Synthesis R. Kumar et al. Special Topic

Nickel-Catalyzed Enantioselective Synthesis of Cyclobutenes via [2+2] Cycloaddition of α,β-Unsaturated Carbonyls with 1,3-Enynes

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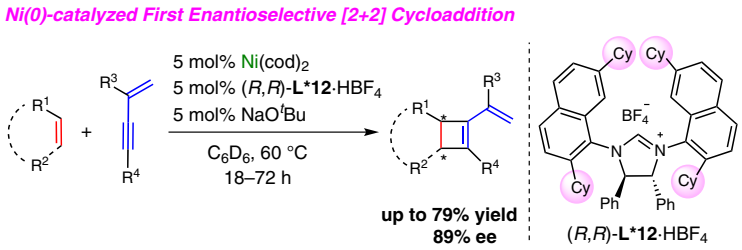

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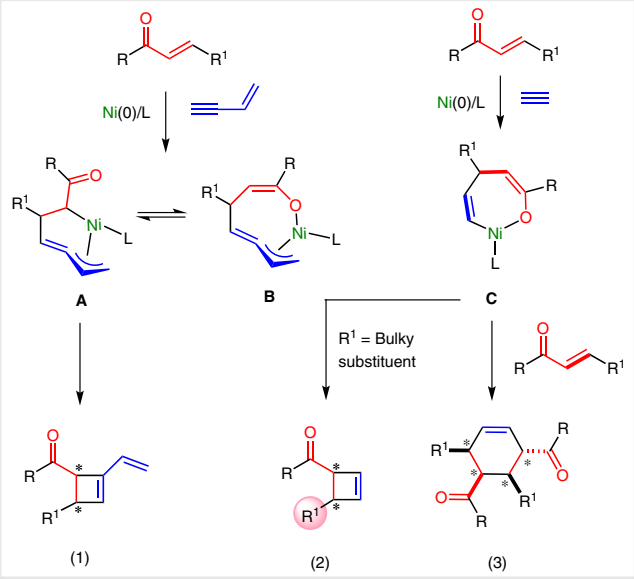
Abstract A Ni(0)/chiral N-heterocyclic carbene (NHC) catalyzed enantioselective and intermolecular [2+2] cycloaddition of α,β-unsaturated carbonyl compounds with conjugated enynes was investigated to produce enantioenriched cyclobutenes (up to 89% ee). The present report reveals the first example of a nickel-catalyzed enantioselective [2+2]-cycloaddition reaction. A newly synthesized imidazolinium salt, **L*12**·HBF_4, was the most effective NHC precursor for the present catalytic reactions.

Key words nickel catalysis, N-heterocyclic carbenes, enantioselective, intermolecular, [2+2] cycloaddition, cyclobutenes

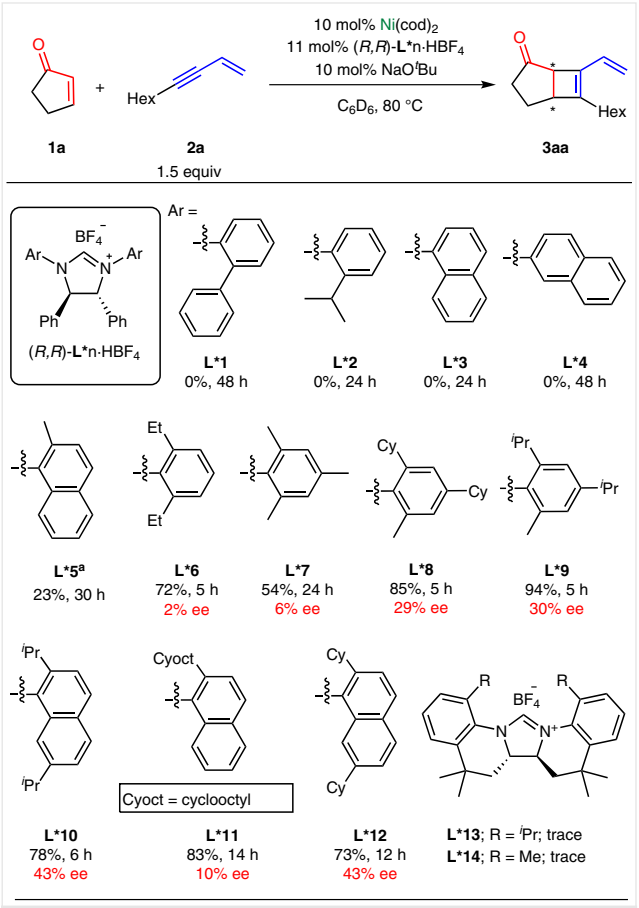
Cyclobutene rings are of particular relevance in chemical synthesis due to the unique reactivity that originates from ring strain.[1] In addition, cyclobutene is also a key component in many natural and pharmaceutically important molecules.[2] The [2+2] cycloaddition of an alkene and an alkyne is the most straightforward method for the synthesis of cyclobutenes. Brønsted or Lewis acid catalyzed and transition-metal-catalyzed [2+2] cycloadditions have been well developed.[3,4] Whereas ample examples of racemic syntheses of cyclobutenes have been reported, catalytic enantioselective syntheses have been significantly less studied.[4c,d] Furthermore, transition-metal-catalyzed enantioselective [2+2]-cycloaddition reactions have been limited to highly strained norbornene types of molecules, that are catalyzed by rhodium[5] and iridium.[6]

Nickel is a prominent candidate as a catalyst for the synthesis of carbo- and heterocycles, and it has been extensively studied for five-, six-, and larger-membered rings.[7] Conversely, there have been few examples of the construction of four-membered rings, and those were developed for non-enantioselective syntheses.[8] We previously reported the Ni(0)-catalyzed intermolecular [2+2] cycloaddition of an alkene/α,β-unsaturated carbonyl with an alkyne/conjugated enyne to synthesize cyclobutenes with the generation of one or two stereogenic centers [Scheme 1,(1) and (2)].[9] In contrast, cyclohexenes were obtained by the reaction of two enones and an alkyne with the generation of four contiguous stereogenic centers [Scheme 1,(3)].[10] These two distinct products were formed due to the structural differences in nickelacycles **A**, **B**, and **C** generated by the oxidative cyclization of α,β-unsaturated carbonyl compounds with a 1,3-enyne and an alkyne, respectively. In the course of the [2+2]-cycloaddition reaction, the coordination of another enone to the nickelacycle might be hampered because of to the pre-occupation of the coordination site of the nickel center either with the conjugated double bond of an enyne [**A** or **B** (1)] or with a bulky substituent (R^1) at the β-position of an enone [**C** (2)]. Since the pioneering discovery of C_2-symmetric chiral *N*-heterocyclic carbenes (NHCs) by Grubbs et al.,[11] which relied on the transfer of the inherent central chirality from the NHC backbone to unsymmetrically *N*-substituted aryl side chains and ultimately to the metal-coordination sphere, a number of metal–chiral NHC systems have been designed. Recently, these NHCs have also been recognized as effective ligands for nickel-catalyzed enantioselective reactions.[12] Very recently, we explored the Ni(0)-catalyzed enantioselective [2+2+2] cycloaddition of two enones and an alkyne in the presence of a chiral NHC [Scheme 1,(3)].[13] Herein, we report the development of an enantioselective variant of a Ni(0)-catalyzed [2+2] cycloaddition of α,β-unsaturated carbonyls with 1,3-enynes to produce enantioenriched cyclobutenes [Scheme 1,(1)].



Scheme 1 Nickel(0)-catalyzed cycloaddition of enone and alkyne

Our study commenced with a survey of chiral NHCs generated in situ from the corresponding C_2-symmetric imidazolinium salts, **L*n**·HBF_4, in the presence of NaO^{t}Bu and Ni(cod)$_2$ at 80 °C using cyclopent-2-en-1-one (**1a**) and dec-1-en-3-yne (**2a**) as model substrates (Scheme 2).[14] First, we examined the reaction with *N*-biphenyl-2-yl-substituted NHC **L*1**, which was an optimal ligand in the case of our Ni(0)-catalyzed enantioselective [2+2+2]-cycloaddition reaction.[13] However, this NHC did not give **3aa** at all. In a similar manner, *N*-2-isopropylphenyl-[12d] and *N*-1-naphthyl-substituted NHCs **L*2** and **L*3** were also unsuccessful, which suggested that mono-*ortho*-substituted NHCs might not be suitable to deliver the desired product, **3aa**. In addition, a mixture of cotrimerization products was detected.[15] It was probably due to the spatial accessibility of the nickel center complexed with less-hindered NHC to another alkyne. In the presence of *N*-2-naphthyl-substituted NHC **L*4**, no reaction occurred. We examined 2,6-disubstituted (bis-*ortho*) NHC **L*5**, which led to the formation of **3aa** in 23% yield along with inseparable cotrimerization products.[15] *N*-2,6-Diethylphenyl-substituted NHC **L*6** gave **3aa** in good yield, albeit with very poor enantioselectivity (72% yield, 2% ee). *N*-Mesityl-substituted NHC **L*7** also gave **3aa** in 54% yield and 6% ee. Montgomery et al. developed a highly efficient chiral NHC **L*8** for the nickel-catalyzed reductive coupling of aldehydes and alkynes.[12a] Indeed, NHC **L*8** worked effectively in our system to afford **3aa** in high yield with a significant improvement in enantioselectivity (85% yield, 29% ee). An analogous NHC salt, **L*9**·HBF_4, was synthesized by replacing the cyclohexyl groups with the isopropyl units, giving **3aa** in optimal chemical yield with almost the same degree of enantioselectivity (94% yield, 30% ee). *N*-(2,7-Diisopropyl-1-naphthyl)-substituted NHC (**L*10**)[16a] gave **3aa** in good yield with an increase in enantioselectivity (78%, 43% ee).



Scheme 2 Catalytic enantioselective [2+2] cycloaddition: Survey of imidazolinium salts. General reaction conditions: (*R*,*R*)-**L*n**·HBF_4 (0.22 mmol), NaO^{t}Bu (0.02 mmol), Ni(cod)$_2$ (0.02 mmol), **1a** (0.2 mmol), **2a** (0.3 mmol), and C_6D_6 (0.5 mL). Experiments were conducted in an NMR tube equipped with a J. Young valve. Isolated yields are given. The enantiomeric excess (ee) was determined by HPLC using a chiral stationary phase. [a] NMR yield, ee was not determined.

Dorta et al. reported that enantioselectivity and reactivity are attributed from all the atropisomers, generated from the respective orientation of naphthyl wingtips (**L*10**·HBF_4 consists of three atropisomers).[16a] They also reported that 2-cyclooctyl-1-naphthyl-substituted NHC (**L*11**·HBF_4 exists as almost a single atropisomer) was an optimal ligand in the Pd-catalyzed α-arylation of amides.[17] However, it was not appropriate to improve the enantioselectivity of **3aa** (83%, 10% ee). This was probably due to the smaller coordination sphere of the nickel center than that of palladium, which resulted an increase of flexibility of the *N*-2-cyclooctyl-1-naphthyl rings in the nickel/**L*11**-complex. Thus, the *N*-(2,7-dicyclohexyl-1-naphthyl)-substituted NHC precursor **L*12**·HBF_4 was synthesized having cyclohexyl groups (smaller than cyclooctyl but bulkier than isopropyl) at the

2- and 7-positions of the naphthyl wingtips to restrict the flexibility of the naphthyl rings in the nickel–**L*12** complex. The newly synthesized NHC salt **L*12**·HBF_4 also appeared virtually as a single major atropisomer in NMR analyses,[16b,18] and superior enantioselectivity (73%, 43% ee) was obtained using the present system (cf. 10% ee in the case of **L*11**·HBF_4). Although the efficiency of **L*12**·HBF_4 and **L*10**·HBF_4 was almost the same in the case of **3aa**, **L*12**·HBF_4 emerged as a promising NHC precursor in the present nickel-catalyzed reactions. Chiral NHCs of the fused ring system were also examined for their role in restricting the flexible behaviors of *N*-substituents (**L*13** and **L*14**).[19] However, only a trace amount of **3aa** was obtained.[15]

Table 1 Further Optimization with **L*10**·HBF_4 and **L*12**·HBF_4[a]

Entry	L*n	Solvent	Temp (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1	**L*10**	C_6D_6	80	6	78	43
2	**L*10**	C_6D_6	60	30	79	48
3	**L*10**	C_6D_6	40	144	50	50
4	**L*12**	C_6D_6	80	12	73	43
5	**L*12**	C_6D_6	60	25	75	44
6	**L*10**	THF	60	24	63	44
7	**L*10**	dioxane	60	24	72	47
8	**L*10**	toluene	60	24	67	50
9	**L*10**	MeCN	60	24	46	29
10	**L*10**	Et_2O	60	24	50	50
11	**L*10**	DMI	60	24	13	43
12[d]	**L*10**	C_6D_6	60	72	75	48
13[e]	**L*10**	C_6D_6	60	24	73	46

[a] General reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), **L*10**·HBF_4 or **L*12**·HBF_4, (0.22 mmol), NaO^{t}Bu (0.02 mmol), Ni(cod)$_2$ (0.02 mmol). All experiments were conducted in an NMR tube equipped with a J. Young valve in C_6D_6. Isolated yields are given; ee was determined by SFC/HPLC using a chiral stationary phase.
[b] Isolated yields are given.
[c] Enantioselectivities were determined by SFC using a chiral stationary phase.
[d] 5 mol% **L*10**·HBF_4, NaO^{t}Bu, and Ni(cod)$_2$ were employed.
[e] 20 mol% **L*10**·HBF_4, NaO^{t}Bu, and Ni(cod)$_2$ were employed.

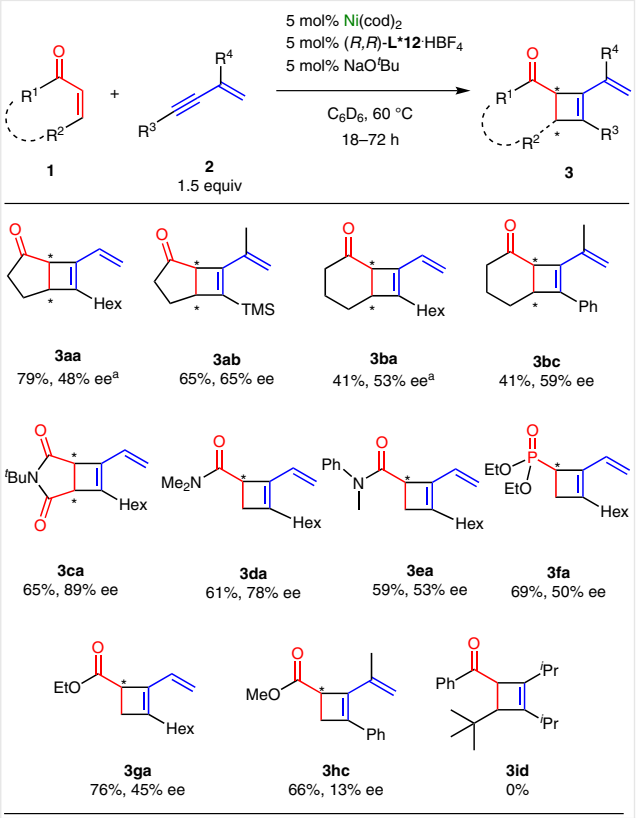
Since the NHCs **L*10** and **L*12** were the most effective ligands, they were subjected to further possible optimization (Table 1). Lowering the temperature to 60 °C was helpful in slightly improving the enantioselectivity (48 and 44% ee with **L*10**·HBF_4 and **L*12**·HBF_4, respectively) without loss in chemical yield (entries 2 and 5). In the case of **L*10**·HBF_4, a further decrease in temperature to 40 °C had no significant influence on the ee (entry 3). Solvent screening with **L*10**·HBF_4 at 60 °C was also not beneficial (entries 6–11). A catalyst loading of 5 mol% gave identical results (entry 12, cf. entry 2). A slight influence on yield and enantioselectivity was observed with a catalyst loading of 20 mol% (entry 13, cf. entries 2 and 12).

An extensive survey of NHC salts and further optimization provided the best results with **L*10**·HBF_4 at 60 °C (entry 12). Since comparable results were obtained with **L*12**·HBF_4 (entry 5), the scope of the substrates was investigated with both ligands, **L*10** and **L*12**.[18] Notably, superior results were obtained with our newly synthesized NHC salts (**L*12**·HBF_4) for most of the substrates (Scheme 3).[18] A bulky alkyne, 3-methyl-1-(trimethylsilyl)but-3-en-1-yne (**2b**), gave the corresponding cyclobutene **3ab** in 65% yield and 65% ee. Cyclohex-2-en-1-one (**1b**) gave the respective bicyclic cyclobutene **3ba** with **2a** in 56% yield and 34% ee. However, superior enantioselectivity was achieved with **L*10**·HBF_4 (41% yield, 53% ee). On the other hand, the reaction of **1b** with sterically hindered enyne **2c** gave **3bc** with a significantly higher enantioselectivity using **L*12**·HBF_4 (41% yield, 59% ee; cf. 14% ee with **L*10**·HBF_4). *N*-*tert*-Butylmaleimide (**3c**) gave the corresponding annulated cyclobutene **3ca** in good enantioselectivity (65% yield, 89% ee). *N*,*N*-Dimethylacrylamide (**1d**) afforded **3da** in good yield and enantioselectivity (61% yield and 78% ee), whereas *N*-methyl-*N*-phenylacrylamide (**1e**) gave **3ea** in 59% yield and 53% ee. The reaction of diethyl vinylphosphonate (**1f**) was also examined with **2a**, which gave a phosphonate containing cyclobutene **3fa** in 69% yield and 50% ee. Remarkably, acrylates **1g** and **1h** also worked well to give the corresponding cyclobutenes **3ga** and **3hc** with **2a** and **2c**, respectively in good chemical yields (**3ga**: 76% and **3hc**: 66%).[20]

Ethyl acrylate (**1g**) reacted with **2a** to give **3ga** with 45% ee, whereas **3hc** was obtained with only 13% ee from the reaction of methyl acrylate (**1h**) with a sterically hindered enyne **2c**. We also examined the catalytic enantioselective [2+2] cycloaddition reaction between an enone with a *tert*-butyl group at the β-position (**1i**) and oct-4-yne (**2d**) or dec-1-en-3-yne(**2a**), but the desired [2+2] cycloaddition product was not obtained.

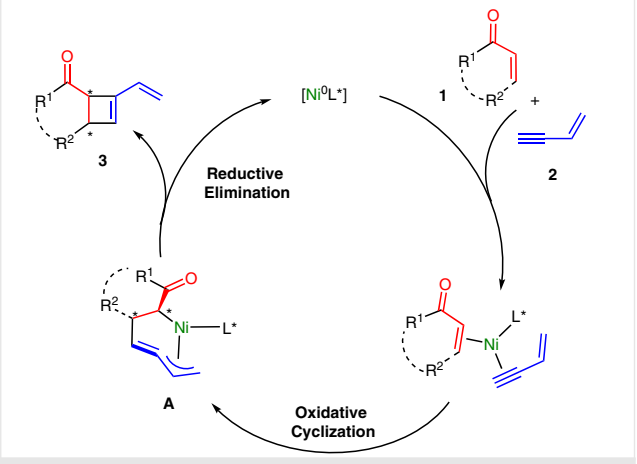
The plausible reaction mechanism depicted in Scheme 4 is based on our previous report.[9a] The simultaneous regioselective coordination of an α,β-unsaturated carbonyl and an 1,3-enyne with a nickel(0)/**L*n** moiety followed by oxidative cyclization gives an enantioenriched η^3-butadienyl intermediate **A**. Subsequent reductive elimination from **A** gives cyclobutene **3** with the generation of one or two stereogenic centers.

In summary, the nickel(0)–NHC-catalyzed enantioselective [2+2]-cycloaddition reaction of α,β-unsaturated carbonyl compounds with 1,3-enynes was studied. A survey of chiral imidazolinium salts suggested that 2,6-disubstitution on the N-aryl group of the NHC was essential for an enantioselective reaction. A wide range of enantioselectivities were obtained for different substrates. However, a newly synthesized chiral NHC **L*12** proved to be the most effective ligand in our study. This also represents the first example of a nickel-catalyzed enantioselective [2+2] cycloaddition reac-



Scheme 3 Nickel(0)-catalyzed cycloaddition of α,β-unsaturated carbonyl and 1,3-enyne. General reaction conditions: **1** (0.4 mmol), **2** (0.6 mmol), **L*12**·HBF_4 (0.02 mmol), NaO^{t}Bu (0.02 mmol), $Ni(cod)_2$ (0.02 mmol). All experiments were conducted in an NMR tube equipped with a J. Young valve in C_6D_6. Isolated yields are given. Enantioselectivities were determined by SFC using a chiral stationary phase. Absolute configuration was not determined. [a] Results are obtained with **L*10**·HBF_4.

tion. The initial study would definitely encourage the pursuit of the most suitable chiral NHCs and reaction conditions, and is presently ongoing in our laboratory.



Scheme 4 A plausible mechanism

All manipulations were conducted under a nitrogen atmosphere using standard Schlenk or dry box techniques. All commercially available reagents were distilled and degassed prior to use. $Ni(cod)_2$ was purified by recrystallization from toluene. All products were characterized by ^{1}H and ^{13}C NMR spectra, which were recorded on a Bruker Avance III AV 400 MHz spectrometer. Chiral NHC salts were synthesized according to reported procedures.[11,12a,16,17,19] Optical rotations were measured in Jasco-DIP 1000 polarimeter with a path length of 1 dm using the Na D line. Enantioselectivities were recorded by means of Jasco-Supercritical Fluid chromatography (SFC), equipped with PU-2080-CO_2 plus CO_2 delivery pump and MD-2018 plus as a photodiode array detector using chiral columns of Diacel Chiralpak (λ = 244–264 nm; temp. = 25 °C; back pressure = 15 MPa).

Ni-Catalyzed Enantioselective [2+2] Cycloaddition of α,β-Unsaturated Carbonyl and 1,3-Enyne; General Procedure

To a vial in a glove box was added chiral NHC salt **L*n**·HBF_4 (0.020 mmol, 5 mol%), NaO^{t}Bu (0.020 mmol, 5 mol%), and C_6D_6 (0.5 mL). This suspension was stirred at r.t. for 10 min. $Ni(cod)_2$ (0.020 mmol, 5 mol%) was added and the suspension was further stirred at r.t. for 5–10 min. Finally, to the solution was added enone **1** (0.4 mmol) followed by enyne **2** (0.4–0.6 mmol, 1.2–1.5 equiv). The mixture was transferred to a J. Young tube, and heated at 60 °C until complete reaction of the α,β-unsaturated carbonyl compounds, as monitored by ^{1}H NMR (18–72 h). The resultant mixture was cooled to r.t., filtered directly through a short plug of silica gel and washed with EtOAc. Volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 5% to 35% EtOAc–hexanes). All cyclobutenes were obtained as single diastereomers and regioisomers. Enantioselectivities were determined via SFC using a chiral stationary phase.

(1*R**,5*S**)-6-Hexyl-7-vinylbicyclo[3.2.0]hept-6-en-2-one (3aa)[9a]

Following the general procedure, cyclopent-2-en-1-one (**1a**, 32.8 mg, 0.40 mmol), dec-1-en-3-yne (**2a**, 81.8 mg, 0.60 mmol), $Ni(cod)_2$ (5.3 mg, 0.020 mmol), chiral NHC precursor **L*10**·HBF_4 (14.3 mg, 0.020 mmol), and NaO^{t}Bu (1.7 mg, 0.018 mmol) were heated at 60 °C for 72 h. Purification by column chromatography (EtOAc/hexane, 5:95) gave **3aa** (65.8 mg, 0.30 mmol, 75%; 48% ee) as a pale yellow oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IC, CO_2: 3.0 mL/min, CH_2Cl_2: 0.3 mL/min): t_R = 7.0 (minor), 7.9 min (major).

$[\alpha]_D^{24}$ +84.53 (*c* 0.10, $CHCl_3$).

(1*R**,5*S**)-7-(Prop-1-en-2-yl)-6-(trimethylsilyl)bicyclo[3.2.0]hept-6-en-2-one (3ab)[9a]

Following the general procedure, cyclopent-2-en-1-one (**1a**, 32.0 mg, 0.39 mmol), 3-methyl-1-(trimethylsilyl)but-3-en-1-yne (**1b**, 86.9 mg, 0.63 mmol), $Ni(cod)_2$ (5.5 mg, 0.02 mmol), chiral NHC precursor **L*12**·HBF_4 (18.4 mg, 0.021 mmol), and NaO^{t}Bu (2.0 mg, 0.021 mmol) were heated at 60 °C for 72 h. Purification by column chromatography (hexane/EtOAc, 95:5) gave **3ab** (57.0 mg, 0.26 mmol, 65%; 65% ee) as a pale yellow oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IC, CO_2: 3.0 mL/min, CH_2Cl_2: 0.3 mL/min): t_R = 4.8 (major), 5.8 min (minor).

$[\alpha]_D^{24}$ +131.76 (*c* 0.10, $CHCl_3$).

(1*R,6*S**)-7-Hexyl-8-vinylbicyclo[4.2.0]oct-7-en-2-one (3ba)**[9a]

Following the general procedure, cyclohex-2-en-1-one (**1b**, 38.4 mg, 0.40 mmol), dec-1-en-3-yne (**2a**, 81.5 mg, 0.60 mmol), Ni(cod)$_2$ (5.6 mg, 0.02 mmol), chiral NHC precursor **L*10**·HBF$_4$ (14.2 mg, 0.019 mmol), and NaO^{t}Bu (1.9 mg, 0.02 mmol) were heated at 60 °C for 48 h. Purification by column chromatography (EtOAc/hexane, 5:95) gave **3ba** (38.0 mg, 0.16 mmol, 41%; 53% ee) as a pale yellow oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IA, CO_2: 4.0 mL/min, CH_2Cl_2: 0.3 mL/min): t_R = 2.6 (minor), 3.3 min (major).

$[\alpha]_D^{24}$ –61.60 (*c* 0.23, $CHCl_3$).

(1*R,6*S**)-7-Phenyl-8-(prop-1-en-2-yl)bicyclo[4.2.0]oct-7-en-2-one (3bc)**[9a]

Following the general procedure, cyclohex-2-en-1-one (**1b**, 38.2 mg, 0.4 mmol), 3-methyl-1-phenylbut-3-en-1-yne (**2c**, 68.2 mg, 0.48 mmol), Ni(cod)$_2$ (5.5 mg, 0.02 mmol), chiral NHC precursor **L*12**·HBF$_4$ (17.0 mg, 0.019 mmol), and NaO^{t}Bu (2.0 mg, 0.02 mmol) were heated at 60 °C for 72 h. Purification by column chromatography (EtOAc/hexane, 5:95) gave **3bc** (39.0 mg, 0.16 mmol, 41%; 59% ee) as a pale yellow oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IA, CO_2: 4.0 mL/min, CH_2Cl_2: 0.3 mL/min): t_R = 4.8 (major), 6.4 min (minor).

$[\alpha]_D^{24}$ +116.63 (*c* 0.10, $CHCl_3$).

(1*R,5*S**)-3-*tert*-Butyl-6-hexyl-7-vinyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ca)**[9a]

Following the general procedure, *N*-*tert*-butylmaleimide (**1c**, 60.1 mg, 0.39 mmol), dec-1-en-3-yne (**2a**, 83.6 mg, 0.61 mmol), Ni(cod)$_2$ (5.6 mg, 0.02 mmol), chiral NHC precursor **L*12**·HBF$_4$ (17.5 mg, 0.02 mmol), and NaO^{t}Bu (2.0 mg, 0.02 mmol) were heated at 60 °C for 36 h. Purification by column chromatography (hexane/EtOAc, 95:5) gave **3ca** (75.5 mg, 0.26 mmol, 65%; 89% ee) as a pale yellow oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IA, CO_2: 3.0 mL/min, *i*-PrOH: 0.1 mL/min): t_R = 2.1 (major), 2.3 min (minor).

$[\alpha]_D^{24}$ +105.82 (*c* 0.33, $CHCl_3$).

3-Hexyl-*N*,*N*-dimethyl-2-vinylcyclobut-2-ene-1-carboxamide (3da)[9a]

Following the general procedure, *N*,*N*-dimethylacrylamide (**1d**, 38.2 mg, 0.39 mmol), dec-1-en-3-yne (**2a**, 86.8 mg, 0.64 mmol), Ni(cod)$_2$ (5.5 mg, 0.02 mmol), chiral NHC precursor **L*12**·HBF$_4$ (17.2 mg, 0.021 mmol), and NaO^{t}Bu (2.0 mg, 0.02 mmol) were heated at 60 °C for 18 h. Purification by column chromatography (EtOAc/hexane, 30:70) gave **3da** (56.1 mg, 0.24 mmol, 61%; 78% ee) as a colorless oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IC, CO_2: 2.4 mL/min, *i*-PrOH: 0.6 mL/min): t_R = 6.7 (major), 7.2 min (minor).

$[\alpha]_D^{24}$ +81.31 (*c* 0.12, $CHCl_3$).

3-Hexyl-*N*-methyl-*N*-phenyl-2-vinylcyclobut-2-ene-1-carboxamide (3ea)

Following the general procedure, *N*-methyl-*N*-phenylacrylamide (**1e**, 64.2 mg, 0.40 mmol), dec-1-en-3-yne (**2a**, 86.0 mg, 0.63 mmol), Ni(cod)$_2$ (5.4 mg, 0.02 mmol), chiral NHC precursor **L*12**·HBF$_4$ (19.1 mg, 0.021 mmol), and NaO^{t}Bu (2.0 mg, 0.02 mmol) were heated at 60 °C for 24 h. Purification by column chromatography [R_f = 0.4 (EtOAc/hexane, 20:80)] gave **3ea** (70.1 mg, 0.24 mmol, 59%; 53% ee) as a colorless oil.

SFC (Daicel Chiralpak IA, CO_2: 2.4 mL/min, *i*-PrOH: 0.6 mL/min): t_R = 5.2 (major), 7.1 min (minor).

$[\alpha]_D^{24}$ + 19.0 (*c* 0.26, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (t, *J* = 7.5 Hz, 2 H, *m*-*H*-Ph), 7.33 (t, *J* = 7.5 Hz, 1 H, *p*-*H*-Ph), 7.19 (d, *J* = 7.5 Hz, 2 H, *o*-*H*-Ph), 6.36 (dd, *J* = 10.6, 17.3 Hz, 1 H, -C*H*=CH$_2$), 4.98 (d, *J* = 10.6 Hz, 1 H, CH=C*H*$_2$), 4.89 (d, *J* = 17.3 Hz, 1 H, -CH=C*H*$_2$), 3.43 (br s, 1 H, COC*H*), 3.30 (s, 3 H, NC*H*$_3$), 2.28 (d, *J* = 13.4 Hz, 1 H, CHC*H*$_2$CH), 2.26 (d, *J* = 13.4 Hz, 1 H, CHC*H*$_2$CH), 2.13 (t, *J* = 7.2 Hz, 2 H, CHC*H*$_2$CH$_2$), 1.42–1.24 (m, 8 H), 0.85 (t, *J* = 6.8 Hz, 3 H, CH$_2$C*H*$_3$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 173.0, 145.9, 144.1, 137.5, 129.6, 128.1, 127.5, 127.1, 113.0, 39.6, 37.3, 33.8, 31.6, 29.1, 28.7, 26.9, 22.5, 14.0.

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{20}H_{27}NO$: 297.2093; found: 297.2090.

Diethyl 3-Hexyl-2-vinylcyclobut-2-en-1-ylphosphonate (3fa)

Following the general procedure, diethyl vinylphosphonate (**1f**, 64.7 mg, 0.39 mmol), dec-1-en-3-yne (**2a**, 80.6 mg, 0.59 mmol), Ni(cod)$_2$ (5.6 mg, 0.020 mmol), chiral NHC precursor **L*12**·HBF$_4$ (17.8 mg, 0.02 mmol), and NaO^{t}Bu (1.8 mg, 0.019 mmol) were heated at 60 °C for 24 h. Purification by column chromatography [R_f = 0.3 (EtOAc/hexane, 35:65)] gave **3fa** (81.0 mg, 0.27 mmol, 69%; 50% ee) as a pale yellow oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IE, CO_2: 2.4 mL/min, *i*-PrOH: 0.3 mL/min): t_R = 5.4 (major), 6.0 min (minor).

$[\alpha]_D^{24}$ + 27.76 (*c* 0.45, $CHCl_3$).

Ethyl 3-Hexyl-2-vinylcyclobut-2-enecarboxylate (3ga)

Following the general procedure, ethyl acrylate (**1g**, 41.2 mg, 0.42 mmol), dec-1-en-3-yne (**2a**, 67.9 mg, 0.5 mmol), Ni(cod)$_2$ (6.2 mg, 0.023 mmol), chiral NHC precursor **L*12**·HBF$_4$ (18.3 mg, 0.021 mmol), and NaO^{t}Bu (2.0 mg, 0.02 mmol) were heated at 60 °C for 24 h. Purification by column chromatography (EtOAc/hexane, 5:95) gave **3ga** (75.6 mg, 0.32 mmol, 76%; 45% ee) as a colorless oil. Spectroscopic data were identical to that previously reported.[9a]

SFC (Daicel Chiralpak IE, CO_2: 3.5 mL/min, CH_2Cl_2: 0.1 mL/min): t_R = 6.3 (major), 6.9 min (minor).

$[\alpha]_D^{24}$ –4.93 (*c* 0.13, $CHCl_3$).

Methyl 3-Phenyl-2-(prop-1-en-2-yl)cyclobut-2-ene-1-carboxylate (3hc)

Following the general procedure, methyl acrylate (**1h**, 35.0 mg, 0.41 mmol), 3-methyl-1-phenylbut-3-en-1-yne (**2c**, 68.2 mg, 0.48 mmol), Ni(cod)$_2$ (5.5 mg, 0.020 mmol), chiral NHC precursor **L*12**·HBF$_4$ (19.6 mg, 0.022 mmol), and NaO^{t}Bu (2.0 mg, 0.02 mmol) were heated at 60 °C for 24 h. Purification by column chromatography [R_f = 0.4 (EtOAc/hexane, 5:95)] gave **3hc** (62.0 mg, 0.27 mmol, 66%; 13% ee) as a colorless oil.

SFC (Daicel Chiralpak IA, CO_2: 4.0 mL/min, CH_2Cl_2: 0.3 mL/min): t_R = 2.2 (minor), 2.7 min (major).

$[\alpha]_D^{24}$ +8.40 (*c* 0.38, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 7.6 Hz, 2 H, Ar-*H*), 7.31 (t, *J* = 7.6 Hz, 2 H, Ar-*H*), 7.23 (m, 1 H, Ar-*H*), 5.11 [s, 1 H, C*H*=C(CH$_3$)], 4.99 [s, 1 H, C*H*=C(CH$_3$)], 3.68–3.70 (m, 4 H, OC*H*$_3$, CH$_2$C*H*), 2.82 (br s, 2 H, C*H*$_2$CH), 1.89 (s, 3 H, C*H*$_3$).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 174.1, 140.8, 138.7, 138.5, 135.2, 128.1, 127.8, 127.3, 115.1, 51.7, 41.9, 30.9, 20.8.

HRMS (EI): *m/z* (M^+) calcd for $C_{15}H_{16}O_2$: 228.1150; found: 228.1146.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561669.

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