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Cobalt(III)-Catalyzed Redox-Neutral Coupling of Acrylamides with Activated Alkenes via C–H Bond Activation

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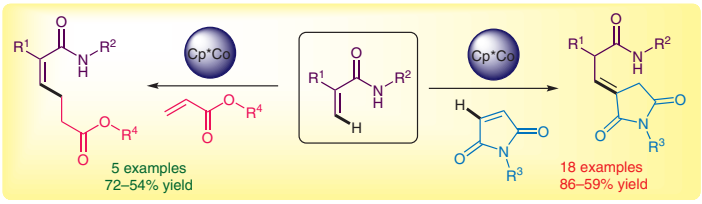
We would like to dedicate this work to Prof. Chien-Hong Cheng on the occasion of his 70th birthday.



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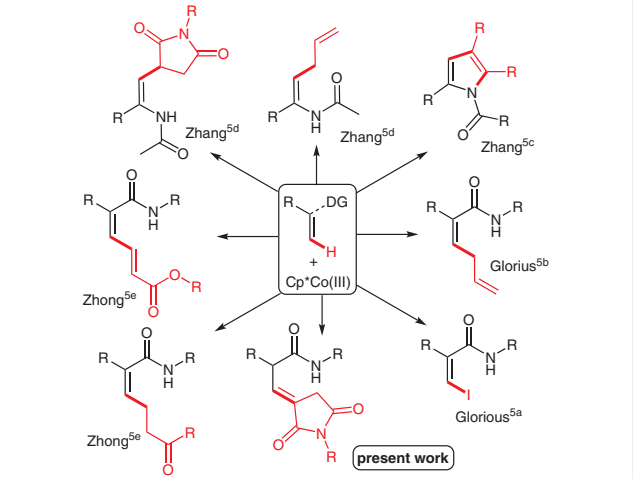
Abstract A cobalt(III)-catalyzed coupling of substituted acrylamides with maleimides in the presence of 30 mol% pivalic acid providing olefin-migrated succinimide derivatives in a redox-neutral manner is described. The coupling reaction was examined with various substituted acrylamides and maleimides. The scope of the C–H alkylation reaction was also examined with substituted acrylates. A possible reaction mechanism involving a five-membered cobaltocycle as a key intermediate is proposed.

Key words acrylamides, maleimides, C–H activation, alkylation, succinimides, acrylates, cobalt

The transition-metal-catalyzed C–H functionalization reaction has evolved as an indispensable tool in synthetic organic chemistry to construct complex organic motifs in a highly atom- and step-economical manner.[1–3] After the seminal findings from Murai and co-workers,[1] transition-metal complexes such as those of Pd, Ru, Rh and Ir have been widely employed to attain carbon–carbon and carbon–heteroatom bond formation via the C–H bond activation reaction.[2] However, these transition-metal salts are less abundant in nature and consequently these transition metals are expensive. Recently, the C–H functionalization of organic molecules catalyzed by first-row transition metals, such as cobalt, nickel, copper and iron, has gained much attention from synthetic organic chemists due to the high abundance and biocompatibility of such metals.[3] In particular, the Cp*Co-catalyzed C–H bond activation reaction has emerged as a promising alternative to second- and third-row metal catalysts for the functionalization of organic molecules.[4] The functionalization of aromatics and heteroaromatics has been extensively studied by employing the Cp*Co(III) catalyst. However, only few examples are reported for functionalization of vinylic C–H bonds, due to the ineffective formation of the key cobaltocycle intermediate.[5]

In 2014, the Glorius group reported the Cp*Co-catalyzed C–H iodination and allylation of acrylamide derivatives.[5a,b] Subsequently, Zhang's group and Zhong's group have explored the vinylic C–H bond activation of enamide derivatives (Scheme 1).[5c–e] On the other hand, succinimide is one of the important cores often found in various natural products and biologically active molecules.[6] The succinimide moiety can be incorporated into the C–H bond of organic molecules via 1,4-addition to maleimides. It is important to note that the maleimide unit is also often found in a range of natural products and biologically active molecules.[7,8] In addition, succinimide derivatives can be readily converted into pyrrolidines, also one of the important cores found in



Scheme 1 Cp*Co(III)-catalyzed functionalization of vinylic C–H bonds (DG = directing group)

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alkaloids.[9] Due to these facts, maleimides have evolved as one of the widely employed coupling partners in C–H bond activation reactions.[10] Herein, we report a cobalt(III)-catalyzed coupling of acrylamides with maleimides via C–H activation. The present protocol provides substituted succinimide derivatives under redox-neutral conditions. The catalytic reaction is compatible with substituted acrylamides as well as maleimides. The scope of the C–H alkylation reaction was also examined with substituted acrylates. A possible reaction mechanism involving a cobaltocycle intermediate is proposed.

Treatment of *N*-isobutylmethacrylamide (**1a**) with *N*-benzylmaleimide (**2a**) (1.2 equiv) in the presence of $Cp^*Co(CO)I_2$ (10 mol%), $AgSbF_6$ (20 mol%) and pivalic acid (PivOH) (30 mol%) in CF_3CH_2OH (TFE) at 120 °C for 16 hours under nitrogen atmosphere yielded product **3aa** in 79% yield (Table 1, entry 13). Initially, the alkylation reaction using NaOPiv was examined with various solvents, such as CH_3CN, 1,2-dichloroethane (1,2-DCE), chlorobenzene, TFE, (trifluoromethyl)benzene, hexafluoro-2-propanol (HFIP) and 1,4-dioxane (entries 1–7). Among them, TFE was very effective, giving product **3aa** in 63% yield (entry 4). 1,2-DCE was partially effective, providing **3aa** in 29% yield (entry 2),

Biographical Sketches

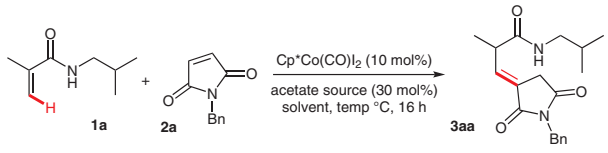
Meledath Sudhakaran Keerthana was born in Kozhikode, Kerala, India, in 1993. She received her integrated MSc degree in chemistry from the Institute for Intensive Research in Basic Sciences (IIRBS), Mahatma Gandhi University in 2017. At present, she is pursuing her PhD under the guidance of Dr. M. Jeganmohan at the Indian Institute of Technology Madras (IIT Madras), India. Her PhD research focuses on the C–H bond functionalization of organic molecules via metal-catalyzed C–H bond activation.

Ramasamy Manoharan was born in Nattuvampalayam, Tamil Nadu, India, in 1989. He received his bachelor's degree from Sri Vasavi College, Bharathiar University in 2009 and his master's degree from Madurai Kamaraj University in 2011. He received his PhD from the Indian Institute of Science Education and Research Pune (IISER Pune) under the guidance of Dr. M. Jeganmohan. His PhD research focused on the C–H bond functionalization of organic molecules via metal-catalyzed C–H bond activation.

Masilamani Jeganmohan was born in Vazhapattampalayam, Tamil Nadu, India, in 1978. He received his master's degree in organic chemistry from the University of Madras in 2001. He earned his PhD from the National Tsing Hua University, Taiwan, under the guidance of Prof. Chien-Hong Cheng in 2005 and pursued postdoctoral work in the same laboratory (2005–2009). Then, he moved to the Ludwig-Maximilians-Universität, Munich, Germany, for postdoctoral study with Prof. Paul Knochel supported by the Alexander von Humboldt Foundation (2009–2010). He started his independent research career in November 2010 at IISER Pune as an assistant professor. In April 2016, he was promoted to associate professor at IISER Pune. At present, he is working as an associate professor at IIT Madras (October 2016–till now). He is the recipient of a DAE Young Scientist Research Award (2011), Science Academy Medal for a Young Associate, Indian Academy of Sciences (2012–2015), Science Academy Medal for Young Scientists, Indian National Science Academy (2013), Alkyl Amines – ICT Young Scientist Award by the Institute of Chemical Technology Mumbai (2013), ISCB Award of Appreciation for Chemical Science, CSIR-CDRI (2014), India and in 2019, Fellow of the Royal Society of Chemistry (FRSC). His research interests include the development of new synthetic methods using metal complexes as catalysts, asymmetric synthesis and natural product synthesis.

while the remaining solvents were totally ineffective. Then, the reaction in TFE was examined with various acetate sources, such as NaOPiv, AgOAc, $Cu(OAc)_2{\cdot}H_2O$, CsOAc and NaOAc. NaOPiv and AgOAc provided product **3aa** in 63% and 47% yield, respectively (entries 4 and 8). Other acetate sources were ineffective. The reaction was also examined in the presence of organic acids, such as acetic acid, PivOH, mesitylenic acid and adamantane-1-carboxylic acid (Adm-1-COOH) (entries 12–15). Among them, PivOH was very effective, yielding **3aa** in 79% yield (entry 13). In addition, the present reaction was examined with various additives, such as $AgSbF_6$, AgOTf, $AgBF_4$ and KPF_6. Among them, $AgSbF_6$ was very effective (79% yield of **3aa**, entry 13), $AgBF_4$ was partially effective (45% yield of **3aa**, entry 17), and AgOTf and KPF_6 were totally ineffective (entries 16 and 18). The efficiency of the cationic cobalt complex $[Cp^*Co(CH_3CN)_3][SbF_6]_2$ was also examined. In this reaction, product **3aa** was obtained in 59% yield (entry 19). This result clearly revealed that the combination of $Cp^*Co(CO)I_2$ and $AgSbF_6$ is more effective than the cationic complex. The reaction condition in entry 20 was done under room temperature, 16h. It is important to note that the yield of product **3aa** decreased drastically at lower temperatures (entries 21 and 22). These optimization studies clearly revealed that $Cp^*Co(CO)I_2$ (10 mol%), $AgSbF_6$ (20 mol%) and PivOH (30 mol%) in TFE at 120 °C for 16 hours are the best conditions for the present reaction.

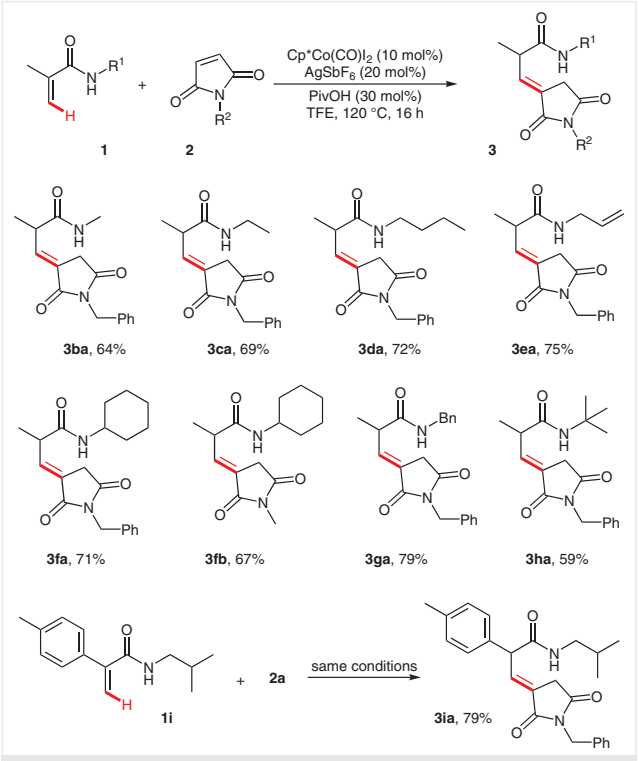
Table 1 Optimization Studies[a]



Entry	Solvent	Acetate source	Additive	Yield (%)[b]
1	CH_3CN	NaOPiv	$AgSbF_6$	NR
2	1,2-DCE	NaOPiv	$AgSbF_6$	29
3	C_6H_5Cl	NaOPiv	$AgSbF_6$	NR
4	TFE	NaOPiv	$AgSbF_6$	63
5	$C_6H_5CF_3$	NaOPiv	$AgSbF_6$	NR
6	HFIP	NaOPiv	$AgSbF_6$	NR
7	1,4-dioxane	NaOPiv	$AgSbF_6$	NR
8	TFE	AgOAc	$AgSbF_6$	47
9	TFE	$Cu(OAc)_2{\cdot}H_2O$	$AgSbF_6$	NR
10	TFE	CsOAc	$AgSbF_6$	NR
11	TFE	NaOAc	$AgSbF_6$	NR
12	TFE	AcOH	$AgSbF_6$	NR
13	TFE	PivOH	$AgSbF_6$	79
14	TFE	Adm-1-COOH	$AgSbF_6$	NR
15	TFE	mesitylenic acid	$AgSbF_6$	NR
16	TFE	PivOH	AgOTf	NR
17	TFE	PivOH	$AgBF_4$	45
18	TFE	PivOH	KPF_6	NR
19	TFE	PivOH	–	59[c]
20	TFE	PivOH	$AgSbF_6$	NR
21	TFE	PivOH	$AgSbF_6$	39[d]
22	TFE	PivOH	$AgSbF_6$	63[e]

[a] Reaction conditions, unless indicated otherwise: **1a** (50 mg), **2a** (1.2 equiv), $Cp^*Co(CO)I_2$ (10 mol%), $AgSbF_6$ (20 mol%), acetate source (30 mol%), solvent (3.0 mL), 120 °C, 16 h.
[b] Isolated yield.
[c] $[Cp^*Co(CH_3CN)_3][SbF_6]_2$ (5 mol%) was used.
[d] 60 °C, 16 h.
[e] 100 °C, 16 h.

The scope of the present alkylation reaction was examined with acrylamides having various *N*-protecting groups under the optimized reaction conditions (Scheme 2). *N*-Methyl-, *N*-ethyl- and *N*-butylacrylamides **1b**, **1c** and **1d** reacted with **2a** providing the expected alkylation products **3ba**, **3ca** and **3da** in 64%, 69% and 72% yield, respectively. *N*-Allylacrylamide **1e** yielded alkylation product **3ea** without affecting the allyl group, in 75% yield. *N*-Cyclohexylacrylamide **1f** reacted with *N*-benzylmaleimide (**2a**), as well as with *N*-methylmaleimide (**2b**), to produce products **3fa** and **3fb** in 71% and 67% yield, respectively.

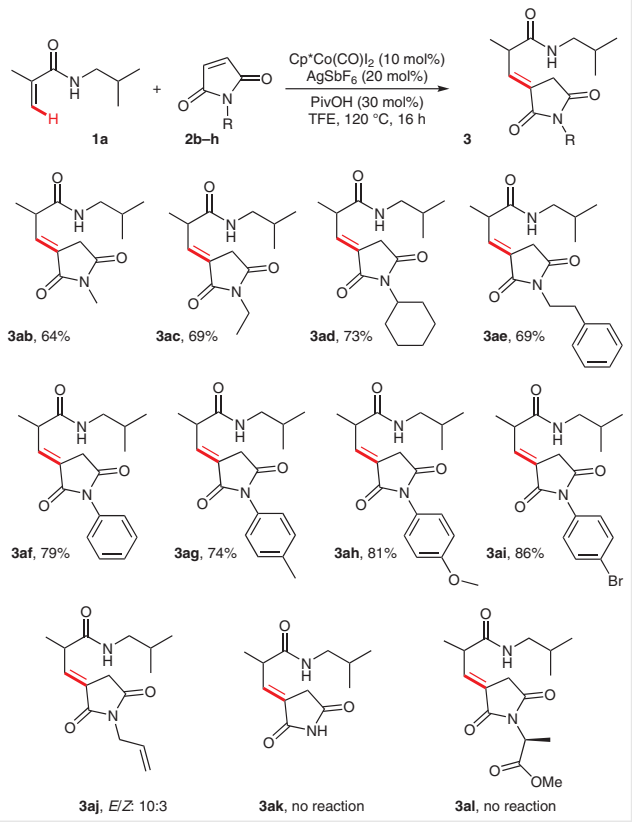


Scheme 2 Scope of acrylamides

N-Benzylacrylamide **1g** reacted with **2a** under the optimized reaction conditions providing product **3ga** in 79% yield. Sterically hindered *N*-*tert*-butylacrylamide **1h** also

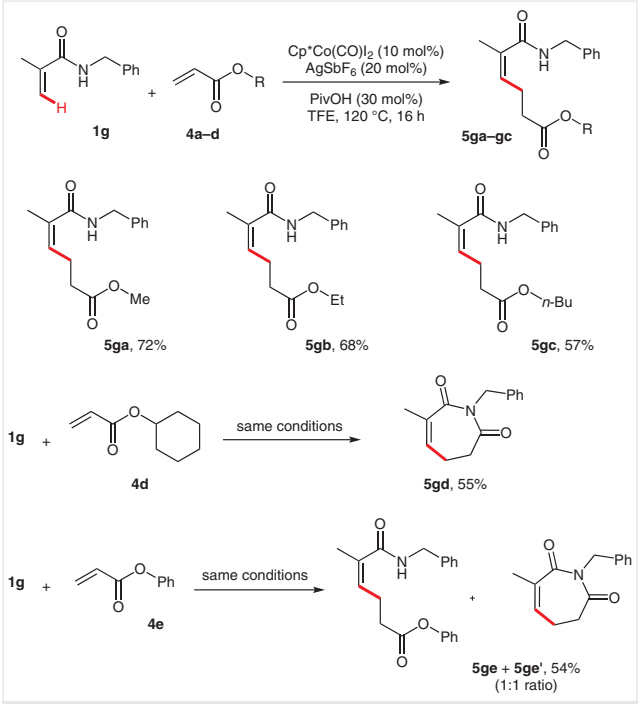
produced the expected product **3ha** in 59% yield. The reaction was also examined with α-arylacrylamides such as *N*-isobutyl-2-(*p*-tolyl)acrylamide (**1i**) which resulted in alkylated product **3ia** in 79% yield. However, the alkylation reaction is not compatible with β-alkyl- or β-aryl-substituted acrylamides due to steric hindrance at the β-position which seems to hinder formation of the key metalacycle.

The present reaction was also further examined with various *N*-substituted maleimides **2b–i** (Scheme 3). Maleimides **2b–e** having an alkyl substituent such as methyl, ethyl, cyclohexyl and phenethyl reacted with **1a** to give the corresponding alkylated products **3ab–ae** in 64%, 69%, 73% and 69% yield, respectively. Then, the scope of maleimides was extended to *N*-aryl-substituted maleimides **2f–i**. *N*-Phenylmaleimide (**2f**) produced the expected product **3af** in 79% yield, while *N*-arylmaleimides **2g–i** having a 4-Me, 4-OMe and 4-Br substituent, respectively, gave the corresponding alkylated products **3ag–ai** in 74%, 81% and 86% yield. *N*-Allylmaleimide (**2j**) produced product **3aj** in 35% yield in a 10:3 *E*/*Z* ratio. However, N–H free maleimide and maleimide **2l** derived from the amino acid L-alanine were found to be ineffective. Similarly, internal olefins such as maleate and fumarate were also ineffective in this reaction.



Scheme 3 Scope of maleimides

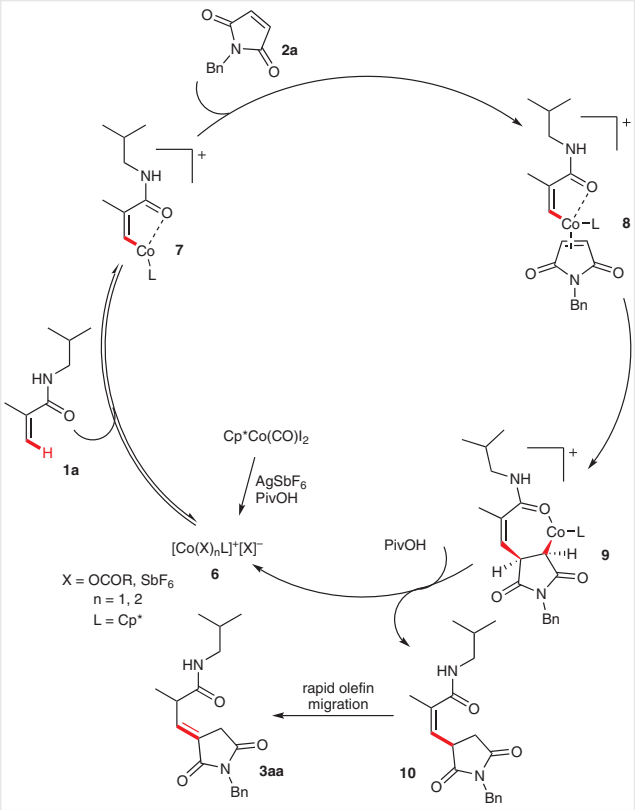
The present alkylation reaction is compatible with substituted acrylates. In these reactions, the linear-selective alkylated product was observed (Scheme 4).[11] It is important to note that in this type of transformation only vinylic C–H alkenylation was observed with acrylates. In the present reaction, interestingly, C–H alkylated product was observed which is not known in the literature. Treatment of *N*-benzylmethacrylamide (**1g**) with methyl acrylate (**4a**) (1.2 equiv) in the presence of $Cp^*Co(CO)I_2$ (10 mol%), $AgSbF_6$ (20 mol%) and PivOH (30 mol%) in TFE at 120 °C for 16 hours provided C–H alkylated product **5ga** in 72% yield (Scheme 4). Ethyl acrylate (**4b**) and *n*-butyl acrylate (**4c**) reacted with **1g** giving the linear-selective alkylated products **5gb** and **5gc** in 68% and 57% yield, respectively. It is interesting to note that in the reaction of **1g** with cyclohexyl acrylate (**4d**), a seven-membered azepine derivative **5gd** was observed in 55% yield under the optimized reaction conditions. However, phenyl acrylate (**4e**) reacted with **1g** to give a 1:1 mixture of alkylated product **5ge** and cyclized product **5ge′** in 54% yield.



Scheme 4 Scope of activated alkenes

Based on known cobalt-catalyzed C–H bond cleavage reactions,[3–5] a possible reaction mechanism is proposed in Scheme 5. The reaction likely commences with the formation of active catalyst **6** from $Cp^*Co(CO)I_2$, $AgSbF_6$ and PivOH. Then, coordination of the oxygen atom of the amide group of **1** followed by C–H bond cleavage leads to the formation of cobaltocycle intermediate **7**. Further, coordination of maleimide **2a** into complex **7** followed by migratory insertion

produces intermediate **9**. Protonation of intermediate **9** by PivOH leads to the formation of alkylated product **10** and regenerates the active catalyst **6** for the next cycle.



Scheme 5 Proposed mechanism

Olefin migration in intermediate **10** furnishes product **3aa**, similar to Kim's observation in the presence of a rhodium catalyst.[10e] It is important to note that the rhodium complex effectively catalyzed the C–H alkylation of β-substituted acrylamides with maleimides; however, it could not catalyze the C–H alkylation of α-substituted acrylamides with maleimides. Interestingly, in the present reaction, a less expensive cobalt complex effectively catalyzed the alkylation of α-substituted acrylamides with maleimides. It is also important to note that the whole catalytic cycle proceeds in the Co(III) state and thus an oxidation step is not needed. The reaction proceeds in a redox-neutral version and organic acid plays the dual role of protonation of the C–Co bond in intermediate **9** and deprotonation of the vinylic C–H bond by the corresponding acetate anion.

In conclusion, we have demonstrated a cobalt-catalyzed C–H alkylation of acrylamides with maleimides to provide olefin-migrated alkylated products in good to excellent yields. The reaction is compatible with various substituted acrylamides and maleimides. The scope of the C–H alkylation reaction was also examined with substituted acrylates. A possible reaction mechanism involving a five-membered cobaltocycle intermediate has been proposed. The reaction proceeds in a redox-neutral version and organic acid plays the dual role of protonation of C–Co in a seven-membered cobalt intermediate and deprotonation of the C–H bond of the acrylamide by the corresponding acetate anion.

All reactions were carried out under N_2 atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with nitrogen prior to use (three times). Anhydrous solvents were used for the reactions. Column chromatographic purifications were performed using silica gel (120–200 mesh ASTM) from Merck, if not indicated otherwise. Standard abbreviations are used for NMR signal coupling. Commercially available metal salts were purchased from Sigma-Aldrich and used without further purification.

Substituted Succinimide Derivatives 3; General Procedure

A 15 mL Schlenk tube with septum containing $Cp^*Co(CO)I_2$ (10 mol%), acrylamide **1** (50 mg, 1 equiv), maleimide **2** (1.2 equiv) and $AgSbF_6$ (20 mol%) was evacuated and purged with nitrogen gas three times ($AgSbF_6$ was transferred inside a glovebox). To the tube were then added PivOH (30 mol%) and TFE (3.0 mL) via syringe; after that, the reaction mixture was evacuated and purged with nitrogen gas three times. Then, the septum was taken out immediately and a screw cap was used to cover the tube under the nitrogen atmosphere, and the reaction mixture was stirred at room temperature for 5 min. Then, the mixture was stirred at 120 °C for 16 h. After cooling to ambient temperature, the mixture was diluted with CH_2Cl_2 and filtered through Celite, and the filtrate was concentrated. The crude residue was purified through a silica gel column (40% ethyl acetate in hexanes as eluent) to give pure product **3**.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3aa)

Colorless semisolid; yield: 92.0 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 2 H), 7.33–7.27 (m, 3 H), 6.84 (d, *J* = 9.8 Hz, 1 H), 5.62 (bs, 1 H), 4.72 (s, 2 H), 3.31 (dd, *J* = 21.4, 2.2 Hz, 1 H), 3.23 (dd, *J* = 21.4, 2.2 Hz, 1 H), 3.16–3.09 (m, 1 H), 3.06 (t, *J* = 6.6 Hz, 2 H), 1.80–1.72 (m, 1 H), 1.36 (d, *J* = 7.2 Hz, 3 H), 0.88 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 171.5, 164.1, 136.9, 135.7, 128.9, 128.7, 128.4, 127.2, 126.4, 47.1, 42.5, 42.4, 31.8, 28.4, 20.0, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{19}H_{24}N_2O_3$)H]: 329.1865; found: 329.1859.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*,2-dimethylpropanamide (3ba)

Colorless semisolid; yield: 92.0 mg (64%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.38 (m, 2 H), 7.32–7.27 (m, 3 H), 6.80 (d, *J* = 9.8 Hz, 1 H), 5.75 (bs, 1 H), 4.71 (s, 2 H), 3.30 (dd, *J* = 21.4, 1.6 Hz, 1 H), 3.22 (dd, *J* = 21.4, 1.6 Hz, 1 H), 3.11 (dq, *J* = 14.2, 7.2 Hz, 1 H), 2.78 (d, *J* = 4.8 Hz, 3 H), 1.34 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 172.1, 169.2, 136.9, 135.6, 128.9, 128.7, 128.1, 127.2, 42.5, 42.2, 31.8, 26.6, 17.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{16}H_{18}N_2O_3$)H]: 287.1396; found: 287.1339.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-ethyl-2-methylpropanamide (3ca)

colorless semisolid; yield: 91.0 mg (69%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.36 (m, 2 H), 7.33–7.23 (m, 3 H), 6.82 (dt, *J* = 9.6, 2.0 Hz, 1 H), 5.69 (s, 1 H), 4.71 (s, 2 H), 3.37–3.18 (m, 4 H), 3.09 (dq, *J* = 14.2, 7.2 Hz, 1 H), 1.34 (d, *J* = 7.2 Hz, 3 H), 1.12 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 171.4, 169.2, 136.9, 135.6, 128.9, 128.7, 128.0, 127.1, 42.4, 42.3, 34.8, 31.9, 17.3, 14.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{17}H_{20}N_2O_3$)H]: 301.1552; found: 301.1552.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-butyl-2-methylpropanamide (3da)

Colorless semisolid; yield: 84.0 mg (72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.37 (m, 2 H), 7.35–7.29 (m, 3 H), 6.82 (dt, *J* = 9.6, 2.2 Hz, 1 H), 5.52 (bs, 1 H), 4.72 (s, 2 H), 3.27 (dd, *J* = 10.8, 2.2 Hz, 2 H), 3.24–3.19 (m, 2 H), 3.09 (dq, *J* = 14.6, 7.2 Hz, 1 H), 1.48–1.43 (m, 2 H), 1.35 (d, *J* = 7.2 Hz, 3 H), 1.32–1.28 (m, 2 H), 0.91 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 172.2, 171.4, 169.6, 169.2, 136.9, 135.7, 129.0, 128.7, 128.1, 127.2, 42.5, 42.4, 39.6, 31.9, 31.6, 20.0, 17.4, 13.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{19}H_{24}N_2O_3$)H]: 329.1865; found: 329.1858.

(*E*)-*N*-Allyl-3-(1-benzyl-2,5-dioxopyrrolidin-3-ylidene)-2-methylpropanamide (3ea)

Colorless semisolid; yield: 94.0 mg (75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.40 (m, 2 H), 7.34–7.27 (m, 3 H), 6.83 (dt, *J* = 9.8, 2.2 Hz, 1 H), 5.80 (ddd, *J* = 16.2, 10.8, 5.8 Hz, 1 H), 5.63 (bs, 1 H), 5.19–5.15 (m, 1 H), 5.14–5.13 (m, 1 H), 4.72 (s, 2 H), 3.86 (t, *J* = 5.8 Hz, 2 H), 3.32 (dd, *J* = 21.2, 2.4 Hz, 1 H), 3.24 (dd, *J* = 21.2, 2.4 Hz, 1 H), 3.13 (dq, *J* = 14.2, 7.2 Hz, 1 H), 1.37 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.2, 172.0, 169.21, 136.8, 135.6, 128.9, 128.9, 128.7, 128.6,128.0, 127.2, 42.4, 42.2, 31.8, 26.5, 17.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{18}H_{20}N_2O_3$)H]: 313.1552; found: 313.1580.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-cyclohexyl-2-methylpropanamide (3fa)

Colorless semisolid; yield: 75.0 mg (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.40 (m, 2 H), 7.33–7.27 (m, 3 H), 6.83 (d, *J* = 9.6 Hz, 1 H), 5.38 (d, *J* = 7.4 Hz, 1 H), 4.72 (s, 2 H), 3.80–3.63 (m, 1 H), 3.31 (dd, *J* = 21.2, 2.2 Hz, 1 H), 3.22 (dd, *J* = 21.2, 2.1 Hz, 1 H), 3.06 (dq, *J* = 14.2, 7.2 Hz, 1 H), 1.91–1.87 (m, 2 H), 1.72–1.60 (m, 4 H), 1.33 (d, *J* = 7.2 Hz, 3 H), 1.18–1.04 (m, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 184.0, 173.5, 170.9, 169.3, 137.2, 135.6, 128.9, 128.9, 128.7, 128.7, 128.0, 126.9, 48.7, 42.4, 38.5, 32.9, 31.8, 27.0, 25.4, 24.8, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{21}H_{26}N_2O_3$)H]: 355.2022; found: 355.2019.

(*E*)-*N*-Cyclohexyl-2-methyl-3-(1-methyl-2,5-dioxopyrrolidin-3-ylidene)propanamide (3fb)

Colorless semisolid; yield: 56.0 mg (67%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (d, *J* = 9.4 Hz, 1 H), 5.84 (d, *J* = 7.2 Hz, 1 H), 3.84–3.68 (m, 1 H), 3.59 (bs, 1 H), 3.34 (d, *J* = 21.4 Hz, 1 H), 3.25 (d, *J* = 21.4 Hz, 1 H), 3.20–3.14 (m, 1 H), 3.06 (s, 3 H), 1.91–1.89 (m, 2 H), 1.74–1.70 (m, 2 H), 1.64–1.61 (m, 1 H), 1.38–1.30 (m, 4 H), 1.19–1.10 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 171.2, 169.7, 136.4, 127.3, 48.9, 42.2, 32.9, 31.7, 25.4, 24.8, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{15}H_{22}N_2O_3$)H]: 279.1709; found: 279.1702.

(*E*)-*N*-Benzyl-3-(1-benzyl-2,5-dioxopyrrolidin-3-ylidene)-2-methylpropanamide (3ga)

Colorless semisolid; yield: 82.0 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.37 (m, 2 H), 7.33–7.30 (m, 2 H), 7.29–7.26 (m, 4 H), 7.21 (d, *J* = 6.8 Hz, 2 H), 6.83 (dt, *J* = 9.6, 2.0 Hz, 1 H), 5.99 (bs, 1 H), 4.69 (s, 2 H), 4.39 (t, *J* = 5.6 Hz, 2 H), 3.25 (dd, *J* = 21.2, 2.2 Hz, 1 H), 3.21–3.08 (m, 2 H), 1.36 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.4, 173.1, 171.3, 169.1, 137.7, 136.6, 135.6, 128.9, 128.8, 128.7, 128.1, 127.9, 127.8, 127.4, 43.9, 42.5, 42.3, 31.8, 29.7, 17.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{22}H_{22}N_2O_3$)H]: 363.1709; found: 363.1721.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-(*tert*-butyl)-2-methylpropanamide (3ha)

Off-white semisolid; yield: 69.0 mg (59%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.40 (m, 2 H), 7.33–7.29 (m, 3 H), 6.83 (d, *J* = 9.6 Hz, 1 H), 5.37 (s, 1 H), 4.72 (s, 2 H), 3.31 (dd, *J* = 21.4, 1.8 Hz, 1 H), 3.22 (dd, *J* = 21.4, 1.8 Hz, 1 H), 3.09–2.94 (m, 1 H), 1.97 (s, 3 H), 1.33 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.5, 171.1, 171.00, 137.6, 128.8, 128.6, 127.9, 121.3, 51.6, 43.0, 42.3, 31.8, 28.6, 27.1, 18.5, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{19}H_{24}N_2O_3$)H]: 329.1865; found: 329.1883.

(*E*)-3-(1-Benzyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-isobutyl-2-(*p*-tolyl)propanamide (3ia)

Colorless semisolid; yield: 74.0 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.30 (m, 2 H), 7.24–7.22 (m, 4 H), 7.13–7.07 (m, 4 H), 5.35 (bs, 1 H), 4.63 (s, 2 H), 4.15 (d, *J* = 8.6 Hz, 1 H), 3.21 (d, *J* = 21.2 Hz, 1 H), 2.99–2.87 (m, 3 H), 2.27 (s, 3 H), 1.65–1.57 (m, 1 H), 0.72 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 170.2, 169.2, 138.3, 135.7, 135.4, 133.7, 133.1, 130.3, 129.9, 129.7, 128.9, 128.8, 128.7, 128.6, 128.2, 128.1, 127.9, 53.3, 47.2, 42.4, 32.1, 28.4, 21.1, 19.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{25}H_{28}N_2O_3$)H]: 405.2178; found: 405.2198.

(*E*)-*N*-Isobutyl-2-methyl-3-(1-methyl-2,5-dioxopyrrolidin-3-ylidene)propanamide (3ab)

Colorless semisolid; yield: 57.0 mg (64%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 9.6 Hz, 1 H), 5.72 (s, 1 H), 3.33 (d, *J* = 21.2 Hz, 1 H), 3.25 (d, *J* = 21.2 Hz, 1 H), 3.20–3.11 (m, 1 H), 3.12–3.08 (m, 2 H), 3.06 (s, 3 H), 1.86–1.69 (m, 1 H), 1.38 (d, *J* = 7.2 Hz, 3 H), 0.90 (d, *J* = 6.6 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 171.6, 169.6, 136.5, 127.2, 47.1, 42.4, 31.8, 28.4, 24.8, 20.0, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{13}H_{20}N_2O_3$)H]: 253.1552; found: 253.1553.

(*E*)-3-(1-Ethyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3ac)

Colorless semisolid; yield: 65.0 mg (69%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (d, *J* = 9.6 Hz, 1 H), 5.70 (s, 1 H), 3.63 (q, *J* = 7.2 Hz, 2 H), 3.31 (d, *J* = 21.2 Hz, 1 H), 3.23 (d, *J* = 21.2 Hz, 1 H), 3.18–3.12 (m, 1 H), 3.08 (t, *J* = 6.4 Hz, 2 H), 1.76 (dt, *J* = 20.2, 6.8 Hz, 1 H), 1.38 (d, *J* = 7.0 Hz, 3 H), 1.20 (t, *J* = 7.2 Hz, 3 H), 0.90 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 171.7, 136.4, 127.4, 47.1, 42.4, 33.8, 31.8, 28.4, 20.0, 17.5, 13.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{14}H_{22}N_2O_3$)H]: 267.1709; found: 267.1716.

(*E*)-3-(1-Cyclohexyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3ad)

Colorless semisolid; yield: 83.0 mg (73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (d, *J* = 9.6 Hz, 1 H), 5.59 (bs, 1 H), 4.05 (tt, *J* = 12.2, 3.6 Hz, 1 H), 3.26 (dd, *J* = 21.2, 2.0 Hz, 1 H), 3.22–3.15 (m, 1 H), 3.15–3.11 (m, 1 H), 3.08 (t, *J* = 6.5 Hz, 2 H), 2.16 (q, *J* = 12.6 Hz, 2 H), 1.83 (d, *J* = 12.8 Hz, 2 H), 1.76 (dd, *J* = 13.6, 6.9 Hz, 2 H), 1.68–1.55 (m, 2 H), 1.37 (d, *J* = 7.2 Hz, 3 H), 1.34–1.31 (dd, *J* = 26.6, 13.2 Hz, 3 H), 0.90 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 171.6, 169.6, 135.9, 127.3, 51.8, 47.1, 42.4, 31.8, 28.8, 28.5, 25.8, 25.0, 20.1, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{18}H_{28}N_2O_3$)H]: 321.2178; found: 321.2235.

(*E*)-3-(2,5-Dioxo-1-phenethylpyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3ae)

Colorless semisolid; yield: 84.0 mg (69%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 2 H), 7.24–7.17 (m, 3 H), 6.82 (d, *J* = 9.7 Hz, 1 H), 5.57 (s, 1 H), 3.83–3.79 (m, 2 H), 3.28 (d, *J* = 21.2 Hz, 1 H), 3.25–3.13 (m, 2 H), 3.08 (t, *J* = 6.6 Hz, 2 H), 2.94–2.87 (m, 2 H), 1.81–1.73 (m, 1 H), 1.38 (d, *J* = 7.2 Hz, 3 H), 0.90 (d, *J* = 6.6 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 172.1, 171.6, 137.7, 137.2, 136.5, 135.9,128.9, 128.8, 128.6, 127.2, 126.7, 47.1, 42.4, 40.0, 33.7, 31.7, 28.5, 20.1, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{20}H_{26}N_2O_3$)H]: 343.2022; found: 343.2038.

(*E*)-3-(2,5-Dioxo-1-phenylpyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3af)

Colorless semisolid; yield: 88.0 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (t, *J* = 7.6 Hz, 2 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.31 (d, *J* = 7.6 Hz, 2 H), 6.96 (d, *J* = 9.6 Hz, 1 H), 5.82 (bs, 1 H), 3.52 (dd, *J* = 21.6, 2.2 Hz, 1 H), 3.42 (dd, *J* = 21.6, 2.2 Hz, 1 H), 3.22 (dq, *J* = 14.2, 7.2 Hz, 1 H), 3.09 (t, *J* = 6.6 Hz, 2 H), 1.85–1.70 (m, 1 H), 1.41 (d, *J* = 7.2 Hz, 3 H), 0.91 (d, *J* = 6.7 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7, 171.7, 168.6, 137.8, 131.8, 129.2, 128.7, 126.9, 126.4, 47.2, 42.5, 32.0, 28.4, 20.1, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{18}H_{22}N_2O_3$)H]: 315.1709; found: 315.1701.

(*E*)-3-(2,5-Dioxo-1-(*p*-tolyl)pyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3ag)

Colorless semisolid; yield: 86.0 mg (74%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.6 Hz, 2 H), 7.23–7.13 (m, 2 H), 6.95 (dt, *J* = 9.6, 2.4 Hz, 1 H), 5.82 (s, 1 H), 3.50 (dd, *J* = 21.4, 2.4 Hz, 1 H), 3.41 (dd, *J* = 21.4, 2.4 Hz, 1 H), 3.21 (dq, *J* = 9.6, 7.2 Hz, 1 H), 3.10–3.04 (m, 2 H), 2.38 (s, 3 H), 1.81–1.73 (m, 1 H), 1.40 (d, *J* = 7.2 Hz, 3 H), 0.90 (d, *J* = 6.6 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.8, 171.6, 168.8, 138.8, 137.8, 129.9, 129.1, 126.9, 126.2, 47.1, 42.5, 32.0, 28.5, 21.2, 20.1, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{19}H_{24}N_2O_3$)H]: 329.1865; found: 329.1857.

(*E*)-*N*-Isobutyl-3-(1-(4-methoxyphenyl)-2,5-dioxopyrrolidin-3-ylidene)-2-methylpropanamide (3ah)

Colorless semisolid; yield: 99.0 mg (81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (d, *J* = 8.8 Hz, 2 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 9.6 Hz, 1 H), 5.64 (s, 1 H), 3.75 (s, 3 H), 3.45–3.39 (m, 1 H), 3.37–3.28 (m, 1 H), 3.16–3.10 (m, 1 H), 3.01 (t, *J* = 6.6 Hz, 2 H), 1.69 (dd, *J* = 13.4, 6.6 Hz, 1 H), 1.33 (d, *J* = 7.2 Hz, 3 H), 0.84 (d, *J* = 6.3 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9, 171.5, 168.8, 159.6, 137.7, 127.6, 126.9, 124.4, 114.5, 55.5, 47.1, 42.5, 31.9, 28.5, 20.1, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{19}H_{24}N_2O_4$)H]: 345.1814; found: 345.1808.

(*E*)-3-(1-(4-Bromophenyl)-2,5-dioxopyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3ai)

Colorless semisolid; yield: 120.0 mg (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.6 Hz, 2 H), 7.23 (d, *J* = 8.6 Hz, 2 H), 6.97 (d, *J* = 9.6 Hz, 1 H), 5.71 (bs, 1 H), 3.51 (dd, *J* = 21.6, 1.8 Hz, 1 H), 3.42 (dd, *J* = 21.6, 1.8 Hz, 1 H), 3.24–3.15 (m, 2 H), 3.09 (t, *J* = 6.6 Hz, 1 H), 1.83–1.73 (m, 1 H), 1.41 (d, *J* = 7.2 Hz, 3 H), 0.91 (d, *J* = 6.6 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 171.4, 168.2, 138.4, 132.3, 130.8, 127.8, 126.5, 122.5, 47.1, 42.6, 32.0, 28.5, 20.0, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for [($C_{18}H_{21}BrN_2O_3$)H]: 393.0814; found: 393.0870.

(*E*)-3-(1-Allyl-2,5-dioxopyrrolidin-3-ylidene)-*N*-isobutyl-2-methylpropanamide (3aj)

Orange liquid; yield: 66 mg (35% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.78 (dt, *J* = 9.6, 2.4 Hz, 1 H), 5.77–5.68 (m, 1 H), 5.56 (s, 1 H), 5.15 (m, 1 H), 4.11 (d, *J* = 5.9 Hz, 2 H), 3.23 (m, 2 H), 3.01 (td, *J* = 6.9, 2.6 Hz, 2 H), 2.08 (dd, *J* = 14.4, 7.1 Hz, 1 H), 1.72–1.65 (m, 2 H), 1.31 (d, *J* = 7.0 Hz, 3 H), 0.83 (d, *J* = 6.7 Hz, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.09, 171.50, 170.78, 169.03, 136.83, 134.16, 134.11, 133.77, 130.55, 129.54, 128.72, 127.13, 118.53, 115.32, 60.39, 47.06, 42.41, 40.94, 37.34, 31.81, 29.67, 28.51, 28.43, 27.51, 25.45, 20.12, 20.02, 17.45, 14.17, 12.87.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for [($C_{15}H_{22}N_2O_3$)Na]: 301.1528; found: 301.1523.

Linear-Selective Alkylated Acrylamide Derivatives 5; General Procedure

A 15 mL Schlenk tube with septum containing Cp*Co(CO)I_2 (10 mol%), *N*-benzylacrylamide **1g** (100 mg, 1 equiv) and $AgSbF_6$ (20 mol%) was evacuated and purged with nitrogen gas three times ($AgSbF_6$ was transferred inside a glovebox). To the tube were then added acrylate **4** (3.0 equiv), PivOH (30 mol%) and TFE (3.0 mL) via syringe; after that, the reaction mixture was evacuated and purged with nitrogen gas three times. Then, the septum was taken out immediately and a screw cap was used to cover the tube under the nitrogen atmosphere, and the reaction mixture was stirred at room temperature for 5 min. Then, the mixture was stirred at 120 °C for 16 h. After cooling to ambient temperature, the mixture was diluted with CH_2Cl_2 and filtered through Celite, and the filtrate was concentrated. The crude residue was purified through a silica gel column (40% ethyl acetate in hexanes as eluent) to give pure product **5**.

Methyl (*Z*)-6-(Benzylamino)-5-methyl-6-oxohex-4-enoate (5ga)

Colorless liquid; yield: 96.0 mg (72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.32 (m, 2 H), 7.32–7.25 (m, 3 H), 6.33–6.31 (m, 1 H), 6.07 (bs, 1 H), 4.50 (d, *J* = 5.6 Hz, 2 H), 3.68 (s, 3 H), 2.53–2.34 (m, 4 H), 1.89 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 168.9, 138.3, 133.9, 132.1, 128.8, 127.9, 127.6, 51.8, 43.9, 32.9, 23.7, 12.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for [($C_{15}H_{19}NO_3$)Na]: 284.1263; found: 284.1259.

Ethyl (*Z*)-6-(Benzylamino)-5-methyl-6-oxohex-4-enoate (5gb)

Colorless liquid; yield: 90 mg (68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 5 H), 6.33 (t, *J* = 6.2 Hz, 1 H), 6.09 (s, 1 H), 4.49 (d, *J* = 5.6 Hz, 2 H), 4.13 (q, *J* = 7.0 Hz, 2 H), 2.49–2.38 (m, 4 H), 1.89 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7, 168.9, 138.3, 133.9, 131.9, 128.7, 127.8, 127.5, 60.5, 43.8, 33.2, 23.6, 14.1, 12.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for [($C_{16}H_{21}NO_3$)Na]: 298.1419; found: 298.1412.

Butyl (*Z*)-6-(Benzylamino)-5-methyl-6-oxohex-4-enoate (5gc)

Colorless liquid; yield: 75.0 mg (57%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.22 (m, 5 H), 6.32 (t, *J* = 6.5 Hz, 1 H), 6.01 (s, 1 H), 4.50 (d, *J* = 5.6 Hz, 2 H), 4.07 (t, *J* = 6.7 Hz, 2 H), 2.44 (m, 4 H), 1.89 (s, 3 H), 1.59 (dd, *J* = 14.7, 7.1 Hz, 2 H), 1.37 (m, 2 H), 0.93 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.8, 168.9, 138.3, 133.9, 132.1, 128.7, 127.9, 127.5, 64.5, 43.9, 33.2, 30.6, 23.7, 19.1, 13.7, 12.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for [($C_{18}H_{25}NO_3$)Na]: 303.181; found: 303.187.

1-Benzyl-6-methyl-3,4-dihydro-1*H*-azepine-2,7-dione (5gd)

Colorless liquid; yield: 36.0 mg (55%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (dd, *J* = 7.8, 6.8 Hz, 3 H), 7.31–7.26 (m, 2 H), 6.31 (td, *J* = 7.2, 1.2 Hz, 1 H), 4.50–4.49 (m, 2 H), 2.57–2.52 (m, 2 H), 2.53–2.48 (m, 2 H), 1.89 (d, *J* = 1.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 168.8, 138.3, 133.0, 132.6, 128.8, 128.7, 127.8, 127.6, 43.9, 32.6, 23.3, 12.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for [($C_{14}H_{15}NO_2$)Na]: 252.0995; found: 252.0999.

Phenyl (*Z*)-6-(Benzylamino)-5-methyl-6-oxohex-4-enoate (5ge) + 1-Benzyl-6-methyl-3,4-dihydro-1*H*-azepine-2,7-dione (5ge′)

Colorless liquid; yield: 86.0 mg (54%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.18 (m, 13 H), 7.06 (d, *J* = 7.7 Hz, 2 H), 6.42 (t, *J* = 7.1 Hz, 1 H), 6.32 (t, *J* = 6.7 Hz, 1 H), 6.09 (s, 1 H), 4.49 (dd, *J* = 9.4, 4.8 Hz, 4 H), 2.70 (t, *J* = 7.3 Hz, 2 H), 2.55 (dq, *J* = 12.8, 6.9 Hz, 6 H), 1.92 (s, 3 H), 1.89 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.22, 171.00, 168.83, 168.71, 150.48, 138.26, 133.44, 133.01, 132.45, 132.30, 129.41, 128.69, 127.81, 127.49, 125.86, 121.42, 43.82, 33.23, 32.54, 23.58, 23.31, 12.85, 12.78.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690866.

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