN 0
CTEMP 22.9 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.20 Hz
RGAIN 42
```





```

Filename = KT302-C-230611
Author = delta
Experiment = carbon13mp
Sample_Id = KT302-C-230611
Solvent = CHLOROFORM-D
Actual_Start_Time = 11-MAY-2023 20:
Revision_Time = 11-MAY-2023 20:

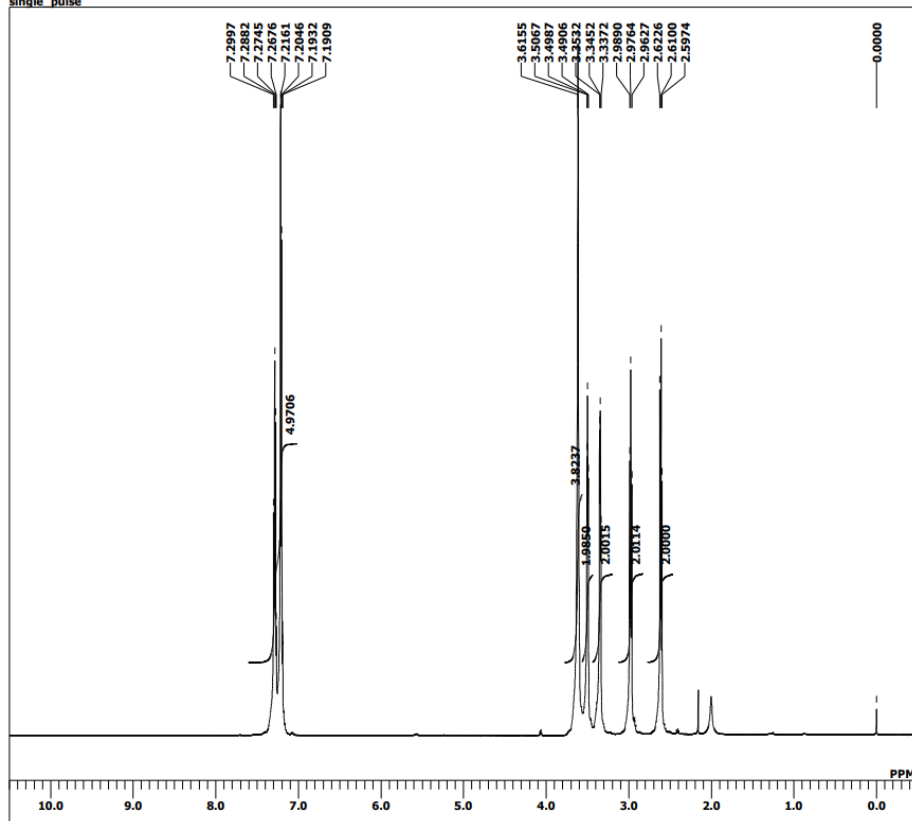
Data_Format = 1D COMPLEX
Dim_Size = 104858
X_Domain = Carbon13
Dim_Title = Carbon13
Dim_Units = [ppm]
Dimensions = X
Site = JNM-ECZ500R/M3
Spectrometer = JNM-ECZ500R/M3

Field_Strength = 11.7473579 [T]
X_Acq_Duration = 0.99357984 [s]
X_Domain = Carbon13
X_Freq = 125.76529768 [MHz]
X_Offset = 100 [ppm]
X_Points = 39303
X_Points_Input = 31442
X_Prescans = 4
X_Resolution = 1.00646164 [Hz]
X_Sweep = 39.55696203 [kHz]
X_Sweep_Clipped = 31.64556962 [kHz]
X_Sweep_Input = 251.0 [ppm]
Irr_Domain = Proton
Irr_Freq = 500.15991521 [MHz]
Irr_Offset = 5.0 [ppm]
Blanking = 5.0 [us]
Clipped = FALSE
Scans = 256
Total_Scans = 256

Relaxation_Delay = 2 [s]
Recvr_Gain = 52
Temp_Set = 22.3 [dC]
X_90_Width = 12.19 [us]
X_Acq_Time = 0.99357984 [s]
X_Angle = 30 [deg]
X_Atn = 11.5 [dB]
X_Data_Points = 32768
X_Points_Default = 39557
X_Pulse = 4.06333333 [us]
Irr_Atn_Dec = 29 [dB]
Irr_Atn_Dec_Calc = 29 [dB]
Irr_Atn_Noise = 29 [dB]
Irr_Bandwidth = 5.97826087 [MHz]
Irr_Bandwidth_Ppm = 11.9526989 [ppm]
Irr_Corresp_Pw90 = 92 [us]
Irr_Dec_Freq = 500.15991521 [MHz]
Irr_Decoupling = TRUE
Irr_Noise = TRUE
Irr_Noise = WALTZ
Irr_Offset_Default = 5 [ppm]
Irr_Pwidth = 92 [us]
Irr_Pwidth_Default = 92 [us]
Decimation_Rate = 0
    
```

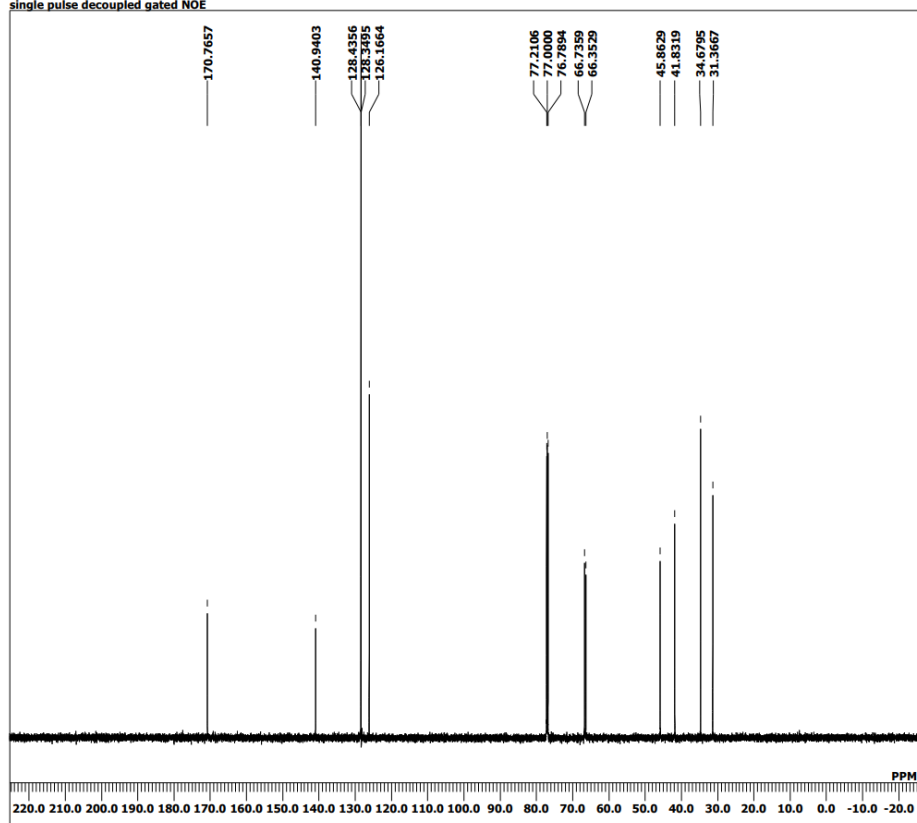
1-(4-Morpholinyl)-3-phenyl-1-propanone (3i)

WEca\data\takeno\KT00332-H-230320-1.als
single_pulse



DATIM 20-03-2023 00:08:21
 DFILE WEca\data\takeno\KT00332-H-230320-1
 OBNUC 1H
 EXMOD single_pulse.ex2
 OBFREQ 600.17 MHz
 OBSET 5.30 KHz
 OBFIN 5.47 Hz
 POINT 13107
 FREQU 9008.87 Hz
 SCANS 8
 ACQTM 1.4549 sec
 PD 5.0000 sec
 PW1 6.88 usec
 IRATN 0
 CTEMP 23.1 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 34

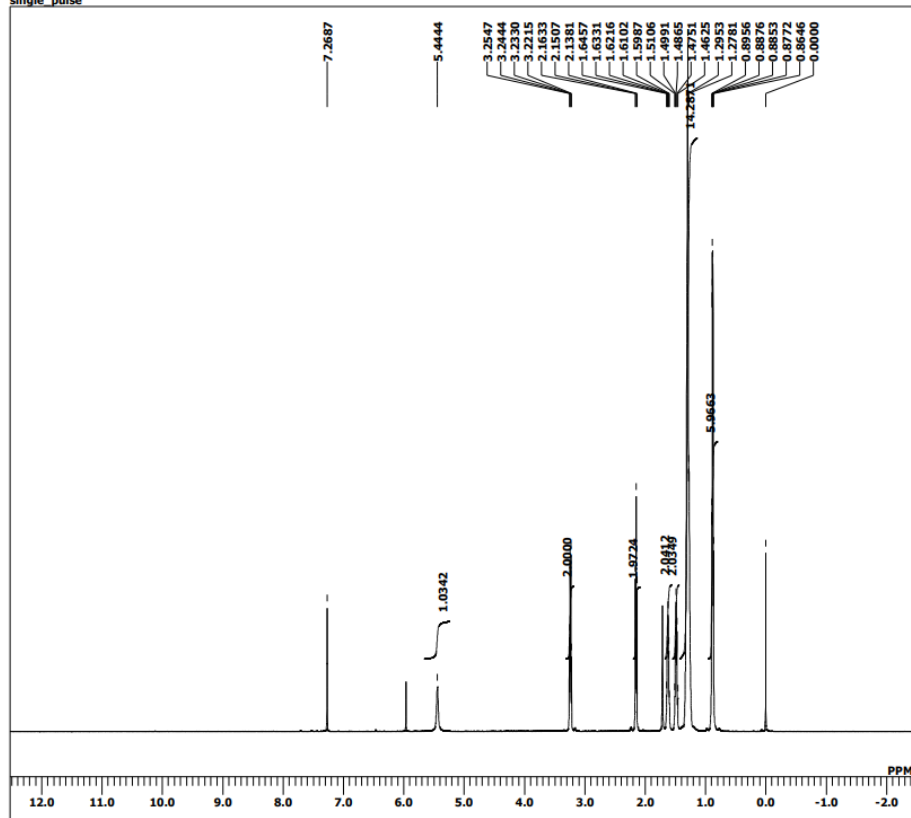
WEca\data\takeno\KT00332-C-230320-1.als
single_pulse decoupled gated NOE



DATIM 20-03-2023 00:06:17
 DFILE WEca\data\takeno\KT00332-C-230320-1
 OBNUC 13C
 EXMOD single_pulse_dec
 OBFREQ 150.92 MHz
 OBSET 8.52 KHz
 OBFIN 1.74 Hz
 POINT 26214
 FREQU 37878.21 Hz
 SCANS 387
 ACQTM 0.6921 sec
 PD 2.0000 sec
 PW1 4.11 usec
 IRATN 0
 CTEMP 23.5 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 50

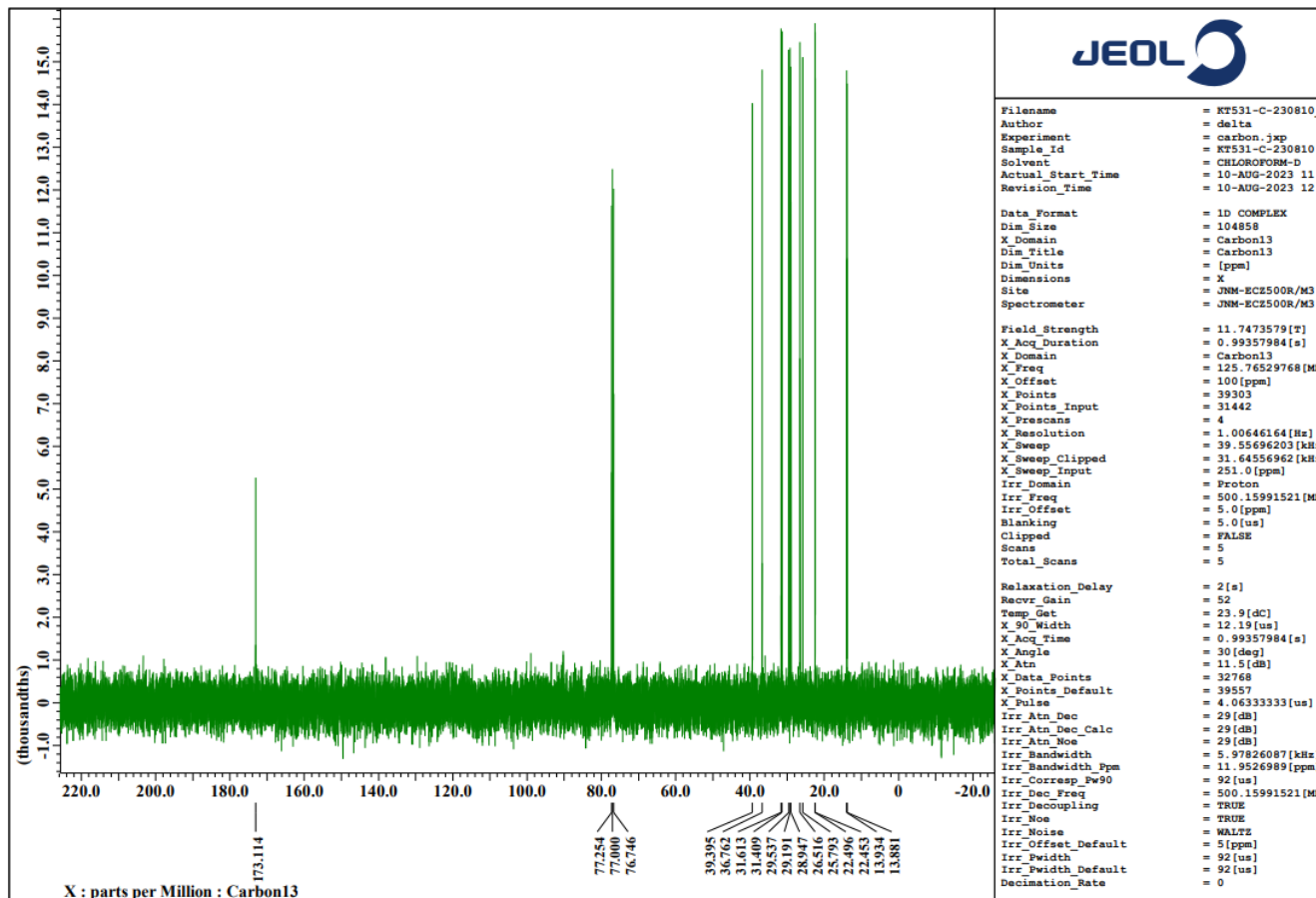
N-Hexylnonanamide (3j)

Weca\data\Takeno\KT00531-6-H-230810-1.als
single_pulse



```

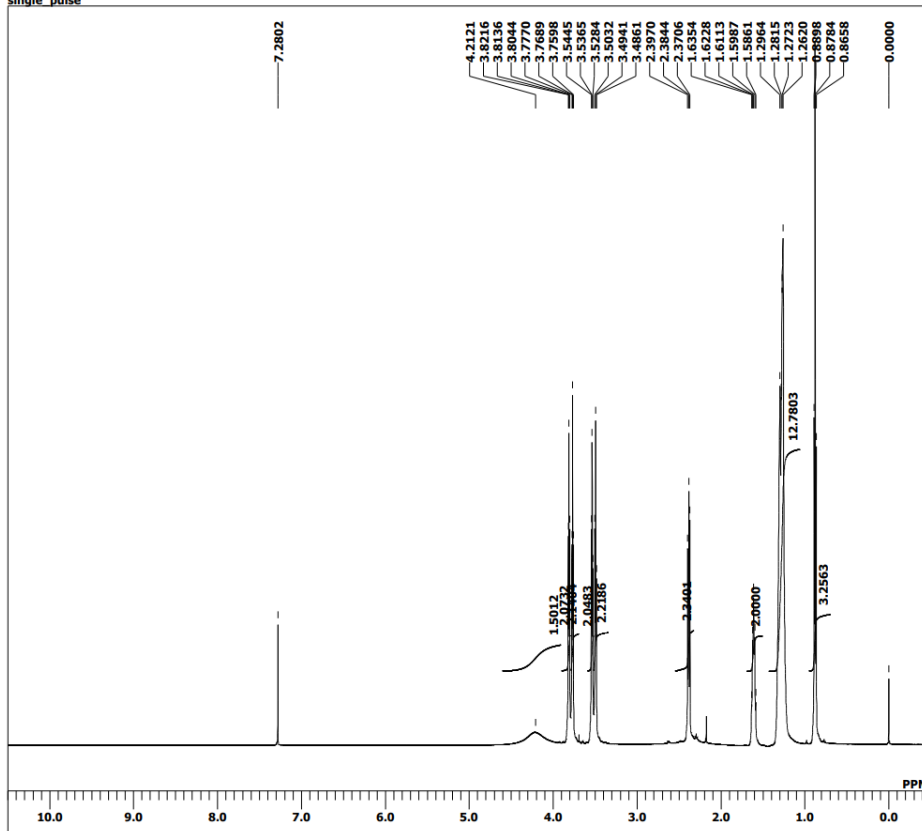
DATIM 09-08-2023 22:21:35
DFILE Weca\data\Takeno\KT00531-6-H-230810-1.
IH
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
OBSET 5.30 KHz
OBFIN 5.47 Hz
POINT 13107
FREQU 9008.87 Hz
SCANS 8
ACQTM 1.4549 sec
PD 5.0000 sec
PW1 6.88 usec
IRATN 0
CTEMP 402.3 c
SOLVNT CDCl3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 40
    
```



Filename	= KT531-C-230810_1
Author	= delta
Experiment	= carbon_jxp
Sample Id	= KT531-C-230810
Solvent	= CHLOROFORM-D
Actual_Start_Time	= 10-AUG-2023 11:22:00
Revision_Time	= 10-AUG-2023 12:00:00
Data_Format	= 1D COMPLEX
Dim_Size	= 104858
X_Domain	= Carbon13
Dim_Title	= Carbon13
Dim_Units	= [ppm]
Dimensions	= X
Site	= JNM-ECE500R/M3
Spectrometer	= JNM-ECE500R/M3
Field_Strength	= 11.7473579 [T] (101.625 MHz)
X_Acq_Duration	= 0.99357984 [s]
X_Domain	= Carbon13
X_Freq	= 125.76529768 [MHz]
X_Offset	= 100 [ppm]
X_Points	= 39303
X_Points_Input	= 31442
X_Prescans	= 4
X_Resolution	= 1.00646164 [Hz]
X_Sweep	= 39.55696203 [kHz]
X_Sweep_Clipped	= 31.64556962 [kHz]
X_Sweep_Input	= 251.0 [ppm]
Irr_Domain	= Proton
Irr_Freq	= 500.15991521 [MHz]
Irr_Offset	= 5.0 [ppm]
Blanking	= 5.0 [us]
Clipped	= FALSE
Scans	= 5
Total_Scans	= 5
Relaxation_Delay	= 2 [s]
Recvr_Gain	= 52
Temp_Get	= 23.9 [dC]
X_90_Width	= 12.19 [us]
X_Acq_Time	= 0.99357984 [s]
X_Angle	= 30 [deg]
X_Atn	= 11.5 [dB]
X_Data_Points	= 32768
X_Points_Default	= 39557
X_Pulse	= 4.06333333 [us]
Irr_Atn_Dec	= 29 [dB]
Irr_Atn_Dec_Calc	= 29 [dB]
Irr_Atn_Noise	= 29 [dB]
Irr_Bandwidth	= 5.97826087 [kHz]
Irr_Bandwidth_Ppm	= 11.9526989 [ppm]
Irr_Corresp_Fw90	= 92 [us]
Irr_Dec_Freq	= 500.15991521 [MHz]
Irr_Decoupling	= TRUE
Irr_Noise	= TRUE
Irr_Noise	= WALTZ
Irr_Offset_Default	= 5 [ppm]
Irr_Pwidth	= 92 [us]
Irr_Pwidth_Default	= 92 [us]
Decimation_Rate	= 0

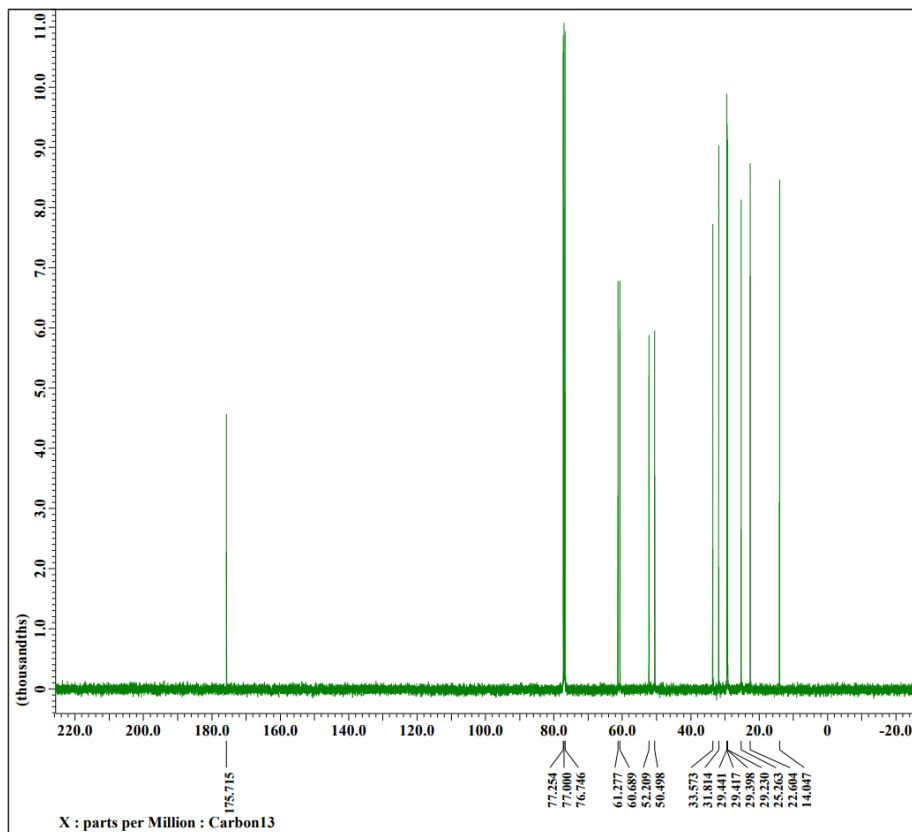
N,N-Bis(2-hydroxyethyl)decanamide (7)

WEca\data\Takeno\KT00391-Isolation-H-CDCl3-230420-1.als
single_pulse



```

DATIM 19-04-2023 23:30:49
DFILE WEca\data\Takeno\KT00391-Isolation-H
1H
single_pulse.ex2
OBNUC EXMOD
OBFRQ 600.17 MHz
OBSET 5.30 KHz
OBFIN 5.47 Hz
POINT 13107
FREQU 9008.87 Hz
SCANS 8
ACQTM 1.4549 sec
PD 5.0000 sec
PW1 6.88 usec
IRATN 0
CTEMP 23.0 c
SLVNT CDCl3
XREF 0.00 ppm
BF 0.12 Hz
RGAIN 34
    
```



JEOL

```

Filename = KT391-C-230512_
Author = delta
Experiment = carbon.jpg
Sample_Id = KT391-C-230512
Solvent = CHLOROFORM-D
Actual_Start_Time = 12-MAY-2023 17:
Revision_Time = 12-MAY-2023 17:

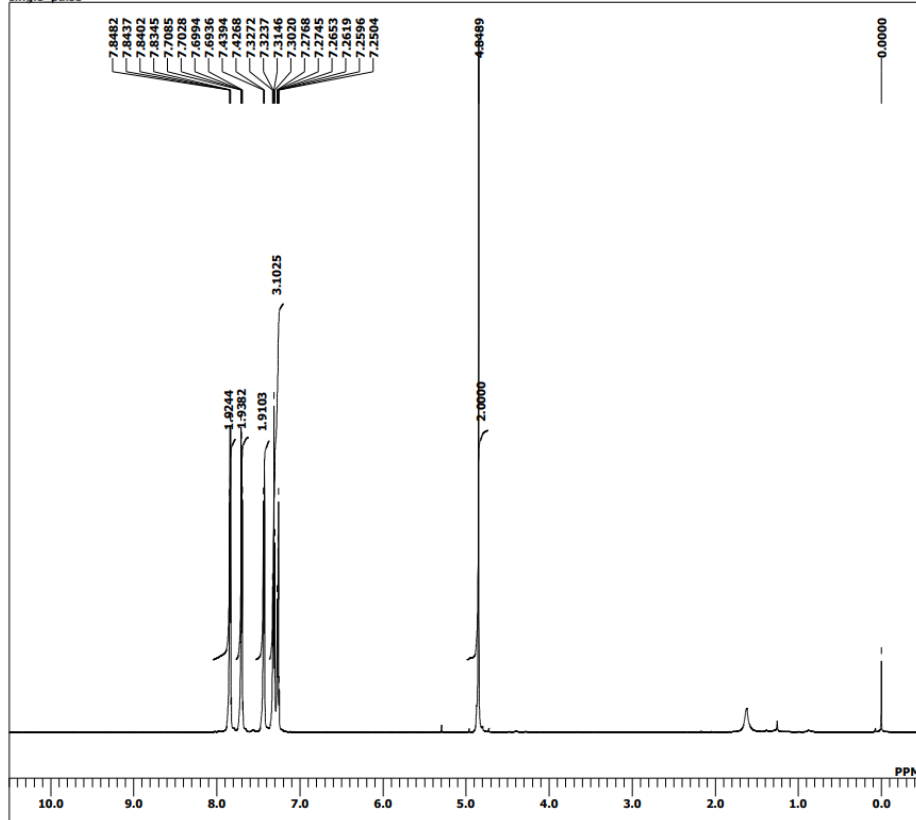
Data Format = 1D COMPLEX
Dim_Size = 104858
X_Domain = Carbon13
Dim_Title = Carbon13
Dim_Units = [ppm]
Dimensions = X
Site = JNM-ECZ500R/M3
Spectrometer = JNM-ECZ500R/M3

Field_Strength = 11.7473579 [T] (
X_Acq_Duration = 0.99357984 [s]
X_Domain = Carbon13
X_Freq = 125.76529768 [MHz]
X_Offset = 100 [ppm]
X_Points = 39303
X_Points_Input = 31442
X_Prescans = 4
X_Resolution = 1.00646164 [Hz]
X_Sweep = 39.55696203 [kHz]
X_Sweep_Clipped = 31.6455962 [kHz]
X_Sweep_Input = 251.0 [ppm]
Irr_Domain = Proton
Irr_Freq = 500.15991521 [MHz]
Irr_Offset = 5.0 [ppm]
Blanking = 5.0 [us]
Clipped = FALSE
Scans = 329
Total_Scans = 329

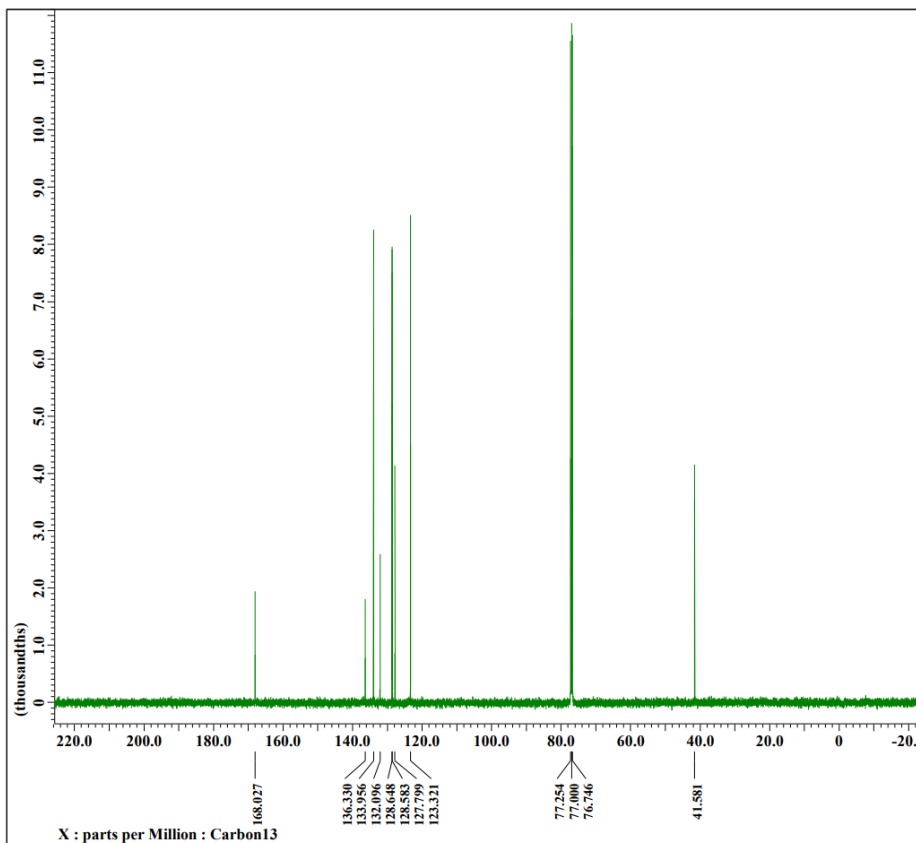
Relaxation_Delay = 2 [s]
Recv_Gain = 52
Temp_Get = 22 [dC]
X_90_Width = 12.19 [us]
X_Acq_Time = 0.99357984 [s]
X_Angle = 30 [deg]
X_Atn = 11.5 [dB]
X_Data_Points = 32768
X_Points_Default = 39557
X_Pulse = 4.06333333 [us]
Irr_Atn_Dec = 29 [dB]
Irr_Atn_Dec_Calc = 29 [dB]
Irr_Atn_Noise = 29 [dB]
Irr_Bandwidth = 5.97826087 [kHz]
Irr_Bandwidth_Ppm = 11.9526989 [ppm]
Irr_Corresp_Pw90 = 92 [us]
Irr_Dec_Freq = 500.15991521 [MHz]
Irr_Decoupling = TRUE
Irr_Noise = TRUE
Irr_Noise = WALTZ
Irr_Offset_Default = 5 [ppm]
Irr_Pwidth = 92 [us]
Irr_Pwidth_Default = 92 [us]
Decimation_Rate = 0
    
```

2-Benzylisoindoline-1,3-dione (11a)

Weca\data\takeno\KT00397-up-H-230523-1.als
single_pulse



DATIM 23-05-2023 05:24:56
 DFILF Weca\data\takeno\KT00397-up-H-23052
 OBNUC 1H
 EXMOD single_pulse.ex2
 OBFRQ 600.17 MHz
 OBSET 5.30 KHz
 OBFIN 5.47 Hz
 POINT 13107
 FREQU 9008.87 Hz
 SCANS 8
 ACQTM 1.4549 sec
 PD 5.0000 sec
 PW1 6.88 usec
 IRATN 0
 CTEMP 22.5 c
 SILVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 44

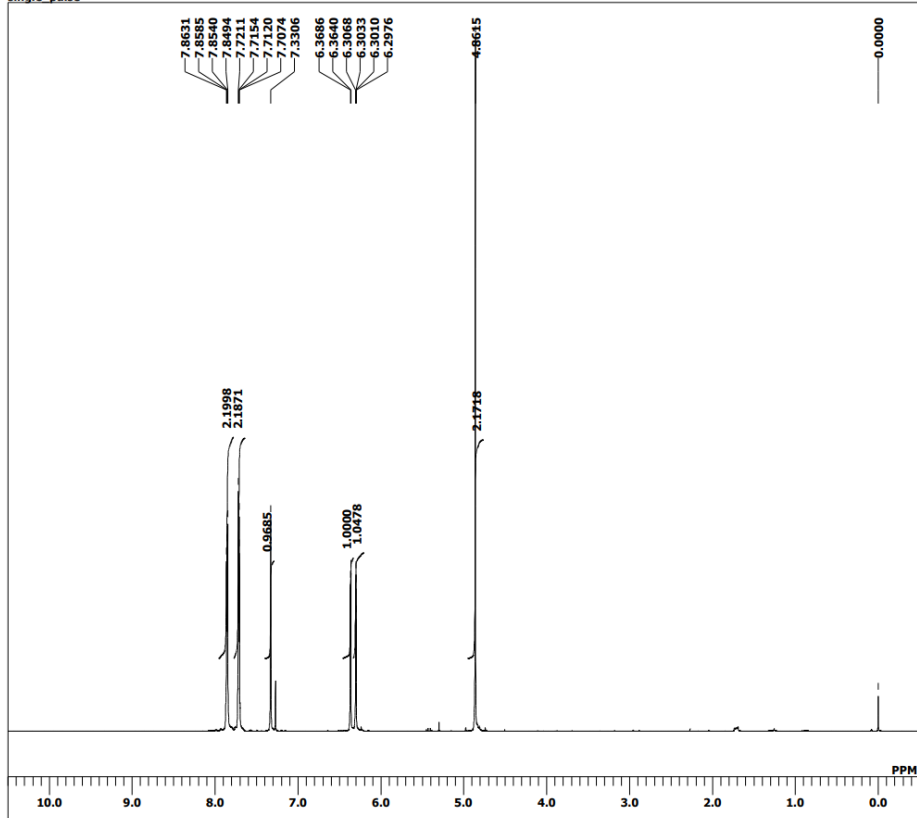


JEOL

Filename = KT00397-C-23052
 Author = delta
 Experiment = carbon_jmp
 Sample_id = KT00397-C-23052
 Solvent = CHLOROFORM-D
 Actual_Start_Time = 24-MAY-2023 10:
 Revision_Time = 24-MAY-2023 11:
 Data Format = 1D COMPLEX
 Dim Size = 104858
 X_Domain = Carbon13
 Dim Title = Carbon13
 Dim Units = [ppm]
 Dimensions = X
 Site = JNM-ECZ500R/M3
 Spectrometer = JNM-ECZ500R/M3
 Field_Strength = 11.7473579 [T] (R
 X_Acq_Duration = 0.99357984 [s]
 X_Domain = Carbon13
 X_Freq = 125.76529768 [MHz]
 X_Offset = 100 [ppm]
 X_Points = 39303
 X_Points_Input = 31442
 X_Prescans = 4
 X_Resolution = 1.00646164 [Hz]
 X_Sweep = 39.35696203 [kHz]
 X_Sweep_Clippped = 31.6456962 [kHz]
 X_Sweep_Input = 251.0 [ppm]
 Irr_Domain = Proton
 Irr_Freq = 500.15991521 [MHz]
 Irr_Offset = 5.0 [ppm]
 Blanking = 5.0 [us]
 Clipped = FALSE
 Scans = 520
 Total_Scans = 520
 Relaxation_Delay = 2 [s]
 Recvr_Gain = 52
 Temp_Get = 22.3 [dC]
 X_90_Width = 12.19 [us]
 X_Acq_Time = 0.99357984 [s]
 X_Angle = 30 [deg]
 X_Atn = 11.5 [dB]
 X_Data_Points = 32768
 X_Points_Default = 39557
 X_Pulse = 4.06333333 [us]
 Irr_Atn_Dec = 29 [dB]
 Irr_Atn_Dec_Calc = 29 [dB]
 Irr_Atn_Noise = 29 [dB]
 Irr_Bandwidth = 5.97826087 [kHz]
 Irr_Bandwidth_Ppm = 11.9526989 [ppm]
 Irr_Corresp_Pw90 = 92 [us]
 Irr_Dec_Freq = 500.15991521 [MHz]
 Irr_Decoupling = TRUR
 Irr_Noise = TRUR
 Irr_Noise = WALTZ
 Irr_Offset_Default = 5 [ppm]
 Irr_Width = 92 [us]
 Irr_Width_Default = 92 [us]
 Decimation_Rate = 0

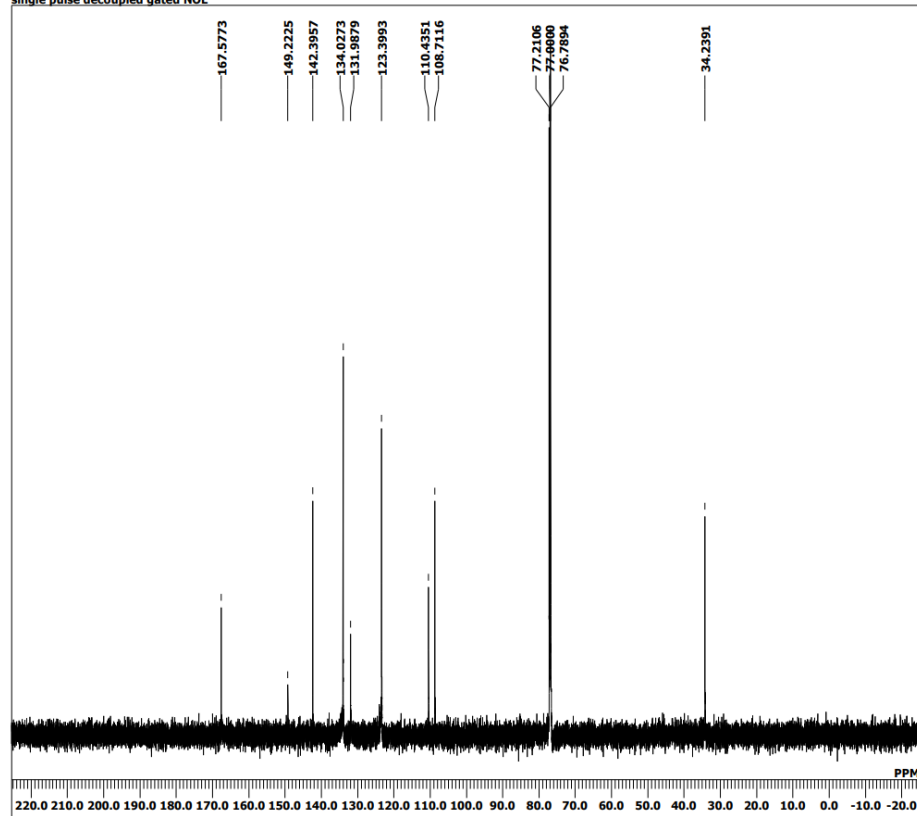
2-(2-Furanylmethyl)-1*H*-isoindole-1,3(2*H*)-dione (11b)

WEca\data\takeno\KT00373-H-230307-1.als
single_pulse



DATIM 07-03-2023 00:54:08
 DFILE WEca\data\takeno\KT00373-H-230307-1
 EXMOD single_pulse.ex2
 OBNUC 1H
 OBFREQ 600.17 MHz
 OBSET 5.30 KHz
 OBFIN 5.47 Hz
 POINT 13107
 FREQU 9008.87 Hz
 SCANS 8
 ACQTM 1.4549 sec
 PD 5.0000 sec
 PW1 6.88 usec
 IRATN 0
 CTEMP 22.9 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 40

WEca\data\takeno\KT00373-C-220510-1.als
single_pulse decoupled gated NOE



DATIM 10-05-2023 05:14:17
 DFILE WEca\data\takeno\KT00373-C-220510-1
 EXMOD single_pulse_dec
 OBNUC 13C
 OBFREQ 150.92 MHz
 OBSET 8.52 KHz
 OBFIN 1.74 Hz
 POINT 26214
 FREQU 37878.21 Hz
 SCANS 285
 ACQTM 0.6921 sec
 PD 2.0000 sec
 PW1 4.11 usec
 IRATN 0
 CTEMP 28.6 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 50

SI-10. References

- 1) S. M. Kemdeo, V. S. Sapkal, G. N. Chaudhari, *Bull. Chem. React. Eng. Catal.*, **2010**, *5*, 39–49.
- 2) H. Ishitani, M. Sasaya, S. Kobayashi, *ACS Sustainable Chem. Eng.*, **2023**, *11*, 5826–5833.
- 3) M. A. Ali, S. M. A. H. Siddiki, W. Onodera, K. Kon, K. Shimizu, *ChemCatChem*, **2015**, *7*, 3555–3561
- 4) M. A. Ali, S. M. A. H. Siddiki, K. Kon, J. Hasegawa, K. Shimizu, *Chem. Eur. J.*, **2014**, *20*, 14256–14260.
- 5) S. Hanada, T. Ishida, Y. Motoyama, H. Nagashima, *J. Org. Chem.*, **2007**, *72*, 7551–7559.
- 6) K. Dong, X. Fang, R. Jackstell, G. Laurenczy, Y. Li, M. Beller, *J. Am. Chem. Soc.*, **2015**, *137*, 6053–6058.
- 7) H. Morimoto, R. Fujiwara, Y. Shimizu, K. Morisaki, T. Ohshima, *Org. Lett.*, **2014**, *16*, 2018–2021.
- 8) C. L. Allen, A. R. Chhatwal, J. M. J. Williams, *Chem. Commun.*, **2012**, *48*, 666–668.
- 9) Z. Wu, K. L. Hull, *Chemical Science*, **2016**, *7*, 969–975.
- 10) Y. Deng, W. Gong, J. He, J.-Q. Yu, *Angew. Chem. Int. Ed.*, **2014**, *126*, 6810–6813.
- 11) A. J. A. Watson, A. C. Maxwell, J. M. J. Williams, *Org. Lett.*, **2009**, *11*, 2667–2670.
- 12) F. Casas, M. Trincado, R. Rodriguez-Lugo, D. Baneerje, H. Grützmacher, *ChemCatChem*, **2019**, *11*, 5241–5251.
- 13) L. Becerra-Figueroa, A. Ojeda-Porras, D. Gamba-Sánchez, *J. Org. Chem.*, **2014**, *79*, 4544–4552.
- 14) R. C. Brewster, J. T. Sutor, A. W. Bennett, S. Wallace, *Angew. Chem. Int. Ed.*, **2019**, *58*, 12409–12414.