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Multi-component coupling synthesis of polycyclic pyrrole derivatives via Ir- and Rh-catalyzed cycloisomerizations with microwave heating

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Abstract—$CuBr_2$-catalyzed three-component coupling of *N*-benzylallylamine, ethyl glyoxalate, and terminal alkynes afforded glycinate-tethered 1,6-enynes, which were further transformed into polycyclic pyrrole-2-carboxylates via iridium-catalyzed cycloisomerization/Diels–Alder cycloaddition/dehydrogenation sequence under conventional and microwave heating conditions. The corresponding β-amino acid analogues were obtained from the Ir-catalyzed reaction of enynes prepared from lithium amides of allylamines with methyl non-2-en-4-ynoate. The Cu-catalyzed Mannich-type condensation was further extended to the synthesis of the glycinate-tethered dienyne and cyclopropylenyne, which were subjected to Rh-catalyzed cycloisomerizations to furnish bicyclic amino acids.

1. Introduction

The design and construction of novel α-amino acid structures has been an important subject in organic and bioorganic chemistry.[1] In particular, rigid α-amino acids with constrained geometries have received great interest, because they are capable of modifying the conformation of peptides.[2] Thus, the rational introduction of unnatural α-amino acid components into peptides enables the optimization of their biological properties. In this regard, recent advances of the transition-metal catalysis would make significant contributions toward the viable access to unique artificial α-amino acids. In fact, Kotha and Undheim, have developed the transition-metal catalyzed approach to constrained α-amino acids, where diynes, dienes, and enynes bearing α-amino acid tethers were employed as synthetic precursors.[3] We also became interested in the utilization of the transition-metal catalysis for the synthesis of biologically important molecules, and have applied the ruthenium-catalyzed [2+2+2] cycloaddition to the assembly of *C*-arylglycosides and its conjugates with α-amino acids.[4] In these previous studies, α-amino-acid-tethered bifunctional substrates were prepared by means of conventional nucleophilic substitution and/or condensation reactions under acidic or basic conditions, although a fully catalytic method that integrates two different catalytic reactions for the substrate formation and the subsequent cyclization into one sequential process is highly desirable. Herein, we wish to report our effort to develop sequential multi-component coupling processes, providing a rapid access to various polycyclic amino acids.[5]

Glycinate-tethered bifunctional molecules are fascinating precursors for the synthesis of constrained cyclic α-amino acids (Fig. 1). Kotha and co-workers synthesized glycinate-tethered 1,7-enynes **1** from a protected glycine through four-step operations. They subjected **1** to enyne metathesis with Grubbs' catalyst and the resultant dienes were converted into constrained phenylalanine derivatives via Diels–Alder cycloaddition and subsequent DDQ oxidation.[6] Similar 1,7-diynes **2** were also prepared and subjected to [2+2+2] cycloaddition with monoalkynes, leading directly to similar constrained phenylalanine derivatives.[6]

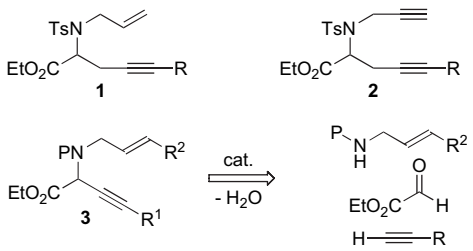

Figure 1.

Keywords: Copper catalyst; Iridium catalyst; Rhodium catalyst; Enynes; Amino acids.
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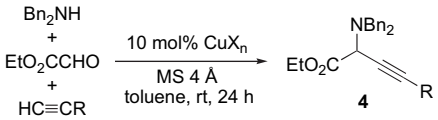
On the other hand, the synthesis of glycinate-tethered 1,6-enynes **3** has remained unexplored to date. This is probably because of the difficulty of the synthesis of α-alkynylated glycines. The parent ethynylglycine is known as antibiotic FR-900130 (L-2-amino-3-butynoic acid), which was isolated from a *Streptomyces catenulae* and characterized as an *N*-acetylated form because of its instability.[7] The chemical synthesis of α-alkynylglycine derivatives has been rare. In 1977, Taub et al. and Metcalf et al. synthesized for the first time α-ethynyl-3,4-dihydroxyphenylalanine via sequential benzylation and acylation of the benzaldehyde imine of 3-(trimethylsilyl)propynylamine.[8] α-Alkynylated glycinates were also synthesized straightforwardly albeit in low to moderate yields via addition of magnesium acetylides to an α-imino ester generated in situ.[9] Further, several research groups have achieved the asymmetric synthesis of alkynylglycinates by taking advantage of chiral auxiliaries, but the previous reports required stoichiometric amounts of harmful metal reagents and/or multi-step synthetic operations.[10] In terms of atom and step economy,[11] a catalytic coupling protocol that minimizes chemical wastes as well as synthetic operations is highly desirable. In this context, Chan and co-workers recently developed the silver-catalyzed alkynylation of α-imino esters under mild conditions, giving *N*-PMP-protected alkynylglycines in high yields.[12] We also envisioned that a single-step assembly of unknown enyne **3** would be realized using transition-metal catalyzed Mannich-type condensation of commercially available ethyl glyoxalate, terminal alkynes, and *N*-protected allylamines only in a single operation (Fig. 1).

2. Results and discussion

2.1. Synthesis of alkynylglycinates via Mannich-type three-component condensation

To this end, copper catalysis is considered to be the method of choice, according to the recent excellent studies of Knochel's group.[13] Thus, several copper salts were examined as catalysts toward the reaction of each 1 equiv of ethyl glyoxalate, dibenzylamine, and phenylacetylene in toluene containing molecular sieve 4 Å at room temperature for 24 h (Scheme 1 and Table 1). The reaction proceeded in the presence of 10 mol % CuBr, and the formation of the desired alkynylglycinate **4a** (R=Ph) was confirmed by the ^{1}H NMR measurement of the crude product. Purification with column chromatography on silica gel or alumina, however, led to the decomposition of **4a** to some other products.[14] To avoid the decomposition, the crude materials were rapidly purified through a short column chromatography on Florisil® to give **4a** in 89% yield (Table 1, run 1). In a similar manner, $CuBr_2$ and $CuCl_2$ gave **4a** in 85 and 79% yields, respectively (runs 2 and 3). In contrast, $Cu(OAc)_2$ and CuI proved to be ineffective. On the basis of these results, further explorations were carried out with $CuBr_2$, which is cheaper and more robust than CuBr. Under the optimal reaction conditions, 1-hexyne and trimethylsilylacetylene similarly gave rise to **4b** (R=^{n}Bu) or **4c** (R=TMS). The former was isolated in 81% yield (run 4), but the latter was decomposed during the chromatography on Florisil® (run 5).



Scheme 1.

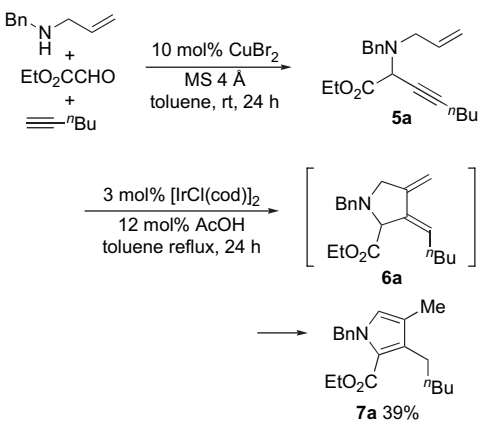
Table 1. Mannich condensation of dibenzylamine, ethyl glyoxalate, and alkynes[a]

Run	R	CuX_2	**4**, Isolated yield (%)
1	Ph	$CuBr_2$	**4a**, 89
2	Ph	$CuBr_2$	**4a**, 85
3	Ph	$CuCl_2$	**4a**, 79
4	^{n}Bu	$CuBr_2$	**4b**, 81
5	Me_3Si	$CuBr_2$	Decomposition

[a] All reactions were carried out with 10 mol % CuX_n in dry benzene at room temperature.

2.2. Synthesis of glycinate-tethered 1,6-enynes and their cycloisomerization

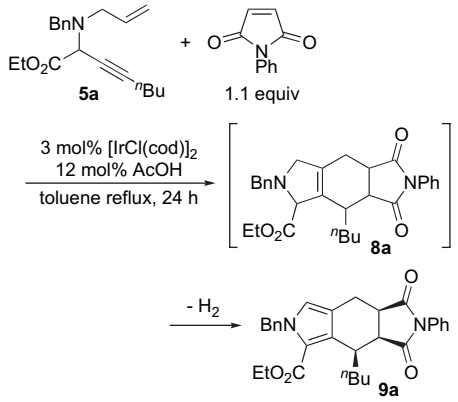
Next, we carried out the synthesis of glycinate-tethered 1,6-enyne **5a** through the Cu-catalyzed three-component coupling of *N*-benzylallylamine, ethyl glyoxalate, and 1-hexyne (Scheme 2). Upon treatment with 10 mol % $CuBr_2$ at room temperature for 24 h, each 1 equiv of these components gave rise to the desired enyne **5a** in ca. 80% yield after filtration through a pad of Florisil®. However, the purification of the product with column chromatography on silica gel again resulted in decomposition. Therefore, we decided to submit the crude enyne directly to the transition-metal-catalyzed cyclization reactions. The cycloisomerization of enynes is known as a powerful method to obtain exocyclic 1,3-dienes, which can be utilized as diene components of Diels–Alder reaction.[15] The crude enyne **5a** was submitted to the reported palladium-catalyzed cycloisomerization conditions (5 mol % $Pd_2(dba)_3$, 10 mol % PPh_3, 10 mol % AcOH, toluene reflux, 24 h)[16] to result in the formation of an intractable product mixture. Similarly, **5a** failed to produce the ring-closing enyne metathesis product,[17] when it was heated with the first generation Grubbs catalyst in refluxing toluene for 24 h. These negative results are ascribed to the instability of the α-alkynylglycinates. Then, we turned our attention to the recently reported iridium catalyst system of Chatani and co-workers.[18] According to their report, crude **5a** was treated



Scheme 2.

with 3 mol % $[IrCl(cod)]_2$ and 12 mol % AcOH in refluxing toluene for 24 h. As a result, **5a** underwent clean cycloisomerization reaction, but the obtained product was the unexpected pyrrole-2-carboxylate **7a**. The formation of **7a** was probably the consequence of the iridium-catalyzed isomerization of exocyclic diene **6a**. Similar isomerization of exocyclic dienes leading to pyrroles has been reported previously.[19]

Encouraged by the above result, we attempted the Diels–Alder trapping of putative exocyclic diene intermediate **6a** by carrying out the cycloisomerization of **5a** in the presence of a dienophile (Scheme 3). Surprisingly, such a one-pot, domino cycloisomerization/Diels–Alder cycloaddition has been less explored to date,[20a,c,e,f] while similar domino processes involving intramolecular Heck reaction[20a–d] or ring-closing enyne metathesis[21] have been developed successfully. Without purification, freshly prepared **5a** was directly subjected to cycloisomerization in the presence of 1.1 equiv *N*-phenylmaleimide in refluxing toluene for 7 h. Gratifyingly, a 1:1 cycloadduct of **5a** with the maleimide was formed, but the following structural analyses revealed that the obtained product was fused pyrrole-2-carboxylate **9a**. In its ^1H NMR spectrum, a singlet peak of the pyrrole proton α to the nitrogen atom appeared at δ 6.73 ppm. In addition, the molecular ion peak M^+ was observed at *m*/*z* 484 instead of *m*/*z* 486 expected for Diels–Alder adduct **8a**. Although the detailed mechanism is unclear, **9a** was presumably formed by the dehydrogenative aromatization of **8a** via C–H activation on the 3,4-dehydroproline ring with Ir species.[22] It is noteworthy that the yield of the cycloisomerization/Diels–Alder reaction/dehydrogenative aromatization resulting in **9a** (62%) was much higher than that of the cycloisomerization leading to **7a** in the absence of the dienophile (39%).

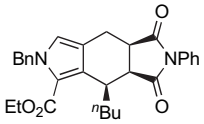
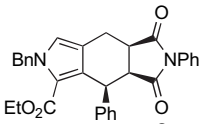
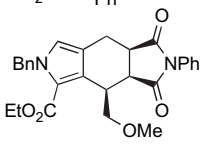
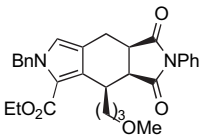
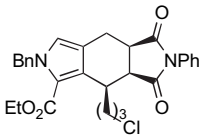
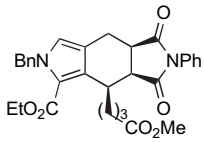
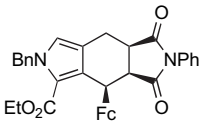
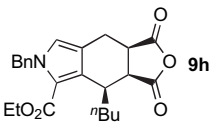
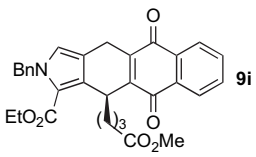


Scheme 3.

2.3. Scope and limitations of four-component coupling synthesis of pyrrole-2-carboxylates

The generality of the present sequential four-component coupling process was exemplified as summarized in Table 2. Although the use of phenylacetylene afforded the corresponding enyne intermediate very cleanly, its cycloisomerization failed to complete within 10 h. To ensure complete conversion of the enyne, the heating was continued for 24 h, resulting **9b** in 54% (run 3). In striking contrast, trimethylsilylacetylene totally failed to give the corresponding product. Similarly, 5-methoxy-1-pentyne, 5-chloro-1-pentyne, and methyl 5-hexynoate gave rise to pyrrolecarboxylates **9d**, **9e**, and **9f** in 51–74% yields (runs 6, 8, and 10), while the use of methyl propargyl ether resulted in the rather lower yield (41%) of **9c** (run 5). The reaction with ethynylferrocene afforded the corresponding adduct **9g** in 54% yield as crystals. Fortunately, recrystallization of the isolated **9g** gave a single crystal favorable for X-ray crystallography. As shown by the ORTEP diagram in Figure 2, the central

Table 2. Synthesis of polycyclic pyrrole-2-carboxylates **9**[a]

Run	Product	Method,[b] yield (%)
1 2	 **9a**	A, 62 B, 59
3 4	 **9b**	A, 54 B, 29
5	 **9c**	A, 41
6 7	 **9d**	A, 51 B, 47
8 9	 **9e**	A, 62 B, 59
10 11	 **9f**	A, 74 B, 68
12	 **9g**	A, 54
13 14	 **9h**	A, 52 B, 53
15 16	 **9i**	A, 35 B, 33

[a] Mannich couplings were carried out with each 1 equiv of *N*-benzylallylamine, ethyl glyoxalate, and an alkyne in the presence of 10 mol % $CuBr_2$ and MS 4 Å in toluene at room temperature for 24 h. Cycloisomerizations were carried out with crude enynes **5**, 1.1 equiv of a dienophile in the presence of 3 mol % $[IrCl(cod)]_2$, 12 mol % AcOH in toluene.

[b] Method A: toluene reflux for 24 h (7 h for runs 1 and 5). Method B: microwave heating (150 °C) for 0.5 h.

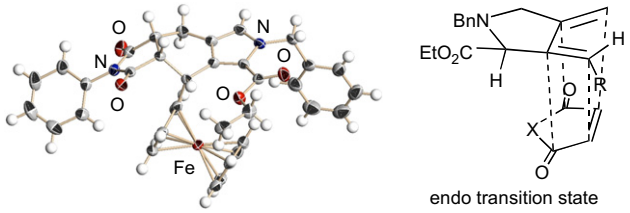


Figure 2.

cyclohexane ring has the all cis geometry as a result of the *endo*-approach of the dienophile to the exocyclic diene intermediate in the Diels–Alder transition state. In accord with the ^{1}H NMR and mass analyses, **9g** has the pyrrole ring that was formed by the dehydrogenation of the 3-pyrroline moiety.

In addition to *N*-phenylmaleimide, maleic anhydride can be used as a dienophile in the cycloisomerization step to afford **9h** in 52% yield (run 13). On the other hand, the use of 1,4-naphthoquinone led to the formation of **9i** possessing both pyrrole and naphthoquinone rings albeit in a lower yield of 35% (run 15). The formation of **9i** is the consequence of the two-fold dehydrogenation under the influence of the iridium catalyst. The use of other allylamines and dienophiles listed in Figure 3 resulted in the formation of intractable products.

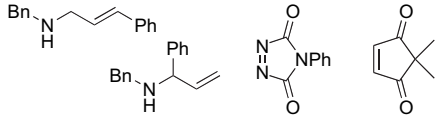
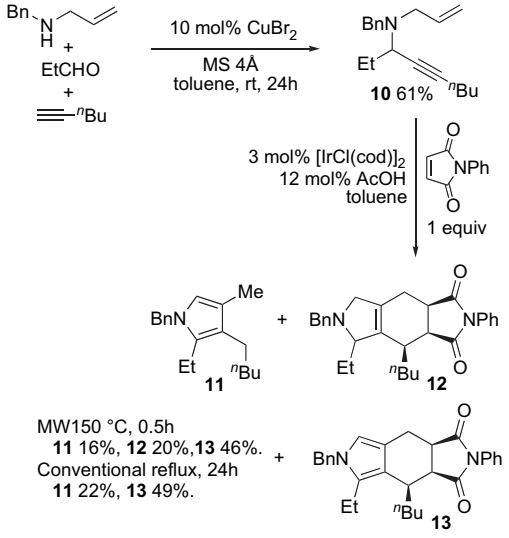


Figure 3.

With the advent of modern microwave reactors, the microwave heating has become a powerful and reliable tool in organic synthesis.[23] This is because microwave irradiation often offers considerable rate acceleration as well as improved product yields. Microwave activation has also proven to be effective to the rapid assembly of heterocycles via multi-component couplings.[24] Thus, the cycloisomerization of enyne **5a** was carried out in a sealed vessel at 150 °C for 0.5 h under microwave irradiation (Table 2, run 2). As a consequence, **9a** was obtained in a comparable yield of 59%. In contrast, the sequential reaction starting from phenylacetylene resulted in a rather lower yield (29%) under the same reaction conditions (run 4). This is presumably the result of the extensive decomposition of the phenylacetylene-derived enyne at 150 °C. Then, other enynes bearing an alkyl group on their alkyne terminals were subjected to microwave-irradiated cycloisomerization to furnish the corresponding adducts in similar yields with those under the conventional heating conditions (runs 7, 9, 11, 14, and 16).

2.4. Impact of ester group on cyclization step: isolation of Diels–Alder intermediate

As described above, the glycinate-tethered enynes were directly converted into the tricyclic pyrrole-2-carboxylates via dehydrogenation of putative Diels–Alder adducts such as **8a**. The ethoxycarbonyl substituent on the 3-pyrroline ring of these intermediates is considered to play an important role in the aromatization stage: the electron-withdrawing ester functionality activates α-C–H bond to facilitate dehydrogenation. To elucidate this, we prepared propanal-derived enyne **10** and submitted it to cycloisomerization (Scheme 4). In the presence of the iridium catalyst, the toluene solution of isolated **10** and 1 equiv of *N*-phenylmaleimide were heated in the microwave reactor at 150 °C for 0.5 h. As expected, Diels–Alder adduct **12**[25] was obtained in 20% yield along with pyrroles **11** and **13**, while only **11** and **13** were obtained in 22 and 49% yields under conventional heating conditions. The reason for the formation of monocyclic pyrrole **11** even in the presence of the dienophile is not clear. The intermediacy of **12** in the formation of **13** was confirmed as follows. Upon treatment with 3 mol % $[IrCl(cod)]_2$ and 12 mol % AcOH in refluxing toluene for 3 h, the isolated **12** was converted into **13** in 76% yield. Interestingly, when the same reaction was carried out in the presence of 1 equiv of *N*-phenylmaleimide, **12** was totally consumed within 0.5 h to give **13** in a similar yield of 73%. In addition, *N*-phenylsuccinimide, which was formed by the hydrogenation of *N*-phenylmaleimide, was also detected by ^{1}H NMR analysis of the crude product mixture. These observations suggest that the dienophiles were not essential for the aromatization of the Diels–Alder adducts, but they facilitate the dehydrogenation as hydrogen acceptors. In fact, the cycloisomerization of **10** was carried out with 3 equiv of *N*-phenylmaleimide under microwave irradiation (150 °C, 0.5 h) to afford **11** and **13** in 12 and 54% yields, respectively. The use of a rhodium complex, $[RhCl(cod)]_2$, in place of the iridium precatalyst resulted in the no reaction.[26] Other catalytic conditions (2.5 mol % $Pd_2(dba)_3$/dppe/2AcOH, toluene, MW 150 °C, 30 min;[16] 5 mol % Cp*RuCl(cod), EtOH, room temperature, 13 h;[27] 5 mol % Cp*RuCl(cod), AcOH, 65 °C, 10 h[27]) also hardly converted **10** into the cyclization products.

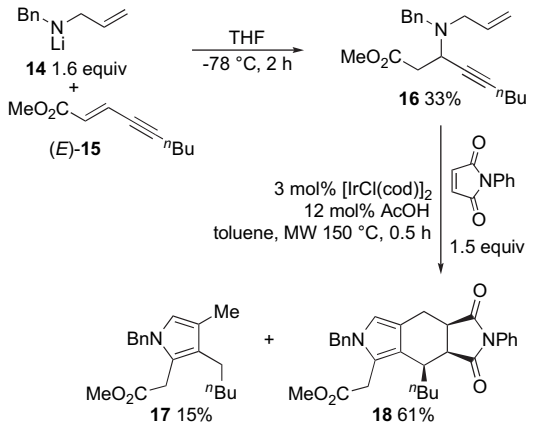


Scheme 4.

2.5. Synthesis of β-amino-acid derivatives via Michael Addition of lithium amides of allylamines to a conjugate enynoate

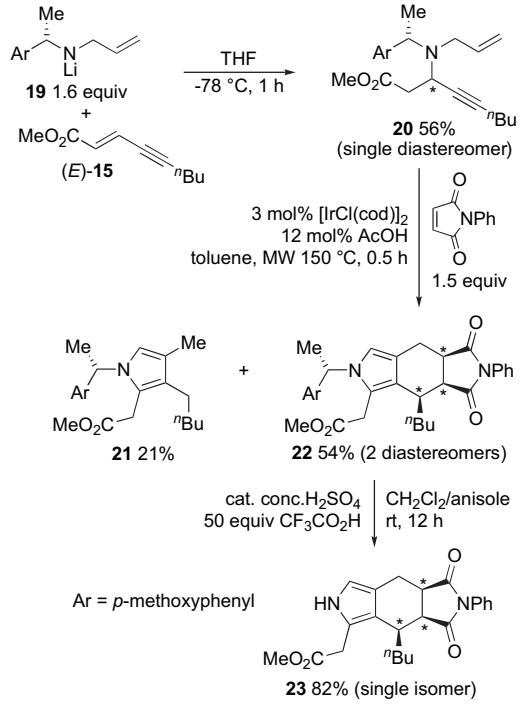
Davies and co-workers have achieved the asymmetric synthesis of cyclic β-amino acids via conjugate addition of

a chiral lithium amide to 2,4-dienoates and subsequent ring-closing metathesis of the resultant β-amino-acid-tethered 1,6-dienes.[28] Inspired by their elegant work, we synthesized the corresponding 1,6-enyne **16** by adapting the Michael addition of lithium amide **14** to methyl non-2-en-4-ynoate **15**, which was prepared according to the report by Takeuchi and co-workers.[29] The reaction of **14** and (*E*)-**15** was executed at −78 °C in THF for 1 h to furnish the desired **16** albeit in a low yield (Scheme 5). In striking contrast, the use of (*Z*)-**15** hardly afforded the Michael adduct. The obtained enyne **16** was then allowed to react with *N*-phenylmaleimide under the microwave heating conditions. To ensure the full conversion of a Diels–Alder intermediate, an excess amount (1.5 equiv) of the dienophile was used. Similarly with the corresponding glycinate derivative **5a**, the reaction reached to completion within 0.5 h at 150 °C to give rise to cycloadduct **18** in 61% yield along with monocyclic pyrrole **17** (15% yield).



Scheme 5.

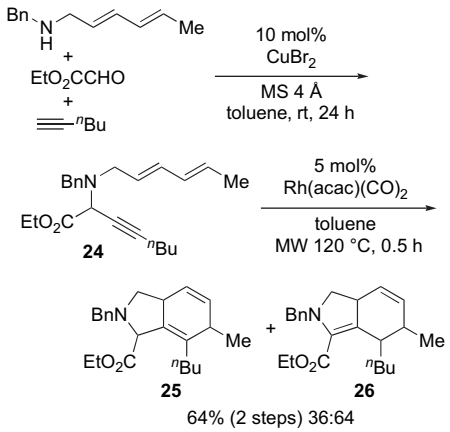
Optically active derivative **20** was further prepared from chiral amide **19** and subjected to microwave-assisted cycloisomerization (Scheme 6). Michael addition of **19** to (*E*)-**15** gave **20** in 56% yield, and the ^{1}H NMR analysis showed that **20** was obtained as a single diastereomer.[25] Under optimal microwave heating conditions, **20** was allowed to react with 1.5 equiv of *N*-phenylmaleimide to result in the formation of pyrroles **21** and **22** in 21 and 54% yields, respectively. To our surprise, the ^{1}H NMR analysis revealed that **22** was obtained as two diastereomers with the ratio of a 1:1.7. Their ^{1}H NMR spectra showed very similar spectral patterns with that of **18**. The *p*-methoxyphenylethyl group of **22** was removed under acidic conditions in a mixed solvent of CH_2Cl_2 and anisole at room temperature,[30] affording *N*-unprotected pyrrole **23** in 82% yield as a single stereoisomer. At first, we suspected the epimerization of the benzylic stereocenter on the chiral auxiliary under the cycloisomerization conditions, but this possibility was ruled out by the following experiment. No detectable change in the diastereomer ratio was observed, when the partially separated higher polar diastereomer of **22** (5.5:1) was treated with 5 mol % iridium catalyst at 150 °C for 30 min under microwave irradiation. According to these results, we tentatively ascribed the diastereomer formation to the racemization of enyne **20** or an exocyclic diene intermediate prior to the diastereoselective Diels–Alder cycloaddition.



Scheme 6.

2.6. Synthesis of other cyclic amino acids using rhodium-catalyzed cycloisomerizations

We finally explored the rhodium-catalyzed intramolecular [4+2] and [5+2] cycloadditions of glycinate-tethered dienyne **24** and cyclopropylenyne **27**, which were readily prepared by our copper-catalyzed Mannich route.[31,32] The Cu-catalyzed Mannich-type condensation of each 1 equiv of *N*-benzylhexa-2,4-dienylamine, ethyl glyoxalate, and 1-hexyne gave rise to dienyne **24**, which was directly subjected to rhodium-catalyzed cycloaddition with microwave heating at 120 °C for 0.5 h (Scheme 7). Recently cationic rhodium catalysts have been found effective for intramolecular diene–alkyne cycloadditions.[31] The cationic rhodium catalyst system, 5 mol % $RhCl(PPh_3)_3$/AgOTf, however, afforded cycloadduct **26** only in a low overall yield (28%). Gratifyingly, the use of a neutral complex with the π-accepting CO ligand, $Rh(acac)(CO)_2$, under the same reaction

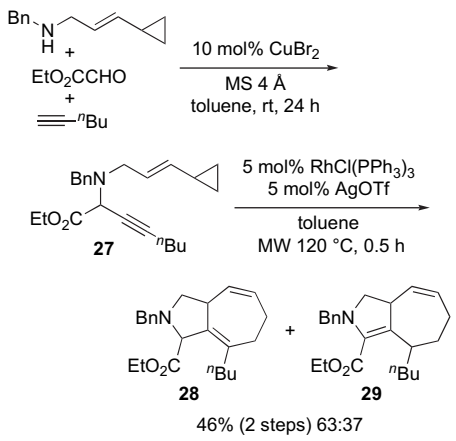


Scheme 7.

conditions improved the product yields. Cyclohexadienes **25** and its olefin isomer **26** were obtained in 64% combined yield with the ratio of 36:64.[25]

Recently, Shibata and co-workers reported that several iridium(I) complexes effectively catalyzed intramolecular [4+2] cycloaddition of dienynes.[33] With the expectation of the direct formation of an aromatization product via sequential [4+2] cycloaddition/dehydrogenation, we carried out the reaction of **24** under the cycloisomerization conditions (1 mol % $[IrCl(cod)]_2$, 4 mol % AcOH, toluene, MW 150 °C, 30 min). Although **24** was completely consumed, none of the expected cycloadducts were detected by ^1H NMR analysis of crude reaction mixture. Next, Vaska's complex, $IrCl(CO)(PPh_3)_2$, was used as a precatalyst, because it proved to be effective for the cycloaddition of dienynes.[33] In the presence of the 3 mol % catalyst, freshly prepared **24** was heated in toluene at 120 °C for 2 h with a microwave reactor, resulting in a complex reaction mixture. Conventional heating conditions also proved to be ineffective for the Ir-catalyzed [4+2] cycloaddition. Consequently, the neutral rhodium catalyst is optimal for the present dienyne cycloisomerization.

In a similar manner, cyclopropylenyne **27** was prepared and treated with 5 mol % $Rh(acac)(CO)_2$ under the microwave irradiation conditions to furnish seven-membered ring products **28** and **29** in 33% combined yield with the ratio of 55:45.[25] Slight improvements in the yield and the selectivity (46%, 63:37) were achieved when the cationic system, 5 mol % $RhCl(PPh_3)_3$/AgOTf, was applied to the same reaction (Scheme 8).



Scheme 8.

3. Conclusion

In conclusion, we successfully developed the straightforward approach to glycinate-tethered bifunctional molecules via Cu-catalyzed Mannich-type condensation of *N*-benzylallylamines, ethyl glyoxalate, and terminal alkynes. The resultant glycinate-derivatives were directly used for the next transition-metal-catalyzed carbocyclizations. The enynes were subjected to the Ir-catalyzed cycloisomerization in the presence of dienophiles to afford tricyclic pyrrole-2-carboxylates as a result of the Diels–Alder reaction of exocyclic diene intermediates and subsequent dehydrogenative aromatization. The corresponding β-amino acid analogues of the tricyclic pyrrole-2-carboxylates were obtained from the Ir-catalyzed reaction of enynes prepared from lithium amides of allylamines with methyl non-2-en-4-ynoate. The glycinate-tethered dienyne and cyclopropylenyne were subjected to rhodium-catalyzed cycloadditions under microwave irradiation to give the expected intramolecular [4+2] and [5+2] cycloadducts in moderate yields.

4. Experimental

4.1. General

Flash chromatography was performed with a silica gel column (Cica silica gel 60N) eluted with mixed solvents [hexane/AcOEt]. TLC analyses were performed with Merck TLC plate silica gel 60 F_{254}. ^1H and ^{13}C NMR spectra were measured on a Gemini 2000 NMR spectrometers as $CDCl_3$ solutions at 25 °C. ^1H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the singlet at 7.26 ppm for chloroform. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quinted; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in hertz. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at δ=77.0 ppm for $CDCl_3$. Infrared spectra were recorded on a JASCO FT/IR-230 spectrometer or a JASCO FT/IR-610 spectrometer. Mass spectra were recorded on a JEOL JMS-T100CS mass spectrometer as MeOH solutions. Elemental analyses were performed with a Perkin–Elmer 2400II CHNS/O elemental analyzer. Melting points were obtained by a Yamato Melting Point Apparatus MP-12 and are uncorrected. Microwave irradiation experiments were carried out with a single-mode microwave reactor (CEM Discover LabMate). Closed reaction vessels were used, and the temperature was monitored by an on-line IR detector. Toluene was distilled from CaH_2. $CuBr_2$ (Kishida, 99.9%) and ethyl glyoxalate (Fluka, 50% toluene solution) were used without further purification. $[IrCl(cod)]_2$ was prepared according to the reported procedures,[34] and rhodium complexes are commercially available.

4.2. General procedure for Cu-catalyzed three-component coupling: synthesis of alkynylglycinate 4b from ethyl glyoxalate, dibenzylamine, and phenylacetylene

To a suspension of $CuBr_2$ (22 mg, 0.1 mmol) and MS 4 Å (500 mg) in toluene (2 mL) were added ethyl glyoxalate solution (ca. 50% in toluene, 0.20 mL), 1-hexyne (82 mg, 1.0 mmol), and dibenzylamine (197 mg, 1.0 mmol) in this order at room temperature under Ar atmosphere. The solution was stirred at room temperature under Ar atmosphere for 24 h. After filtration through a glass frit, the filtrate was concentrated in vacuo. The residue was purified by short column chromatography on Florisil® eluted with ether to give **4b** (295 mg, 81%) as pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 0.95 (t, J=7.2 Hz, 3H), 1.29 (t, J=7.2 Hz, 3H), 1.42–1.62 (m, 4H), 2.31 (dt, J=7.2, 2.4 Hz, 2H), 3.63 (d, J=13.5 Hz, 2H), 3.79 (d, J=13.5 Hz, 2H), 4.18 (q, J=7.2 Hz, 1H), 4.19 (q, J=7.2 Hz, 1H), 4.21

(t, J=2.4 Hz, 1H), 7.21–7.34 (m, 6H), 7.41–7.44 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.63, 14.20, 18.51, 21.94, 30.88, 55.26, 55.63, 61.19, 72.48, 87.09, 126.88, 128.04, 128.92, 138.92, 169.23; IR (neat) 1742 cm^{-1}; MS (EI): m/z (%): 363 (3) $[M]^+$, 234 (2) $[M-Et]^+$, 290 (100) $[M-CO_2Et]^+$, 198 (30) $[M-CO_2Et-C_6H_5Me]^+$; EA calcd (%) for $C_{24}H_{29}NO_2$ (363.49): C 79.30, H 8.04, N 3.85; found: C 79.25, H 8.09, N 3.84.

Compound **4a**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 1.31 (t, J=7.2 Hz, 3H), 3.72 (d, J=13.8 Hz, 2H), 3.89 (d, J=13.8 Hz, 2H), 4.22 (q, J=7.2 Hz, 1H), 4.23 (q, J=7.2 Hz, 1H), 4.46 (s, 1H), 7.24–7.35 (m, 11H), 7.45–7.54 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 55.5, 56.2, 61.5, 82.1, 86.6, 122.6, 127.1, 128.1, 128.2, 128.3, 128.8, 131.9, 138.8, 168.7; IR (neat) 1741 cm^{-1}; MS (EI): m/z (%): 383 (4) $[M]^+$, 254 (0.8) $[M-Et]^+$, 310 (100) $[M-CO_2Et]^+$, 218 (35) $[M-CO_2Et-C_6H_5Me]^+$; EA calcd (%) for $C_{26}H_{25}NO_2$ (383.48): C 81.43, H 6.57, N 3.65; found: C 81.56, H 6.52, N 3.57.

Compound **10**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.93 (t, J=7.2 Hz, 3H), 0.94 (t, J=7.2 Hz, 3H), 1.40–1.69 (m, 6H), 2.25 (t, J=6.9, 2.1 Hz, 2H), 2.92 (dd, J=14.4, 7.8 Hz, 1H), 3.21 (ddt, J=14.4, 4.5, 1.8 Hz, 1H), 3.32 (tt, J=7.5, 1.8 Hz, 1H), 3.35 (d, J=14.1 Hz, 1H), 3.81 (d, J=14.1 Hz, 1H), 5.08 (m, 1H), 5.22 (m, 1H), 5.83 (dddd, J=18.0, 9.0, 7.8, 4.5 Hz, 1H), 7.19–7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.5, 18.3, 21.8, 27.3, 31.3, 53.9, 54.1, 54.8, 78.1, 84.9, 116.6, 126.7, 128.2, 128.8, 137.3, 140.5; MS (ESI): calcd for $C_{19}H_{27}N$ (269.21): found m/z 270.21 $[M+Na]^+$; EA calcd (%) for $C_{19}H_{27}N$ (269.42): C 84.70, H 10.10, N 5.20; found: C 84.81, H 9.93, N 5.25.

4.3. Synthesis of β-amino-acid-tethered enyne 16

To a solution of *N*-benzylallylamine (219 mg, 1.49 mmol) in dry THF (3.5 mL) was added ^{n}BuLi (1.6 M in hexane, 0.9 mL, 1.44 mmol) at −78 °C under Ar atmosphere. The solution was stirred at this temperature for 1 h, and then the solution was added to the solution of enynoate (*E*)-**15** in dry THF (3.5 mL) at −78 °C under Ar. After stirring another 1 h, the reaction was quenched with satd NH_4Cl (20 mL), and the reaction mixture was extracted with Et_2O (20 mL×3). The combined organic layer was washed with brine (20 mL), dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane/AcOEt 30:1) to give **16** (92.1 mg, 33%) as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (t, J=7.2 Hz, 3H), 1.38–1.56 (m, 4H), 2.23 (dt, J=6.6, 2.1 Hz, 2H), 2.57 (dd, J=14.4, 6.6 Hz, 1H), 2.68 (dd, J=14.4, 9.0 Hz, 1H), 2.90 (dd, J=14.1, 8.1 Hz, 1H), 3.20 (ddt, J=14.1, 4.8, 2.0 Hz, 1H), 3.33 (d, J=14.1 Hz, 1H), 3.65 (s, 3H), 3.80 (d, J=14.1 Hz, 1H), 4.01 (ddt, J=14.1, 9.0, 2.0 Hz, 1H), 5.08–5.24 (m, 2H), 5.78 (dddd, J=17.6, 9.6, 8.4, 4.2 Hz, 1H), 7.20–7.30 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 18.2, 21.8, 31.0, 39.8, 49.3, 51.4, 54.7, 76.0, 86.0, 117.2, 126.9, 128.2, 128.9, 136.6, 139.7, 171.3; IR (neat) 1745 cm^{-1}; MS (ESI): calcd for $C_{20}H_{27}NO_2$ (313.20): found m/z 336.18 $[M+Na]^+$; EA calcd (%) for $C_{20}H_{27}NO_2$ (313.43): C 76.64, H 8.68, N 4.47; found: C 76.33, H 9.08, N 4.37.

Compound **20**: oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (t, J=7.5 Hz, 3H), 1.40 (d, J=6.6 Hz, 3H), 1.38–1.52 (m, 4H), 2.19 (dt, J=7.2, 2.1 Hz, 2H), 2.49 (dd, J=14.4, 7.5 Hz, 1H), 2.56 (dd, J=14.4, 8.1 Hz, 1H), 3.16 (dd, J=15.0, 7.2 Hz, 1H), 3.55 (s, 3H), 3.79 (s, 3H), 3.94 (q, J=6.6 Hz, 1H), 4.02 (tt, J=8.1, 2.1 Hz, 1H), 5.03 (m, 1H), 5.14 (m, 1H), 5.78 (dddd, J=17.2, 10.2, 7.2, 4.8 Hz, 1H), 6.82 (d, J=9.0 Hz, 2H), 7.25 (d, J=9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 15.4, 18.3, 21.8, 30.9, 41.1, 46.9, 50.5, 51.4, 55.2, 57.3, 78.8, 85.5, 113.3, 116.0, 128.9, 136.9, 138.3, 158.5, 171.3; IR (neat) 1743 cm^{-1}; MS (ESI): calcd for $C_{22}H_{31}NO_3$ (357.23): found m/z 380.19 $[M+Na]^+$; EA calcd (%) for $C_{22}H_{31}NO_3$ (357.49): C 73.91, H 8.74, N 3.92; found: C 73.65, H 8.64, N 3.95.

4.4. Synthesis of pyrrole-2-carboxylate 7a from ethyl glyoxalate, *N*-benzylallylamine, and 1-hexyne

To a suspension of $CuBr_2$ (22 mg, 0.1 mmol) and MS 4 Å (500 mg) in toluene (2 mL) was added ethyl glyoxalate solution (ca. 50% in toluene, 0.20 mL), 1-hexyne (82 mg, 1.0 mmol), and *N*-benzylallylamine (147 mg, 1.0 mmol) in this order at room temperature under Ar atmosphere. The solution was stirred at room temperature under Ar atmosphere for 24 h. After filtration through a pad of Florisil®, the filtrate was concentrated in vacuo. The residue was diluted with degassed toluene (5 mL) and to this solution was added $[IrCl(cod)]_2$ (21 mg, 0.03 mmol) and AcOH (7 μL, 0.12 mmol). The solution was refluxed for 24 h under Ar. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (35:1) to give **7a** (123 mg, 39%) as pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, J=7.2 Hz, 3H), 1.27 (t, J=7.2 Hz, 3H), 1.31–1.52 (m, 6H), 2.00 (d, J=0.6 Hz, 3H), 2.70 (d, J=7.5 Hz, 2H), 4.21 (q, J=7.2 Hz, 2H), 6.60 (d, J=0.6 Hz, 1H), 7.03–7.07 (m, 2H), 7.19–7.31 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.92, 14.23, 14.35, 22.73, 26.12, 30.82, 32.21, 52.31, 59.39, 117.96, 118.63, 126.46, 126.87, 126.91, 128.32, 133.92, 138.94, 161.60; IR (neat) 1691 cm^{-1}; MS (EI): m/z (%): 313 (74) $[M]^+$, 256 (100) $[M-Bu]^+$, 184 (58) $[M-CO_2Et-CH_2{=}CHEt]^+$; EA calcd (%) for $C_{22}H_{27}NO_2$ (313.43): C 76.64, H 8.68, N 4.47; found: C 76.74, H 8.64, N 4.40.

4.5. General procedure for four-component coupling: synthesis of tricyclic pyrrole-2-carboxylate 9a from ethyl glyoxalate, *N*-benzylallylamine, 1-hexyne, and *N*-phenylmaleimide

To a suspension of $CuBr_2$ (22 mg, 0.1 mmol) and MS 4 Å (500 mg) in toluene (2 mL) was added ethyl glyoxalate solution (ca. 50% in toluene, 0.20 mL), 1-hexyne (82 mg, 1.0 mmol), and *N*-benzylallylamine (147 mg, 1.0 mmol) in this order at room temperature under Ar atmosphere. The solution was stirred at room temperature under Ar atmosphere for 24 h. After filtration through a pad of Florisil®, the filtrate was concentrated in vacuo. The residue was diluted with degassed toluene (5 mL) and to this solution was added $[IrCl(cod)]_2$ (21 mg, 0.03 mmol), AcOH (7 μL, 0.12 mmol), and *N*-phenylmaleimide (200 mg, 1.1 mmol). The solution was refluxed for 24 h under Ar. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (40:1–5:1)

to give **9a** (299 mg, 62%) as pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79 (t, J=7.2 Hz, 3H), 1.05–1.30 (m, 5H), 1.32 (t, J=7.2 Hz, 3H), 1.60–1.69 (m, 1H), 2.80 (ddd, J=15.0, 8.0, 0.9 Hz, 1H), 3.18–3.40 (m, 3H), 4.13–4.20 (m, 1H), 4.24 (dq, J=10.8, 7.2 Hz, 1H), 4.32 (dq, J=10.8, 7.2 Hz, 1H), 5.54 (s, 2H), 6.73 (s, 1H), 7.09–7.12 (m, 2H), 7.23–7.63 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (DEPT) 14.10 (CH_3), 14.52 (CH_3), 19.87 (CH_2), 22.91 (CH_2), 29.52 (CH_2), 30.19 (CH_2), 35.01 (CH), 39.88 (CH), 45.81 (CH), 52.44 (CH_2), 59.84 (CH_2), 117.62, 118.59, 124.86 (CH), 126.30 (CH), 126.66 (CH), 127.26 (CH), 128.45 (CH), 129.07 (CH), 131.53, 131.76, 138.33, 161.27, 177.36, 179.09; IR ($CHCl_3$) 1709 cm^{-1}; MS (EI): m/z (%): 484 (84) $[M]^+$, 427 (74) $[M-Bu]^+$, 411 (100) $[M-CO_2Et]^+$; EA calcd (%) for $C_{30}H_{32}N_2O_4$ (484.59): C 74.36, H 6.66, N 5.78; found: C 73.97, H 6.68, N 5.52.

The microwave heating was carried out as follows: to a dry degassed toluene (5 mL) solution of the freshly prepared enyne in a 6 mL reaction tube were added $[IrCl(cod)]_2$ (20 mg, 0.03 mmol), AcOH (7 μL, 0.12 mmol), and *N*-phenylmaleimide (200 mg, 1.1 mmol). The tube was sealed with a Teflon cap and heated in a microwave reactor at 150 °C for 0.5 h. The purification as above afforded **9a** (287 mg, 59%).

Compound **9b**: mp 201.0–201.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 (t, J=7.2 Hz, 3H), 3.28–3.35 (m, 2H), 3.50–3.57 (m, 2H), 4.14 (q, J=7.2 Hz, 2H), 5.33 (d, J=6.9 Hz, 1H), 5.45 (d, J=12.6 Hz, 1H), 5.63 (d, J=12.6 Hz, 1H), 6.47–6.50 (m, 2H), 6.83 (s, 1H), 7.07–7.35 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 18.1, 38.4, 40.3, 45.8, 52.4, 59.9, 117.6, 117.7, 124.8, 126.3, 126.8, 126.0, 127.3, 128.3, 128.3, 128.5, 128.7, 129.0, 129.6, 131.3, 137.9, 138.9, 160.8, 176.4, 178.6; IR ($CHCl_3$) 1711 cm^{-1}; MS (EI): m/z (%): 504 (36) $[M]^+$, 458 (100) $[M-HOEt]^+$; EA calcd (%) for $C_{32}H_{28}N_2O_4$ (504.58): C 76.17, H 5.59, N 5.55; found: C 76.59, H 5.56, N 5.42.

Compound **9c**: mp 136.8–137.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, J=7.2 Hz, 3H), 2.92–3.00 (m, 1H), 3.09 (dd, J=15.0, 9.0 Hz, 1H), 3.18 (s, 3H), 3.29–3.42 (m, 2H), 3.52 (dd, J=9.6, 3.0 Hz, 1H), 3.81 (dd, J=9.6, 3.9 Hz, 1H), 4.22 (dq, J=10.5, 7.2 Hz, 1H), 4.27 (dd, J=7.2, 3.6 Hz, 1H), 4.31 (dq, J=10.5, 7.2 Hz, 1H), 5.40 (d, J=15.0 Hz, 1H), 5.63 (d, J=15.0 Hz, 1H), 6.71 (s, 1H), 7.13–7.17 (m, 2H), 7.27–7.52 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 20.2, 34.4, 40.2, 42.3, 52.4, 58.7, 59.9, 74.9, 117.4, 119.5, 124.4, 126.3, 127.0, 127.3, 128.2, 128.5, 128.9, 130.2, 132.2, 138.1, 160.9, 177.3, 179.2; IR ($CHCl_3$) 1707 cm^{-1}; MS (EI): m/z (%): 472 (46) $[M]^+$, 440 (14) $[M-HOMe]^+$, 427 (100) $[M-OEt]^+$; EA calcd (%) for $C_{28}H_{28}N_2O_5$ (472.53): C 71.17, H 5.97, N 5.93; found: C 71.46, H 5.86, N 5.79.

Compound **9d**: oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J=7.2 Hz, 3H), 1.36–1.78 (m, 4H), 2.80 (ddd, J=15.0, 9.0, 1.5 Hz, 1H), 3.17–3.37 (m, 5H), 3.23 (s, 3H), 4.13–4.21 (m, 1H), 4.24 (dq, J=10.8, 7.2 Hz, 1H), 4.30 (dq, J=10.8, 7.2 Hz, 1H), 5.49 (d, J=15.3 Hz, 1H), 5.54 (d, J=15.3 Hz, 1H), 6.72 (s, 1H), 7.09–7.13 (m, 2H), 7.27–7.53 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 19.7, 26.7, 27.3, 34.6, 39.7, 45.6, 52.3, 58.2, 59.7, 72.3, 117.6, 118.3, 124.8, 126.2, 126.6, 127.1, 128.3, 128.3, 128.8, 131.1, 131.6, 138.1, 160.9, 177.0, 178.8; IR ($CHCl_3$) 1710 cm^{-1}; MS (EI): m/z (%): 500 (100) $[M]^+$, 427 (97) $[M-CO_2Et]^+$, 395 (35) $[M-CO_2Et-HOMe]^+$; EA calcd (%) for $C_{30}H_{32}N_2O_5$ (500.59): C 71.98, H 6.44, N 5.60; found: C 72.05, H 6.44, N 5.52.

Compound **9e**: oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J=7.2 Hz, 3H), 1.36–1.46 (m, 1H), 1.55–1.65 (m, 1H), 1.75–1.89 (m, 2H), 2.80 (ddd, J=15.0, 9.0, 1.2 Hz, 1H), 3.20–3.38 (m, 3H), 3.42 (t, J=6.6 Hz, 2H), 4.15–4.22 (m, 1H), 4.25 (dq, J=10.8, 7.2 Hz, 1H), 4.31 (dq, J=10.8, 3.6 Hz, 1 H), 5.52 (s, 2H), 6.74 (s, 1 H), 7.08–7.11 (m, 2H), 7.26–7.54 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 19.9, 27.7, 30.3, 34.3, 39.9, 45.0, 45.6, 52.6, 60.0, 117.7, 118.6, 125.1, 126.3, 126.7, 127.3, 128.5, 128.5, 129.1, 130.9, 131.7, 138.1, 161.0., 177.0, 178.8; IR ($CHCl_3$) 1709 cm^{-1}; MS (EI): m/z (%): 504 (45) $[M]^+$, 458 (38) $[M-HOEt]^+$, 427 (100) $[M-C_6H_5]^+$, 381 (31) $[M-HOEt-C_6H_5]^+$; EA calcd (%) for $C_{29}H_{29}ClN_2O_4$ (505.00): C 68.97, H 5.79, N 5.55; found: C 69.13, H 5.74, N 5.40.

Compound **9f**: mp 57–59 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J=7.2 Hz, 3H), 1.40–1.72 (m, 4H), 2.16–2.31 (m, 2H), 2.77 (ddd, J=15.0, 9.0, 1.2 Hz, 1H), 3.18–3.40 (m, 3H), 3.60 (s, 3H), 4.15–4.22 (m, 1H), 4.24 (dq, J=10.8, 7.2 Hz, 1H), 4.32 (dq, J=10.8, 7.2 Hz, 1H), 5.49 (d, J=15.3 Hz, 1H), 5.57 (d, J=15.3 Hz, 1H), 6.73 (s, 1H), 7.10–7.13 (m, 2H), 7.27–7.53 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 19.8, 22.7, 29.7, 33.9, 34.6, 39.8, 45.6, 51.4, 52.4, 59.9, 117.6, 118.6, 124.9, 126.2, 126.7, 127.2, 128.4, 129.0, 130.9, 131.7, 138.2, 161.0, 173.3, 177.1, 178.8; IR ($CHCl_3$) 1711 cm^{-1}; MS (EI): m/z (%): 528 (100) $[M]^+$, 455 (50) $[M-CO_2Et]^+$, 427 (38) $[M-(CH_2)_3CO_2Me]^+$; EA calcd (%) for $C_{31}H_{32}N_2O_6$ (528.60): C 70.44, H 6.10, N 5.30; found: C 70.46, H 6.04, N 5.29.

Compound **9g**: mp 207.6–208.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (t, J=7.2 Hz, 3H), 3.08 (dd, J=15.8, 8.7 Hz, 1H), 3.15 (dd, J=15.8, 8.4 Hz, 1H), 3.26 (dd, J=9.0, 8.7 Hz, 1H), 3.34 (dd, J=9.3, 5.4 Hz, 1H), 3.69–3.70 (m, 1H), 3.97 (s, 5H), 4.03–4.06 (m, 1H), 4.07–4.09 (m, 1H), 4.18–4.20 (m, 1H), 4.30 (dq, J=10.8, 7.2 Hz, 1H), 4.42 (dq, J=10.8, 7.2 Hz, 1H), 5.24 (d, J=5.4 Hz, 1H), 5.47 (d, J=15.3 Hz, 1H), 5.71 (d, J=15.3 Hz, 1H), 6.83 (s, 1H), 6.99–7.03 (m, 2H), 7.12–7.15 (m, 2H), 7.27–7.41 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 19.4, 34.7, 39.2, 48.3, 52.9, 60.1, 67.3, 67.4, 67.8, 68.5, 69.1, 87.7, 117.6, 118.7, 125.0, 126.2, 126.5, 127.2, 128.1, 128.4, 128.6, 131.5, 131.9, 138.5, 161.1, 176.4, 178.5; IR ($CHCl_3$) 1708 cm^{-1}; MS (EI): m/z (%): 612 (100) $[M]^+$, 547 (2) $[M-Cp]^+$, 501 (17) $[M-CO_2Et-CpH]^+$; EA calcd (%) for $C_{36}H_{32}FeN_2O_4$ (612.50): C 70.59, H 5.27, N 4.57; found: C 70.58, H 5.15, N 4.61.

Compound **9h**: oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79 (t, J=7.2 Hz, 3H), 1.00–1.28 (m, 5H), 1.31 (t, J=7.2 Hz, 3H), 1.52–1.63 (m, 1H), 2.80 (ddd, J=15.6, 9.0, 1.2 Hz, 1H), 3.16 (dd, J=15.6, 9.6 Hz, 1H), 3.35–3.52 (m, 2H), 4.04–4.11 (m, 1H), 4.23 (dq, J=10.8, 7.2 Hz, 1H), 4.30 (dq, J=10.8, 7.2 Hz, 1H), 5.47 (d, J=15.0 Hz, 1H), 5.56 (d, J=15.0 Hz, 1H), 6.70 (s, 1H), 7.06–7.09 (m, 2H),

7.27–7.34 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 14.5, 19.4, 22.7, 29.5, 30.6, 34.6, 39.7, 46.6, 52.5, 60.0, 116.4, 118.8, 124.9, 126.7, 127.4, 128.5, 130.2, 138.1, 161.1, 172.1, 174.2; IR ($CHCl_3$) 1779, 1693 cm^{-1}; MS (EI): *m/z* (%): 409 (56) $[M]^+$, 353 (100) $[M-CH_2{=}CHEt]^+$, 336 (39) $[M-CO_2Et]^+$; EA calcd (%) for $C_{24}H_{27}NO_5$ (409.47): C 70.40, H 6.65, N 3.42; found: C 70.74, H 6.67, N 3.31.

Compound **9i**: mp 109.4–110.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 (t, *J*=7.2 Hz, 3H), 1.35–1.45 (m, 2H), 1.75–2.02 (m, 2H), 2.16 (t, *J*=7.5 Hz, 2H), 3.45 (dd, *J*=22.5, 3.0 Hz, 1H), 3.55 (s, 3H), 4.03 (dd, *J*=22.5, 2.1 Hz, 1H), 4.30 (dq, *J*=7.2, 3.6 Hz, 1H), 4.32 (dq, *J*=7.2, 3.6 Hz, 1H), 4.95–5.01 (m, 1H), 5.48 (d, *J*=15.3 Hz, 1H), 5.65 (d, *J*=15.3 Hz, 1H), 6.80 (s, 1H), 7.07–7.10 (m, 2H), 7.21–7.33 (m, 3H), 7.69–7.75 (m, 2H), 8.09–8.16 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 21.0, 21.9, 33.3, 34.2, 36.0, 51.4, 52.6, 59.9, 116.7, 117.2, 124.7, 126.1, 126.4, 126.6, 127.3, 128.5, 129.9, 131.9, 132.2, 138.3, 144.1, 146.8, 161.0, 173.5, 183.7, 184.3; IR ($CHCl_3$) 1731, 1689, 1660 cm^{-1}; MS (EI): *m/z* (%): 511 (26) $[M]^+$, 480 (5) $[M-OMe]^+$, 466 (2) $[M-OEt]^+$, 438 (6) $[M-CO_2Et]^+$, 410 (100) $[M-(CH_2)_3CO_2Me]^+$; EA calcd (%) for $C_{31}H_{29}NO_6$ (511.57): C 72.78, H 5.71, N 2.74; found: C 72.92, H 5.63, N 2.63.

Compound **11**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.90 (t, *J*=6.6 Hz, 3H), 1.01 (t, *J*=7.5 Hz, 3H), 1.31–1.51 (m, 6H), 2.02 (d, *J*=0.6 Hz, 3H), 2.36 (t, *J*=7.5 Hz, 2H), 2.47 (q, *J*=7.5 Hz, 2H), 4.95 (s, 2H), 6.30 (s, 1H), 7.00 (d, *J*=6.9 Hz, 2H), 7.20–7.32 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.2, 14.0, 15.3, 17.5, 22.5, 24.8, 31.5, 32.0, 49.9, 116.8, 117.8, 119.6, 126.6, 127.2, 128.7, 131.0, 139.4; MS (ESI): calcd for $C_{19}H_{27}N$ (269.21): found *m/z* 270.21 $[M+Na]^+$; EA calcd (%) for $C_{19}H_{27}N$ (269.42): C 84.70, H 10.10, N 5.20; found: C 84.58, H 10.45, N 5.34.

Compound **12**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.87 (t, *J*=6.6 Hz, 3H), 0.90 (t, *J*=7.2 Hz, 3H), 1.18–1.32 (m, 5H), 1.53 (m, 1H), 1.58–1.70 (m, 2H), 2.50–2.57 (m, 2H), 2.88 (m, 1H), 3.16 (dd, *J*=9.9, 6.6 Hz, 1H), 3.22 (m, 1H), 3.32 (dt, *J*=9.9, 7.2 Hz, 1H), 3.53 (d, *J*=13.2 Hz, 1H), 3.51–3.58 (m, 1H), 3.71 (m, 1H), 4.06 (d, *J*=13.2 Hz, 1H), 7.22–7.51 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.0, 13.8, 20.3, 22.7, 24.2, 29.7, 30.1, 34.1, 38.8, 44.8, 59.2, 61.9, 73.1, 126.4, 126.9, 128.4, 128.5, 128.7, 129.3, 132.0, 132.2, 138.5, 140.3, 177.8, 179.5; IR ($CHCl_3$) 1712 cm^{-1}; MS (ESI): calcd for $C_{29}H_{34}N_2O_2$ (442.26): found *m/z* 443.42 $[M+H]^+$; EA calcd (%) for $C_{29}H_{34}N_2O_2$ (442.59): C 78.70, H 7.74, N 6.33; found: C 79.06, H 7.71, N 6.00.

Compound **13**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.85 (t, *J*=7.2 Hz, 3H), 1.06 (t, *J*=7.2 Hz, 3H), 1.20–1.45 (m, 5H), 1.74 (m, 1H), 2.41–2.62 (m, 2H), 2.90 (dd, *J*=14.4, 7.2 Hz, 1H), 3.13 (dd, *J*=14.4, 8.7 Hz, 1H), 3.27–3.42 (m, 3H), 4.98 (d, *J*=16.5 Hz, 1H), 5.04 (d, *J*=16.5 Hz, 1H), 6.42 (s, 1H), 6.98 (d, *J*=6.0 Hz, 2H), 7.24–7.50 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 15.3, 17.5, 20.8, 22.6, 29.9, 30.1, 34.9, 40.8, 46.2, 50.1, 116.2, 116.5, 118.3, 126.4, 126.6, 127.4, 128.6, 128.8, 129.2, 130.4, 132.2, 138.9, 178.3, 179.8; IR ($CHCl_3$) 1709 cm^{-1}; MS (ESI): calcd for $C_{29}H_{32}N_2O_2$ (440.25): found *m/z* 463.19 $[M+Na]^+$; EA calcd (%) for $C_{29}H_{32}N_2O_2$ (440.58): C 79.06, H 7.32, N 6.36; found: C 79.11, H 7.38, N 6.25.

Compound **17**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.89 (t, *J*=6.9 Hz, 3H), 1.26–1.50 (m, 6H), 2.03 (d, *J*=0.9 Hz, 3H), 2.38 (t, *J*=7.5 Hz, 2H), 3.46 (s, 2H), 3.56 (s, 3H), 5.03 (s, 2H), 6.40 (s, 1H), 6.99 (d, *J*=6.9 Hz, 2H), 7.20–7.33 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.2, 13.9, 22.5, 24.7, 30.4, 30.8, 31.8, 50.4, 51.8, 116.9, 119.6, 121.1, 122.6, 126.6, 127.3, 128.7, 138.7, 171.4; IR ($CHCl_3$) 1739 cm^{-1}; MS (ESI): calcd for $C_{20}H_{27}NO_2$ (313.20): found *m/z* 336.18 $[M+Na]^+$; EA calcd (%) for $C_{20}H_{27}NO_2$ (313.43): C 76.64, H 8.68, N 4.47; found: C 76.57, H 8.74, N 4.48.

Compound **18**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.83 (t, *J*=6.9 Hz, 3H), 1.13–1.45 (m, 5H), 1.74 (m, 1H), 2.91 (dd, *J*=15.0, 7.2 Hz, 1H), 3.13 (dd, *J*=15.0, 8.4 Hz, 1H), 3.24–3.43 (m, 3H), 3.50 (d, *J*=6.9 Hz, 2H), 3.57 (s, 3H), 5.04 (d, *J*=16.5 Hz, 1H), 5.10 (d, *J*=16.5 Hz, 1H), 6.52 (s, 1H), 6.98 (dd, *J*=6.0, 2.1 Hz, 2H), 7.23–7.51 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 20.7, 22.6, 29.8, 29.9, 30.3, 34.9, 40.7, 45.7, 50.6, 51.9, 116.6, 117.9, 120.5, 121.3, 126.5, 126.6, 127.6, 128.6, 128.8, 129.2, 132.2, 138.2, 171.0, 178.0, 179.7; IR ($CHCl_3$) 1737, 1709 cm^{-1}; MS (ESI): calcd for $C_{30}H_{32}N_2O_4$ (484.24): found *m/z* 507.20 $[M+Na]^+$; EA calcd (%) for $C_{30}H_{32}N_2O_4$ (484.59): C 74.36, H 6.66, N 5.78; found: C 74.48, H 6.73, N 5.58.

Compound **21**: oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.88 (t, *J*=6.9 Hz, 3H), 1.25–1.48 (m, 6H), 1.71 (d, *J*=6.9 Hz, 3H), 2.03 (d, *J*=0.9 Hz, 3H), 2.36 (tt, *J*=7.5, 3.9 Hz, 2H), 3.38 (d, *J*=16.2 Hz, 1H), 3.51 (d, *J*=16.2 Hz, 1H), 3.56 (s, 3H), 3.77 (s, 3H), 5.29 (q, *J*=6.9 Hz, 1H), 6.52 (s, 1H), 6.81 (d, *J*=9.0 Hz, 2H), 6.92 (d, *J*=9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.4, 14.0, 22.4, 22.5, 24.7, 30.5, 30.8, 31.8, 51.8, 54.0, 55.2, 113.9, 115.4, 116.6, 121.1, 122.3, 127.1, 136.2, 158.7, 171.6; IR ($CHCl_3$) 1738 cm^{-1}; MS (ESI): calcd for $C_{22}H_{31}NO_3$ (357.23): found *m/z* 380.19 $[M+Na]^+$; EA calcd (%) for $C_{22}H_{31}NO_3$ (357.49): C 73.91, H 8.74, N 3.92; found: C 73.99, H 8.73, N 3.85.

Compound **22**: mp 185.6–186.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): (more polar isomer) δ 0.83 (t, *J*=6.9 Hz, 3H), 1.15–1.41 (m, 5H), 1.71 (m, 1H), 1.75 (d, *J*=6.6 Hz, 3H), 2.88 (dd, *J*=15.0, 7.8 Hz, 1H), 3.13 (dd, *J*=15.0, 9.0 Hz, 1H), 3.20–3.38 (m, 3H), 3.45 (d, *J*=17.0 Hz, 1 H), 3.55 (s, 3H), 3.57 (d, *J*=17.0 Hz, 1H), 3.78 (s, 3H), 5.31 (q, *J*=6.6 Hz, 1H), 6.63 (s, 1H), 6.83 (d, *J*=8.7 Hz, 2H), 6.95 (d, *J*=8.7 Hz, 2H), 7.23–7.51 (m, 5H); (less polar isomer) δ 0.81 (t, *J*=7.2 Hz, 3H), 1.05–1.45 (m, 6H), 1.74 (d, *J*=6.9 Hz, 3H), 2.93 (dd, *J*=14.2, 6.3 Hz, 1H), 3.13 (dd, *J*=14.2, 8.4 Hz, 1H), 3.25–3.40 (m, 3H), 3.37 (d, *J*=17.1 Hz, 1H), 3.58 (d, *J*=17.1 Hz, 1H), 3.60 (s, 3H), 3.77 (s, 3H), 5.31 (q, *J*=6.9 Hz, 1H), 6.66 (s, 1H), 6.78 (d, *J*=8.7 Hz, 2H), 6.87 (d, *J*=8.7 Hz, 2H), 7.22–7.50 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): (more polar isomer) δ 14.0, 20.7, 22.5, 22.6, 29.9, 30.0, 30.3, 34.9, 40.7, 46.0, 51.9, 54.3, 55.2, 113.8, 114.0, 116.2, 120.5, 120.8, 126.6,

127.2, 128.6, 129.2, 132.2, 135.5, 158.9, 171.2, 178.1, 179.8; (less polar isomer) δ 13.9, 20.9, 22.4, 22.5, 29.7, 29.8, 30.4, 34.8, 40.7, 45.6, 51.9, 54.2, 55.1, 113.8, 114.0, 116.3, 120.5, 120.9, 126.6, 126.8, 128.5, 129.1, 132.2, 135.7, 158.9, 171.2, 179.0, 179.7; IR ($CHCl_3$) 1736, 1709 cm^{-1}; MS (ESI): calcd for $C_{32}H_{36}N_2O_5$ (528.26): found *m/z* 551.21 $[M+Na]^+$; EA calcd (%) for $C_{32}H_{36}N_2O_5$ (528.64): C 72.70, H 6.86, N 5.30; found: C 72.52, H 7.01, N 5.33.

4.6. Procedure for removal of chiral auxiliary of 22

To a solution of **22** (12.3 mg, 0.023 mmol) in CH_2Cl_2 (1 mL)/anisole (0.4 mL) were added CF_3CO_2H (0.1 mL) and concd H_2SO_4 (1 drop) at room temperature. After stirring for 12 h, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with 5% Na_2CO_3 (5 mL). The aqueous solution was dried with Na_2SO_4, concentrated in vacuo, and purified by flash column chromatography on silica gel eluted with hexane/AcOEt (5:1) to give **23** (7.5 mg, 82%) as pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.84 (t, J=7.5 Hz, 3H), 1.11–1.40 (m, 5H), 1.73 (m, 1H), 2.88 (dd, J=15.0, 7.5 Hz, 1H), 3.16 (dd, J=15.0, 8.4 Hz, 1H), 3.23–3.41 (m, 3H), 3.60 (d, J=17.1 Hz, 1H), 3.66 (d, J=17.1 Hz, 1H), 3.71 (s, 3H), 6.60 (d, J=1.8 Hz, 1H), 7.21–7.25 (m, 2H), 7.36–7.50 (m, 3H), 8.44 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 20.7, 22.5, 30.0, 31.2, 34.5, 40.7, 45.8, 52.1, 113.1, 117.5, 118.7, 119.4, 126.6, 128.6, 129.3, 132.2, 171.6, 178.0, 179.6; IR ($CHCl_3$) 3100–3700, 1736, 1710 cm^{-1}; MS (ESI): calcd for $C_{23}H_{26}N_2O_4$ (394.19): found *m/z* 417.17 $[M+Na]^+$; EA calcd (%) for $C_{23}H_{26}N_2O_4$ (394.46): C 70.03, H 6.64, N 7.10; found: C 70.21, H 6.42, N 7.13.

4.7. Synthesis of dienyne 24 and its Rh-catalyzed cycloisomerization

To a suspension of $CuBr_2$ (11 mg, 0.05 mmol) and MS 4 Å (252 mg) in toluene (0.6 mL) were added ethyl glyoxalate solution (ca. 50% in toluene, 0.10 mL), 1-hexyne (41 mg, 0.5 mmol), and *N*-benzylpenta-2,4-dienylamine (92.6 mg, 0.5 mmol) in this order at room temperature under Ar atmosphere. The solution was stirred at room temperature under Ar atmosphere for 24 h. After filtration through a pad of Florisil®, the filtrate was concentrated in vacuo. To a dry degassed toluene (5 mL) solution of the obtained dienyne **24** in a 6 mL reaction tube was added $Rh(acac)(CO)_2$ (6.3 mg, 0.024 mmol). The tube was sealed with a Teflon cap and heated in a microwave reactor at 120 °C for 0.5 h. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (50:1) to give **25** (41.2 mg, 23%) as pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J=7.2 Hz, 3H), 1.13 (d, J=7.5 Hz, 3H), 1.23 (t, J=7.5 Hz, 3H), 1.20–1.47 (m, 4H), 1.95–2.14 (m, 2H), 2.75 (dd, J=11.0, 7.2 Hz, 1H), 2.72–2.86 (m, 1H), 3.05 (dd, J=14.1, 6.9 Hz, 1H), 3.05–3.13 (m, 1H), 3.65 (d, J=13.5 Hz, 1H), 3.87 (d, J=13.5 Hz, 1H), 4.14 (q, J=7.2 Hz, 2H), 4.43 (s, 1H), 5.57 (ddd, J=9.6, 3.0, 1.8 Hz, 1H), 5.74 (ddd, J=9.6, 2.4, 1.8 Hz, 1H), 7.23–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 14.3, 19.1, 22.5, 29.8, 30.0, 32.9, 40.9, 54.9, 55.0, 59.9, 66.1, 124.8, 127.1, 128.3, 128.7, 133.8, 133.9, 134.2, 139.2, 172.8; IR ($CHCl_3$) 1730 cm^{-1}; MS (ESI): calcd for $C_{23}H_{31}NO_2$ (353.24): found *m/z* 376.22 $[M+Na]^+$. This compound was not suitable for elemental analysis because of ready aromatization under air. EA calcd (%) for $C_{23}H_{31}NO_2$ (353.50): C 78.15, H 8.84, N 3.96; found: C 77.64, H 9.38, N 3.93.

Further elution with hexane/AcOEt (30:1) to give **26** (71.4 mg, 41%) as pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, J=7.2 Hz, 3H), 1.11 (d, J=7.2 Hz, 3H), 1.14 (t, J=7.2 Hz, 3H), 1.27 (sext, J=7.2 Hz, 2H), 1.33–1.47 (m, 2H), 1.98–2.20 (m, 3H), 2.87 (m, 1H), 3.26–3.35 (m, 2H), 3.83 (s, 2H), 3.91 (s, 1H), 3.98 (dq, J=7.2, 1.5 Hz, 1H), 5.56 (dt, J=9.9, 2.1 Hz, 1H), 5.67 (dt, J=9.6, 2.1 Hz, 1H), 7.21–7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 14.0, 19.3, 22.9, 29.7, 29.9, 32.0, 40.1, 58.3, 59.7, 60.6, 67.4, 123.4, 127.2, 128.3, 129.3, 131.8, 133.0, 133.5, 138.6, 173.6; IR ($CHCl_3$) 1728 cm^{-1};MS (ESI): calcd for $C_{23}H_{31}NO_2$ (353.24): found *m/z* 376.22 $[M+Na]^+$; EA calcd (%) for $C_{23}H_{31}NO_2$ (353.50): C 78.15, H 8.84, N 3.96; found: C 77.89, H 9.07, N 3.99.

4.8. Synthesis of cyclopropylenyne 27 and its Rh-catalyzed cycloisomerization

To a suspension of $CuBr_2$ (11 mg, 0.05 mmol) and MS 4 Å (254 mg) in toluene (0.6 mL) was added ethyl glyoxalate solution (ca. 50% in toluene, 0.10 mL), 1-hexyne (41 mg, 0.5 mmol), and *N*-benzyl-3-cyclopropylallylamine (93.9 mg, 0.5 mmol) in this order at room temperature under Ar atmosphere. The solution was stirred at room temperature under Ar atmosphere for 24 h. After filtration through a pad of Florisil®, the filtrate was concentrated in vacuo. To a dry degassed toluene (5 mL) solution of the obtained cyclopropylenyne **27** in a 6 mL reaction tube were added $RhCl(PPh_3)_3$ (23.2 mg, 0.025 mmol) and AgOTf (6.6 mg, 0.025 mmol). The tube was sealed with a Teflon cap and heated in a microwave reactor at 120 °C for 0.5 h. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel eluted with hexane/AcOEt (100:1) to give a 1.7:1 mixture of **28** and **29** (81.4 mg, 46%) as pale yellow oil. Compound **28**: ^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J=7.2 Hz, 3H), 1.25 (t, J=7.5 Hz, 3H), 1.17–1.46 (m, 4H), 1.92–2.24 (m, 4H), 2.68 (m, 1H), 2.97 (t, J=8.4 Hz, 1H), 3.22 (t, J=8.4 Hz, 1H), 3.67 (d, J=12.9 Hz, 1H), 3.82 (m, 1H), 3.84 (d, J=12.9 Hz, 1H), 4.10 (dq, J=10.5, 7.5 Hz, 1H), 4.20 (dq, J=10.5, 7.5 Hz, 1H), 4.28 (s, 1H), 5.35–5.41 (m, 1H), 5.47–5.56 (m, 1H), 7.22–7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 14.2, 22.7, 26.7, 30.0, 30.2, 35.3, 39.6, 55.2, 58.3, 60.0, 66.9, 127.1, 128.3, 128.8, 128.9, 129.3, 136.6, 138.2, 138.9, 172.5; IR ($CHCl_3$) 1727 cm^{-1}; MS (ESI): calcd for $C_{23}H_{31}NO_2$ (353.24): found *m/z* 376.22 $[M+Na]^+$; EA calcd (%) for $C_{23}H_{31}NO_2$ (353.50): C 78.15, H 8.84, N 3.96; found: C 78.02, H 9.21, N 3.72. Compound **29**: ^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J=7.2 Hz, 3H), 1.25 (t, J=7.5 Hz, 3H), 1.20–1.43 (m, 4H), 1.92–2.26 (m, 5H), 2.49 (dd, J=8.4, 6.0 Hz, 1H), 2.64 (m, 1H), 3.33 (t, J=8.4 Hz, 1H), 3.73 (s, 2H), 3.84 (m, 1H), 4.11 (q, J=7.5 Hz, 2H), 4.17 (s, 1H), 5.38–5.43 (m, 1H), 5.52–5.60 (m, 1H), 7.21–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 14.1, 22.8, 26.3, 29.7, 30.4, 35.0, 40.5, 56.8, 59.7, 60.3, 68.7, 127.1, 128.2, 129.0, 129.9, 131.9,

136.1, 137.5, 138.5, 173.0; IR ($CHCl_3$) 1726 cm^{-1}; MS (ESI): calcd for $C_{23}H_{31}NO_2$ (353.24): found *m/z* 376.22 $[M+Na]^+$; EA calcd (%) for $C_{23}H_{31}NO_2$ (353.50): C 78.15, H 8.84, N 3.96; found: C 77.89, H 9.32, N 3.76.

4.9. Crystallographic structural determination of 9g

A single crystal was mounted on a quartz fiber, and diffraction data were collected at 173 K on a Brucker SMART APEX CCD diffractometer with graphite-monochromated Mo Kα radiation (λ=0.71073 Å). An absorption correction was made using SADABS. The structure was solved by direct methods and refined by full-matrix least squares on F^2 by using SHELXTL.[35] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in calculated positions. The supplementary crystallographic data for this paper [CCDC 269756] can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

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