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Diels–Alder reactions of acyclic α-cyano α,β-alkenones: a new approach to highly substituted cyclohexene system

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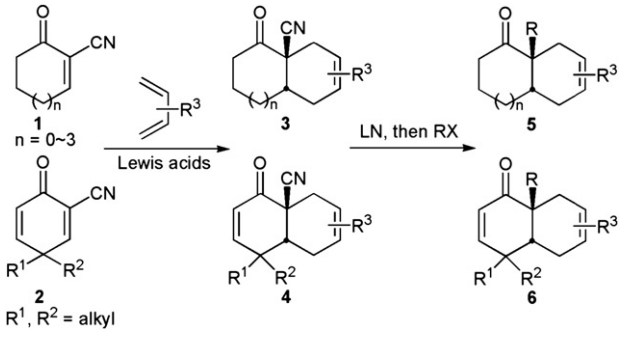
ABSTRACT

The Diels–Alder reactions of a variety of acyclic α-cyano α,β-unsaturated ketones **8** have been investigated. With the assistance of boron trichloride, these compounds were found to undergo the cycloaddition readily with dienes to give the corresponding adducts **9** in good to high yields. In addition, some of **9** could be further subjected to the reductive alkylation reactions using lithium naphthalenide (LN) and an appropriate alkylating agent, thus allowing for the generation of highly substituted cyclohexenes **10** with the replacement of the cyano group with an alkyl substituent.

1. Introduction

The Diels–Alder cycloaddition of α,β-unsaturated ketones with dienes is a very useful method for forming substituted cyclohexenes.[1,2] For these substrates, it is well known that their reactivity toward electron-rich dienes could be enhanced with the aid of an α electron-withdrawing activating group. Predictably, the synthetic utility of the Diels–Alder reactions will be expanded if those activating groups are amendable to further elaboration after the cycloadditions. In our long-term research efforts directed to the Diels–Alder chemistry, we have recently developed an efficient and versatile synthetic route leading to the fused bicyclic ring systems bearing an angular alkyl group based on the Diels–Alder reactions of 2-cyano 2-cycloalkenones **1** and 2-cyano-2,5-cyclohexa-dienones **2**. It was found that with the activation by a nitrile functionality, the cycloadditions of **1** and **2** with various dienes took place smoothly in a highly regio- and/or stereoselective manner to produce bicycles **3** and **4** possessing up to four stereogenic centers (Scheme 1).[3,4] Moreover, the angular cyano group of the resulting adducts could be reductively cleaved by using lithium naphthalenide (LN) as a reducing reagent, and subsequently, the in situ generated enolates were able to be trapped with an alkylating agent (RX), thereafter tactically allowing for the installation of an alkyl group to the ring junction position in providing **5** and **6**. The combination of cycloaddition with reductive alkylation had therefore practically turned **1** and **2** into the synthetic equivalents of their 2-alkyl substituted counterparts, which always show to be less reactive in Diels–Alder reactions. So far, we have successfully applied this strategy into the total syntheses of a few clerodane diterpenoid natural products.[5,6]



Scheme 1. Diels–Alder reactions of **1** and **2** and reductive alkylation of the resulting adducts.

Following the studies of **1** and **2**, we were continuously interested in applying the strategy to their acyclic analogs for preparing substituted mono cyclohexenes. Herein we wish to report

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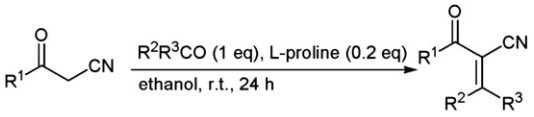
our findings on the Diels–Alder reactions of acyclic α-cyano α,β-unsaturated ketones as well as the reductive alkylation reactions of the resulting adducts. Although there are numerous examples reported on the Diels–Alder reactions of acyclic α,β-unsaturated ketones bearing an α activating substituent, such as ester,[7] chloro,[8] sulfonyl,[9] bromo,[10] or fluoro[11] functional groups, to our knowledge, the detailed studies on the acyclic α-cyano α,β-unsaturated ketones have never been reported before.

2. Results and discussion

The α-cyano α,β-unsaturated ketones used for the current studies were easily prepared by the Knoevenagel condensation between aldehydes or ketones and β-ketonitriles **7a**–**e**, which were either commercially available (**7d** and **7e**) or synthesized by the base-mediated acylation of acetonitrile with the corresponding esters (**7a**–**c**).[12] As shown in Scheme 2, the condensation reactions were all carried out in alcoholic solution under the catalysis of L-proline for 24 h, to yield **8a**–**h** in high yields (82–99%).[13] For those reactions with aldehydes, only the single *E*-isomers were produced (**8a**–**d**, **8f**, and **8h**) and their stereogeometries were confirmed either by NOE experiments (**8a**–**c**, **8f**) or by X-ray analysis (**8d** and **8h**). We thus obtained the dienophilic substrates with considerable structural diversity and used them for the following study.



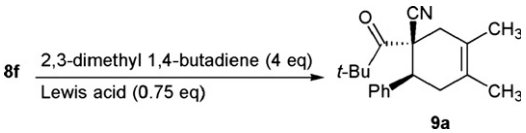
7a (R^1 = methyl)
7b (R^1 = ethyl)
7c (R^1 = cyclopropyl)
7d (R^1 = *t*-butyl)
7e (R^1 = phenyl)

8a (R^1 = methyl, R^2 = H, R^3 = phenyl, 90%)
8b (R^1 = ethyl, R^2 = H, R^3 = phenyl, 98%)
8c (R^1 = ethyl, R^2 = H, R^3 = 2-furyl, 86%)
8d (R^1 = cyclopropyl, R^2 = H, R^3 = 2-naphthyl, 95%)
8e (R^1 = cyclopropyl, R^2 = R^3 = methyl, 90%)
8f (R^1 = *t*-butyl, R^2 = H, R^3 = phenyl, 99%)
8g (R^1 = *t*-butyl, R^2 = R^3 = cyclohexyl, 82%)
8h (R^1 = phenyl, R^2 = H, R^3 = 2-furyl, 95%)

Scheme 2. Preparation of α-cyano α,β-unsaturated ketones.

Our previous studies on **1** and **2** revealed that their Diels–Alder reactivity as well as the regio- and/or stereoselectivity of the reactions could be greatly enhanced by the assistance of the Lewis acid.[3,4] Therefore, in the current investigation, several Lewis acids traditionally used for the activation of dienophiles were initially screened by the reaction of **8f** with 2,3-dimethyl-1,3-butadien (Table 1). It was found that with the use of titanium (IV) chloride ($TiCl_4$), the desired cycloaddition did not occur in CH_2Cl_2 at 0 °C or under refluxing conditions (Table 1, entries 1 and 2). Still with $TiCl_4$, the adduct **9a** was formed in 50% yield only when the reaction was carried out in refluxing benzene (entry 3). Similarly, the use of tin

Table 1
Optimization of Lewis acid-mediated reaction conditions

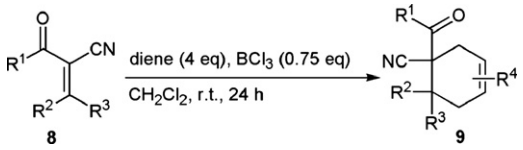


9a

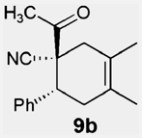
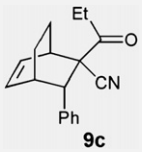
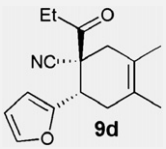
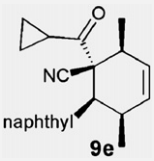
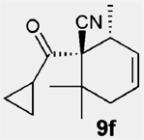
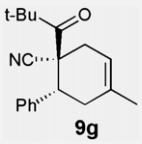
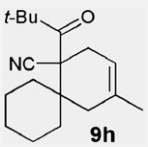
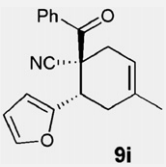
Entry	Reaction conditions	Time (h)	Yield[a] (%)
1	$TiCl_4/CH_2Cl_2$/0 °C	56	—
2	$TiCl_4/CH_2Cl_2$/reflux	56	—
3	$TiCl_4$/benzene/reflux	48	50
4	$SnCl_4/CH_2Cl_2$/reflux	56	—
5	$SnCl_4$/benzene/reflux	48	65
6	$ZnCl_2$/benzene/reflux	48	68
7	$BF_3{\cdot}OEt_2/CH_2Cl_2$/25 °C	36	78
8	BCl_3/CH_2Cl_2/25 °C	24	80
9	BCl_3/benzene/25 °C	24	81

[a] Isolated yield.

Table 2
BCl_3-mediated Diels–Alder reactions of **8** with dienes



8 **9**

Entry	Substrate	Diene	Adduct	Yield (%)[a]
1[d]	**8a**		 **9b**	75
2	**8b**		 **9c**	86
3	**8c**		 **9d**	82
4[b]	**8d**		 **9e**	62
5[b,c]	**8e**		 **9f**	64
6[d]	**8f**		 **9g**	68
7[c]	**8g**		 **9h**	65
8[d]	**8h**		 **9i**	88

[a] Yield refers to purified product.
[b] Only single diastereoisomer was formed.
[c] The regiochemistry (*ortho*-like for **9f** and *para*-like for **9h**) was determined by ^1H–^1H COSY experiment.
[d] The structure was confirmed by X-ray analysis.

(IV) chloride ($SnCl_4$) gave no detectable formation of the product in CH_2Cl_2 (entry 4) and 65% of **9a** in refluxing benzene (entry 5). It was also noted that in refluxing benzene, zinc chloride ($ZnCl_2$) displayed a comparable capability in promoting the reaction as $TiCl_4$ and $SnCl_4$ to afford **9a** in 68% yield (entry 6). We further discovered that the use of boron-containing Lewis acids, i.e., boron trifluoride etherate ($BF_3{\cdot}OEt_2$) and boron trichloride (BCl_3) in CH_2Cl_2 could result in the formation of **9a** in much higher yields under the relatively milder reaction conditions (entries 7 and 8) and moreover, BCl_3 appeared to be even better than $BF_3{\cdot}OEt_2$ in term of permitting a shorter time for the reaction to attain the completion. With BCl_3, we also observed that the replacement of CH_2Cl_2 with benzene almost caused no improvement on the yield of **9a** (entry 9). Considering the higher toxicity of benzene than CH_2Cl_2, we therefore applied the reaction conditions indicated in entry 8 to the substrates **8a**–**h** (Table 2).

Under the standard reaction conditions (Table 1, entry 8), the cyclization reactions of **8a**–**h** with a range of dienes including 2,3-dimethyl-1,3-butadiene (Table 2, entries 1 and 3), cyclohexa-1,3-diene (entry 2), 2,4-hexadiene (entry 4), *trans*-1,3-pentadiene (entry 5) or isoprene (entries 6–8) occurred smoothly in giving the formation of the corresponding adducts **9b**–**i** in good to high yields (62–88%). From the results in Table 2, it seems to be difficult to reach the formidable conclusion on the correlation between the β substitution of **8** and their reactivity. Even though, the results in entries 1 and 3 (2,3-dimethyl-1,3-butadiene) as well as entries 6–8 (isoprene) may imply that the 2-furyl group is more effective than phenyl and cyclohexyl groups at strengthening the reactivity of the dienophile. Besides, the generation of the single diastereomers **9e** and **9f** in entries 4 and 5 suggests that the cycloadditions should proceed in a stereo-controlled fashion. The NOE experiments of **9e** confirmed that it was produced in an *endo*-to-keto route as evidenced by the correlations between the methine protons at the C-2, C-5, and C-6 positions (Fig. 1). Based on this and previous experiences,[3,4] we envisioned that adduct **9f** should also be produced in the same *endo* transition state, albeit its NOE and NOESY spectra failed to show any diagnostic signals. It is also worthy to note that the cycloaddition reactions strictly followed the *para*- or *ortho*-like rule as indicated by the exclusive formation of **9f**–**i** as the single regioisomers. In this manner, we were thus able to achieve a series of cyclohexene derivatives with high functionalities.

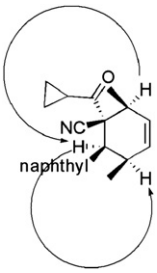
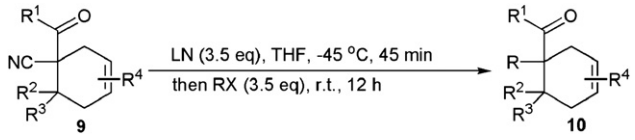
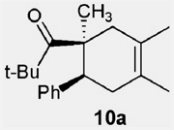
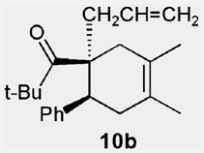
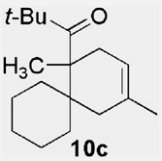
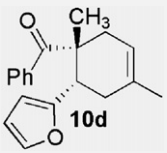


Figure 1. NOE correlations of **9e**.

After completing the investigation on the Diels–Alder reactions, we further surveyed the possibility of applying the resulting adducts into the reductive alkylation process according to the established protocol.[3,4] It was found that the subjection of **9b**–**f** to the reduction alkylation conditions with lithium naphthalenide (LN)[14] and methyl iodide gave no desired methylated products but only complex mixtures, whereas **9a**, **9h**, and **9i** could undergo the reductive methylation and allylation reactions easily. As shown in Table 3, treatment of **9a**, **9h** and **9i** with LN in THF at −45 °C for 45 min followed by the addition of methyl iodide or allyl bromide to the reaction mixtures led to the generation of alkylated products **10a**–**d** in fairly good yields (68–88%).

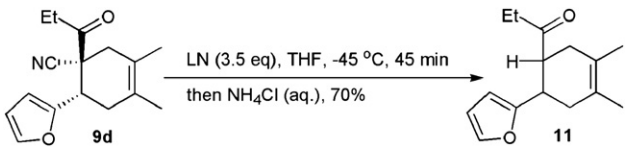
Table 3
LN-Induced reductive alkylation reactions of **9a**, **9h**, and **9i**



Entry	Substrate	Product	Yield[a] (%)
1[b]	**9a**	 **10a**	80
2[b]	**9a**	 **10b**	72
3	**9h**	 **10c**	68
4[c]	**9i**	 **10d**	88

[a] Yield refers to purified product.
[b] Only single diastereoisomer was formed. The stereochemistry was determined by NOE experiments.
[c] The structure was confirmed by X-ray analysis.

While compounds **9b**–**f** failed for the reductive methylation, the reductive decyanation of **9d** could occur upon the sequential treatment with LN and an aqueous ammonium chloride solution, to give compound **11**[15] in 70% yield (Scheme 3). We thus speculated that interference of α acidic proton(s) of the carbonyl group to the initially formed enolate intermediates might account for the failure of **9b**–**f**. To prove this, we further performed a deuterium incorporation experiment with **9b** by treating it with LN (−45 °C, 45 min) and then D_2O. However, the reaction only produced a complex mixture and the ^{13}C NMR spectra of the major component did not display any carbonyl carbon signal, implying that the carbonyl group might be reduced. Currently, the exploration for the true reason is still underway in our group.



Scheme 3. Reductive decyanation of **9d**.

3. Conclusion

In conclusion, we have demonstrated that with the assistance of BCl_3, **8** could undergo the Diels–Alder reactions easily with the electron-rich dienes to provide the adducts with wide structural diversity in good yields. Besides, the high regio- and/or stereoselectivity were observed for these reactions. In regards of these, as

well as the convenient access to the starting materials and the great potential in the elaboration of cyano and keto functionalities, it is reasonable to believe that this protocol will be of considerable use in synthetic chemistry. In addition, we have further proved that the cyano group of the products with *t*-butyl and phenyl keto moieties could be replaced by an alkyl group through a simple reductive alkylation operation, to result in the generation of a few compounds, which are otherwise difficult to be achieved. Currently, the application of this method into the syntheses of more complex molecules is being explored by us.

4. Experimental

4.1. General

All of starting materials were obtained from commercial suppliers and used without further purification. Diels–Alder and reductive alkylation reactions were all performed under an atmosphere of argon. Tetrahydrofuran was distilled from sodium–benzophenone, and dichloromethane and benzene were distilled from calcium hydride before use. TLC analysis was performed on Merck 25 DC-Alufolien Kieselgel 60F_{254} aluminum-backed plates and visualized by UV or permanganate treatment. All of the compounds were purified by flash chromatography on Merck Art.9385 Kieselgel 60 silica gel (230–400 mesh). NMR spectra (^{1}H, ^{13}C, DEPT, COSY) were recorded on a Varian Unity 400 or a Bruker DMX-600 spectrometer using deuterio-chloroform ($CDCl_3$) as solvent. High-resolution mass spectra (HRMS) were determined by using a JEOL JMS-HX110 high-resolution mass spectrometer in an electron impact (EI, 70 eV) mode. The X-ray analyses were carried out on a Bruker SMART APEX instrument.

4.2. General procedure for Knoevenagel condensation for the preparation of 8

*4.2.1. (E)-2-Benzylidene-3-oxobutanenitrile (**8a**).* To a solution of 3-oxobutanenitrile (1.96 g, 23.56 mmol, 1.0 equiv) in 30 mL of absolute ethanol, L-proline (0.54 g, 4.71 mmol, 0.2 equiv) and benzaldehyde (2.5 g, 23.56 mmol, 1.0 equiv) were successively added. The resulting reaction mixture was stirred at room temperature for 24 h and then concentrated in vacuo. The crude residue was subjected to chromatographic purification on silica gel (hexane–EtOAc 9.5:0.5) to give 3.63 g of **8a** as a white solid (90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (s, 1H), 7.99 (d, J=8.0 Hz, 2H), 7.57–7.47 (m, 3H), 2.56 (d, J=1.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.9 (CO), 152.7 (CH), 133.1 (CH), 131.1 (C), 130.9 (CH), 128.9 (CH), 116.7 (CN), 109.6 (C), 27.3 (CH_3); IR (neat): 2925, 2854, 2218, 1777, 1382, 1598 cm^{-1}; HRMS (EI) calcd for $C_{11}H_9NO$: 171.0684; found: 171.0678.

*4.2.2. (E)-2-Benzylidene-3-oxopentanenitrile (**8b**).* The typical procedure for the preparation of **8a** was followed using 3-oxopentanenitrile (2.29 g, 23.56 mmol, 1.0 equiv), L-proline (0.54 g, 4.71 mmol, 0.2 equiv), and benzaldehyde (2.5 g, 23.56 mmol, 1.0 equiv). Flash chromatography on silica gel (hexane–EtOAc 8:2) gave **8b** as a white solid (4.27 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.99 (d, J=7.6 Hz, 2H), 7.55–7.24 (m, 3H), 2.96 (q, J=7.2 Hz, 2H), 1.22 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.8 (CO), 152.7 (CH), 133.2 (CH), 131.5 (C), 131.2 (CH), 129.2 (CH), 117.1 (CN), 109.1 (C), 33.8 (CH_2), 7.7 (CH_3); IR (neat): 3060, 2982, 2224, 1682, 1601, 1571, 1450 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{11}NO$: 185.0841; found: 185.0839.

*4.2.3. (E)-2-(Furan-2-ylmethylene)-3-oxopentanenitrile (**8c**).* The typical procedure for the preparation of **8a** was followed using 3-oxopentanenitrile (2.52 g, 26.02 mmol, 1.0 equiv), L-proline (0.60 g, 5.20 mmol, 0.2 equiv), and 2-furfural (2.5 g, 26.02 mmol, 1.0 equiv). Flash chromatography on silica gel (hexane–EtOAc 8:2) gave **8c** as a yellow solid (3.92 g, 86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J=2.4 Hz, 1H), 7.74 (d, J=2.0 Hz, 1H), 7.94 (d, J=3.2 Hz, 1H), 6.65 (dd, J=3.6, 3.6 Hz, 1H), 2.91 (q, J=7.2 Hz, 2H), 1.18 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6 (CO), 148.9 (C), 148.3 (CH), 136.8 (CH), 122.3 (CH), 116.9 (CN), 113.9 (CH), 104.7 (C), 33.6 (CH_2), 7.6(CH_3); IR (neat): 3133, 3037, 2978, 2212, 1695, 1608, 1534, 1167 cm^{-1}; HRMS (EI) calcd for $C_{10}H_9NO_2$: 175.0633; found: 175.0633.

*4.2.4. (E)-2-(Cyclopropanecarbonyl)-3-(naphthalen-2-yl)-acrylonitrile (**8d**).* The typical procedure for the preparation of **8a** was followed using 3-cyclopropyl-3-oxopropanenitrile (1.75 g, 16.00 mmol, 1.0 equiv), L-proline (0.37 g, 3.20 mmol, 0.2 equiv), and 2-naphthal (2.5 g, 16.00 mmol, 1.0 equiv). Flash chromatography on silica gel (hexane–EtOAc 9.5:0.5) gave **8d** as a yellow crystal (3.76 g, 95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 8.30 (s, 1H), 8.20 (d, J=8.8 Hz, 1H), 7.94–7.85 (m, 3H), 7.63–7.53 (m, 2H), 2.76–2.69 (m, 1H), 1.30–1.10 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.4 (CO), 152.2 (CH), 135.2 (C), 134.4 (CH), 132.6 (C), 129.2 (CH), 129.0 (CH), 128.9 (CH), 127.7 (CH), 127.0 (CH), 125.1 (CH), 117.8 (CN), 109.3 (C), 18.5 (CH), 13.2 (CH_2), 13.2 (CH_2); IR (neat): 3057, 3010, 2212, 1678, 1578, 1384, 1146 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{13}NO$: 247.0997; found: 247.1002.

*4.2.5. 2-(Cyclopropanecarbonyl)-3-methylbut-2-enenitrile (**8e**).* The typical procedure for the preparation of **8a** was followed using 3-cyclopropyl-3-oxopropanenitrile (2.0 g, 18.33 mmol, 1.0 equiv), L-proline (0.42 g, 3.67 mmol, 0.2 equiv), and acetone (1.35 mL, 18.4 mmol, 1.0 equiv). Flash chromatography on silica gel (hexane–EtOAc 9:1) gave **8e** as a yellow oil (2.46 g, 90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47–2.44 (m, 1H), 2.25 (s, 3H), 2.24 (s, 3H), 1.07–0.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9 (CO), 170.7 (C), 117.3 (CN), 112.3 (C), 27.1 (CH_3), 22.9 (CH_3), 20.2 (CH), 12.4 (CH_2); IR (KBr): 3012, 2214, 1685, 1586, 1384, 1164 cm^{-1}; HRMS (EI) calcd for $C_9H_{11}NO$: 149.0841; found: 149.0849.

*4.2.6. (E)-2-Benzylidene-4,4-dimethyl-3-oxopentanenitrile (**8f**).* The typical procedure for the preparation of **8a** was followed using 4,4-dimethyl-3-oxopentanenitrile (2.95 g, 23.56 mmol, 1.0 equiv), L-proline (0.54 g, 4.71 mmol, 0.2 equiv), and benzaldehyde (2.5 g, 23.56 mmol, 1.0 equiv) Flash chromatography on silica gel (hexane–EtOAc 9:1) gave **8f** as a white solid (4.97 g, 99%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.96–7.93 (m, 2H), 7.50–7.41 (m, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9 (CO), 156.0 (CH), 132.8 (CH), 131.9 (C), 131.0 (CH), 129.0 (CH), 118.1 (CN), 107.2 (C), 44.5 (C), 26.3 (CH_3); IR (neat): 2973, 2232, 1704, 1583, 1456 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1161.

*4.2.7. 2-Cyclohexylidene-4,4-dimethyl-3-oxopentanenitrile (**8g**).* The typical procedure for the preparation of **8a** was followed using 4,4-dimethyl-3-oxopentanenitrile (1.96 g, 19.97 mmol, 1.0 equiv), L-proline (0.46 g, 3.99 mmol, 0.2 equiv), and cyclohexanone (2.5 g, 19.97 mmol, 1.0 equiv). Flash chromatography on silica gel (hexane–EtOAc 9.5:0.5) gave **8g** as a colorless oil (3.36 g, 82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.56 (t, J=6.2 Hz, 2H), 2.27 (t, J=5.8 Hz, 2H), 1.76–1.61 (m, 6H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.1 (CO), 170.3 (C), 115.7 (CN), 107.8 (C), 45.3 (C), 34.8 (CH_2), 32.3 (CH_2), 28.1 (CH_2), 27.9 (CH_2), 26.7 (CH_3), 25.4 (CH_2); IR (neat): 2938, 2862, 2212, 1697, 1609, 1478, 1450 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{19}NO$: 205.1467; found: 205.1465.

*4.2.8. (E)-2-Benzoyl-3-(furan-2-yl)acrylonitrile (**8h**).* The typical procedure for the preparation of **8a** was followed using 3-oxo-3-

phenylpropanenitrile (3.78 g, 26.02 mmol, 1.0 equiv), L-proline (0.60 g, 5.20 mmol, 0.2 equiv), and 2-furfural (2.5 g, 26.02 mmol, 1.0 equiv). Flash chromatography on silica gel (hexane–EtOAc 7:3) gave **8h** as a yellow crystal (5.52 g, 95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.84–7.82 (m, 2H), 7.42 (d, J=1.6 Hz, 1H), 7.60–7.55 (m, 1H), 7.48–7.45 (m, 3H), 6.66–6.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.2 (CO), 148.9 (C), 148.5 (CH), 140.2 (CH), 135.9 (C), 133.1 (CH), 128.9 (CH), 128.5 (CH), 122.2 (CH), 116.8 (CN), 114.0 (CH), 105.2 (C); IR (neat): 3149, 3115, 3032, 2208, 1664, 1582, 1461, 1278 cm^{-1}; HRMS (EI) calcd for $C_{14}H_9NO_2$: 223.0633; found: 223.0633.

4.3. General procedure for BCl_3-catalyzed Diels–Alder reactions

*4.3.1. 3,4-Dimethyl-6-phenyl-1-pivaloylcyclohex-3-ene carbonitrile (**9a**).* To a solution of **8f** (1.2 g, 5.63 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (50 mL), boron trichloride (1 M in hexane, 4.22 mL, 4.22 mmol, 0.75 equiv) was added slowly via a syringe at room temperature under an atmosphere of argon and the resulting reaction mixture was stirred for 30–45 min at room temperature. The 2,3-dimethyl-1,3-butadiene (2.55 mL, 22.51 mmol, 4.0 equiv) was then introduced to the reaction mixture and the resulting solution was stirred for 24 h at room temperature. The reaction mixture was slowly poured into ice-cooled water (50 mL) and extracted with CH_2Cl_2 (4×25 mL) and the combined organic layers were dried over Na_2SO_4, filtered and then concentrated in vacuo. The crude products were purified by flash chromatography on silica gel (hexane–EtOAc 9.5:0.5) to afford **9a** as a colorless crystal (1.33 g, 80%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33–7.22 (m, 5H), 3.44 (dd, J=12.5, 5.2 Hz, 1H), 2.82 (dd, J=15.2, 15.3 Hz, 1H), 2.68 (d, J=16.8 Hz, 1H), 2.35 (d, J=16.8 Hz, 1H), 2.23 (dd, J=17.9, 4.9 Hz, 1H), 1.72 (s, 3H), 1.67 (s, 3H), 0.91 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.6 (CO), 139.5 (C), 129.0 (CH), 128.4 (CH), 127.8 (CH), 126.3 (C), 121.3 (C), 120.9 (CN), 52.0 (C), 46.5 (C), 45.8 (CH), 44.1 (CH_2), 35.4 (CH_2), 25.2 (CH_3), 18.8 (CH_3), 18.5 (CH_3); IR (neat): 2973, 2913, 2232, 1702, 1477, 1453, 1078 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{25}NO$: 295.1936; found: 295.1929.

*4.3.2. 1-Acetyl-3,4-dimethyl-6-phenylcyclohex-3-enecarbonitrile (**9b**).* The typical procedure for the preparation of **9a** was followed using **8a** (1.2 g, 7.01 mmol, 1.0 equiv), boron trichloride (BCl_3) (5.26 mL, 5.26 mmol, 0.75 equiv), and 2,3-dimethyl-1,3-butadiene (3.17 mL, 28.04 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) afforded **9b** as a white solid (1.34 g, 75%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32–7.24 (m, 5H), 3.12 (dd, J=12.2, 5.2 Hz, 1H), 2.82 (d, J=17.1 Hz, 1H), 2.75–2.70 (m, 1H), 2.26 (d, J=17.1 Hz, 1H), 2.21 (dd, J=17.9, 4.7 Hz, 1H), 1.85 (s, 3H), 1.69 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 202.8 (CO), 138.7 (C), 128.6 (CH), 128.0 (CH), 127.8 (CH), 125.8 (C), 121.2 (C), 120.4 (CN), 54.8 (C), 46.3 (CH), 39.8 (CH_2), 36.2 (CH_2), 29.4 (CH_3), 18.5 (CH_3), 18.4 (CH_3); IR (neat): 2915, 2862, 2236, 1721, 1455, 1358, 1197 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{19}NO$: 253.1467; found: 253.1461.

*4.3.3. 3-Phenyl-2-propionylbicyclo[2.2.2]oct-5-ene-2-carbonitrile (**9c**).* The typical procedure for the preparation of **9a** was followed using **8b** (1.2 g, 6.48 mmol, 1.0 equiv), boron trichloride (4.86 mL, 4.86 mmol, 0.75 equiv), and 1,3-cyclohexadiene (2.47 mL, 25.91 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.3:9.7) yielded **9c** as a white solid (1.87 g, 86%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35–7.32 (m, 2H), 7.28–7.25 (m, 3H), 6.56 (dd, J=8.0, 7.0 Hz, 1H), 6.04 (dd, J=7.8, 6.7 Hz, 1H), 3.65 (s, 1H), 3.13–3.11 (m, 1H), 2.91–2.90 (m, 1H), 2.90–2.83 (m, 1H), 2.78–2.75 (m, 1H), 2.38–2.34 (m, 1H), 2.23–2.18 (m, 1H), 1.51–1.46 (m, 1H), 1.33–1.30 (m, 1H), 1.14 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6 (CO), 139.0 (C), 138.1 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 127.2 (CH), 120.1 (CN), 57.5 (C), 45.6 (CH), 37.8 (CH), 33.5 (CH), 32.0 (CH_2), 22.8 (CH_2), 17.8 (CH_2), 8.5 (CH_3); IR (neat): 3055, 2945, 2231, 1727, 1498, 1451, 1127 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{19}NO$: 265.1467; found: 265.1469.

*4.3.4. 6-(Furan-2-yl)-3,4-dimethyl-1-propionylcyclohex-3-enecarbonitrile (**9d**).* The typical procedure for the preparation of **9a** was followed using **8c** (1.2 g, 6.85 mmol, 1.0 equiv), boron trichloride (5.14 mL, 5.14 mmol, 0.75 equiv), and 2,3-dimethyl-1,3-butadiene (3.1 mL, 27.40 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) gave **9d** as a colorless oil (1.44 g, 82%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (d, J=1.8 Hz, 1H), 6.30 (dd, J=3.3, 1.9 Hz, 1H), 6.21 (d, J=3.3 Hz, 1H), 3.34 (dd, J=12.3, 5.3 Hz, 1H), 2.79 (dd, J=17.1, 1.9 Hz, 1H), 2.68–2.61 (m, 2H), 2.28–2.16 (m, 3H), 1.69 (s, 3H), 1.66 (s, 3H), 0.93 (t, J=1.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 205.4 (CO), 152.8 (C), 142.0 (CH), 125.1 (C), 121.4 (C), 119.8 (CN), 110.6 (CH), 107.2 (CH), 53.9 (C), 39.9 (CH), 39.4 (CH_2), 35.1 (CH_2), 33.9 (CH_2), 18.6 (CH_3), 18.5 (CH_3), 7.4 (CH_3); IR (KBr): 2981, 2941, 2240, 1723, 1455, 1380, 1149, 1111 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{19}NO_2$: 257.1416; found: 257.1410.

*4.3.5. 1-(Cyclopropanecarbonyl)-2,5-dimethyl-6-(naphthalene-2-yl)cyclohex-3-ene carbonitrile (**9e**).* The typical procedure for the preparation of **9a** was followed using **8d** (1.2 g, 4.85 mmol, 1.0 equiv), boron trichloride (3.64 mL, 3.64 mmol, 0.75 equiv), and 2,4-hexadiene (2.21 mL, 19.41 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) gave **9e** as a white solid (1.01 g, 62%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.82–7.78 (m, 3H), 7.60–7.43 (m, 3H), 5.94 (dt, J=10.1, 3.4 Hz, 1H), 5.57 (dt, J=10.1, 1.9 Hz, 1H), 3.75 (d, J=6.7 Hz, 1H), 3.03–2.99 (m, 1H), 2.75–2.71 (m, 1H), 2.56–2.54 (m, 1H), 1.25 (d, J=7.2 Hz, 3H), 1.14 (d, J=7.6 Hz, 3H), 0.89–0.86 (m, 1H), 0.80–0.78 (m, 1H), 0.62–0.60 (m, 1H), 0.36–0.35 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 205.3 (CO), 136.2 (C), 133.1 (CH), 132.3 (C), 127.9 (CH), 127.7 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 127.0 (CH), 126.1 (CH), 125.8 (CH), 121.3 (CN), 56.5 (C), 50.4 (CH), 39.9 (CH), 35.6 (CH), 20.1 (CH), 17.1 (CH_3), 15.7 (CH_3), 13.7 (CH_2), 12.7 (CH_2); IR (neat): 3020, 2970, 2235, 1699, 1453, 1380, 1132 cm^{-1}; HRMS (EI) calcd for $C_{23}H_{23}NO$: 329.1780; found: 329.1770.

*4.3.6. 1-(Cyclopropanecarbonyl)-2,6,6-trimethylcyclohex-3-enecarbonitrile (**9f**).* The typical procedure for the preparation of **9a** was followed using **8e** (1.2 g, 8.04 mmol, 1.0 equiv), boron trichloride (6.03 mL, 6.03 mmol, 0.75 equiv), and *trans*-1,3-pentadiene (3.2 mL, 32.17 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) gave **9f** as a colorless oil (1.12 g, 64%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.65 (dt, J=7.6, 2.5 Hz, 1H), 5.42 (dd, J=11.8, 1.2 Hz, 1H), 2.98–2.96 (m, 1H), 2.63–2.60 (m, 1H), 2.46–2.42 (m, 1H), 1.82–1.78 (m, 1H), 1.24 (s, 3H), 1.22–1.20 (m, 1H), 1.06–1.03 (m, 3H), 1.03 (d, J=7.1, 3H), 0.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 204.1 (CO), 128.8 (CH), 124.5 (CH), 120.0 (CN), 63.9 (C), 39.1 (CH_2), 37.0 (C), 33.1 (CH), 27.6 (CH_3), 21.8 (CH), 21.3 (CH_3), 17.2 (CH_3), 14.7 (CH_2), 12.7 (CH_2); IR (neat): 2969, 2232, 1701, 1458, 1378, 1127 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{19}NO$: 217.1467; found: 217.1466.

*4.3.7. 4-Methyl-6-phenyl-1-pivaloylcyclohex-3-enecarbonitrile (**9g**).* The typical procedure for the preparation of **9a** was followed using **8f** (1.2 g, 5.63 mmol, 1.0 equiv), boron trichloride (4.22 mL, 4.22 mmol, 0.75 equiv), and isoprene (2.25 mL, 22.51 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) provided **9g** as a colorless crystal (1.07 g, 68%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34 (d, J=7.2 Hz, 2H), 7.26–7.20 (m, 3H), 5.40 (dd, J=3.5, 1.3 Hz, 1H), 3.48 (dd, J=12.4, 5.1 Hz, 1H), 2.78 (t,

J=15.3 Hz, 1H), 2.66–2.63 (m, 1H), 2.53 (dd, J=17.0, 5.5 Hz, 1H), 2.34 (dd, J=18.0, 4.9 Hz, 1H), 1.77 (s, 6H), 0.89 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.7 (CO), 139.5 (C), 134.8 (C), 129.1 (CH), 128.4 (CH), 127.8 (CH), 121.1 (CN), 115.9 (CH), 51.0 (C), 46.0 (C), 45.6 (CH), 38.5 (CH_2), 34.1 (CH_2), 25.2 (CH_3), 23.1 (CH_3); IR (neat): 2983, 2972, 2232, 1704,1397, 1368 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{23}NO$: 281.1780; found: 281.1783.

*4.3.8. 4-Methyl-1-pivaloylspiro[5.5]undec-3-ene-1-carbonitrile (**9h**).* The typical procedure for the preparation of **9a** was followed using **8g** (1.2 g, 5.85 mmol, 1.0 equiv), boron trichloride (4.38 mL, 4.38 mmol, 0.75 equiv), and isoprene (2.34 mL, 23.38 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) yielded **9h** as a colorless oil (1.04 g, 65%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.22 (dd, J=7.3, 1.5 Hz, 1H), 2.54–2.51 (m, 1H), 2.38–2.31 (m, 2H), 2.14–2.11 (m, 1H), 1.77–1.71 (m, 2H), 1.69 (s, 3H), 1.63–1.60 (m, 1H), 1.55–1.52 (m, 2H), 1.45–1.35 (m, 2H), 1.34 (s, 9H), 1.29–1.24 (m, 2H), 1.10–1.05 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.9 (CO), 133.9 (C), 122.8 (CN), 115.1 (CH), 53.4 (C), 47.7 (C), 40.5 (C), 35.3 (CH_2), 34.2 (CH_2), 33.9 (CH_2), 28.8 (CH_2), 27.0 (CH_3), 25.3 (CH_2), 23.6 (CH_3), 21.8 (CH_2), 21.3 (CH_2); IR (neat): 2250, 1722, 1380, 1360 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{27}NO$: 273.2093; found: 273.2089.

*4.3.9. 1-Benzoyl-6-(furan-2-yl)-4-methylcyclohex-3-enecarbonitrile (**9i**).* The typical procedure for the preparation of **9a** was followed using **8h** (1.2 g, 5.38 mmol, 1.0 equiv), boron trichloride (4.03 mL, 4.03 mmol, 0.75 equiv), and isoprene (2.15 mL, 21.5 mmol, 4.0 equiv). Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) offered **9i** as a colorless crystal (1.38 g, 88%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66–7.65 (m, 2H), 7.49 (dd, J=7.3, 1.0 Hz, 1H), 7.37–7.35 (m, 2H), 7.23 (dd, J=1.7, 1.0 Hz, 1H), 6.24–6.22 (m, 2H), 5.46 (dd, J=3.5, 1.9 Hz, 1H), 3.76 (dd, J=11.7, 5.4 Hz, 1H), 2.92–2.88 (m, 1H), 2.75–2.67 (m, 2H), 2.40 (dd, J=17.9, 5.1 Hz, 1H), 1.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 196.7 (CO), 153.1 (C), 141.9 (CH), 136.0 (C), 133.8 (C), 132.9 (CH), 128.3 (CH), 128.2 (CH), 119.9 (CN), 116.0 (CH), 110.4 (CH), 107.5 (CH), 51.2 (C), 39.8 (CH), 36.0 (CH_2), 32.6 (CH_2), 23.0 (CH_3); IR (neat): 2969, 2914, 2855, 2237, 1686, 1597, 1236 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{17}NO_2$: 291.1259; found: 291.1252.

4.4. General procedure for the reductive alkylation reactions

*4.4.1. 2,2-Dimethyl-1-(1,3,4-trimethyl-6-phenylcyclohex-3-enyl)propan-1-one (**10a**).* To a solution of **9a** (0.1 g, 0.34 mmol, 1.0 equiv) in THF (5 mL) pre-cooled at −45 °C, lithium naphthalenide THF solution[14] (0.34 M, 3.5 mL, 1.19 mmol, 3.5 equiv) was added via a syringe under the protection of an argon atmosphere. The resulting dark green solution was continued to stir at −45 °C for 45 min and added with methyl iodide (0.07 mL, 1.19 mmol, 3.5 equiv). The reaction mixture was stirred at room temperature for 12 h then poured into saturated NH_4Cl aqueous solution (10 mL) and extracted with EtOAc (2×20 mL). The combined organic extract was washed with saturated NaCl aqueous solution (10 mL) and then concentrated. Chromatographic purification on silica gel (hexane–EtOAc 0.2:9.8) afforded **10a** as a colorless oil (770 mg, 80%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16–7.08 (m, 5H), 3.32 (d, J=6.9 Hz, 1H), 2.83 (d, J=16.8 Hz, 1H), 2.57 (d, J=18.4 Hz, 1H), 2.13 (d, J=8.4 Hz, 1H), 2.10 (d, J=9.8 Hz, 1H), 1.72 (s, 3H), 1.68 (s, 3H), 1.25 (s, 3H), 0.87 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 217.7 (CO), 145.0 (C), 129.0 (CH), 127.9 (CH), 126.2 (CH), 124.3 (C), 123.8 (C), 52.8 (C), 46.4 (CH), 46.1 (C), 37.2 (CH_2), 35.5 (CH_2), 27.3 (CH_3), 26.1 (CH_3), 19.8 (CH_3), 18.6 (CH_3); IR (neat): 2966, 2929, 1678, 1478, 1453, 1365, 988 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{28}O$: 284.2140; found: 284.2146.

*4.4.2. 1-(1-Allyl-3,4-dimethyl-6-phenylcyclohex-3-enyl)-2,2-dimethylpropan-1-one (**10b**).* The typical procedure for preparing **10a** was employed using **9a** (0.1 g, 0.34 mmol, 1.0 equiv), lithium naphthalenide (3.5 mL, 1.19 mmol, 3.5 equiv), and allyl bromide (0.1 mL, 1.18 mmol, 3.5 equiv). Flash chromatography on silica gel (hexane–EtOAc 0.2:9.8) afforded **10b** as a colorless oil (80 mg, 72%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16–7.06 (m, 5H), 5.67–5.63 (m, 1H), 5.01–4.93 (m, 2H), 3.29 (dd, J=12.3, 5.3 Hz, 1H), 2.77 (d, J=16.6 Hz, 1H), 2.60–2.57 (m, 1H), 2.54 (dd, J=13.2, 6.9 Hz, 1H), 2.38 (d, J=16.6 Hz, 1H), 2.33 (dd, J=13.1, 8.2 Hz, 1H), 2.04 (d, J=18.0 Hz, 1H), 1.76 (s, 3H), 1.69 (s, 3H), 0.69 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 217.2 (CO), 145.1 (C), 135.3 (CH), 129.3 (CH), 128.1 (CH), 126.3 (CH), 124.4 (C), 123.9 (C), 117.8 (CH_2), 57.2 (C), 46.7 (CH), 46.1 (C), 43.4 (CH_2), 35.6 (CH_2), 33.3 (CH_2), 26.8 (CH_3), 19.9 (CH_3), 18.6 (CH_3); IR (neat): 3062, 3029, 2972, 2926, 1676, 1453, 1365, 1056 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{30}O$: 310.2297; found: 310.2296.

*4.4.3. 1-(1,4-Dimethylspiro[5.5]undec-3-en-1-yl)-2,2-dimethylpropan-1-one (**10c**).* The typical procedure for preparing **10a** was employed using **9h** (0.1 g, 0.37 mmol, 1.0 equiv), lithium naphthalenide (3.8 mL, 1.30 mmol, 3.5 equiv), and allyl bromide (0.14 mL, 1.30 mmol, 3.5 equiv). Flash chromatography on silica gel (hexane–EtOAc 0.2:9.8) afforded **10c** as a colorless oil (65 mg, 68%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.22 (dd, J=2.9, 1.4 Hz, 1H), 2.70 (d, J=17.7 Hz, 1H), 2.23 (d, J=18.0 Hz, 1H), 1.79–1.78 (m, 1H), 1.71 (d, J=18.0 Hz, 1H), 1.62 (s, 3H), 1.58–1.56 (m, 3H), 1.47–1.46 (m, 2H), 1.38–1.33 (m, 3H), 1.27 (s, 3H), 1.21 (s, 9H), 1.15–1.11 (m, 1H), 1.04–0.98 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 219.1 (CO), 132.0 (C), 118.7 (CH), 54.6 (C), 47.3 (C), 39.2 (C), 35.2 (CH_2), 34.6 (CH_2), 33.0 (CH_2), 29.4 (CH_3), 29.1 (CH_2), 26.0 (CH_2), 23.6 (CH_3), 22.1 (CH_2), 21.8 (CH_2), 18.5 (CH_3); IR (neat): 2929, 2867, 1682, 1454, 1366, 982 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{30}O$: 262.2297; found: 262.2294.

*4.4.4. 6-(Furan-2-yl-1,4-dimethylcyclohex-3-enyl)-phenyl-methanone (**10d**).* The typical procedure for preparing **10a** was employed using **9i** (0.1 g, 0.34 mmol, 1.0 equiv), lithium naphthalenide (3.5 mL, 1.19 mmol, 3.5 equiv) and methyl iodide (0.08 mL, 1.20 mmol, 3.5 equiv). Flash chromatography on silica gel (hexane–EtOAc 0.2:9.8) afforded **10d** as a colorless crystal (85 mg, 88%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49–7.47 (m, 2H), 7.40 (t, J=7.4 Hz, 1H), 7.35–7.32 (m, 2H), 7.15 (d, J=1.8 Hz, 1H), 6.19 (dd, J=3.2, 1.8 Hz, 1H), 5.95 (d, J=3.2 Hz 1H), 5.35 (t, J=1.5 Hz, 1H), 3.60 (dd, J=6.0, 2.9 Hz, 1H), 2.52–2.47 (m, 2H), 2.29 (d, J=18.6 Hz, 1H), 2.03–1.99 (m, 1H), 1.70 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.8 (CO), 157.0 (C), 140.5 (CH), 139.7 (C), 131.0 (C), 130.4 (CH), 127.9 (CH), 127.3 (CH), 119.2 (CH), 110.1 (CH), 105.9 (CH), 48.8 (C), 39.9 (CH), 32.6 (CH_2), 32.1 (CH_2), 23.9 (CH_3), 23.2 (CH_3); IR (neat): 2960, 2911, 2846, 1672, 1500, 1441, 1274, 1169 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{20}O_2$: 280.1463; found: 280.1467.

*4.4.5. 1-[6-(Furan-2-yl)-3,4-dimethylcyclohex-3-enyl]-propan-1-one (**11**).* To a solution of **9d** (0.16 g, 0.62 mmol, 1.0 equiv) in THF (8 mL) pre-cooled at −45 °C, lithium naphthalenide THF solution (0.34 M, 6.4 mL, 2.17 mmol, 3.5 equiv) was added via a syringe under the protection of an argon atmosphere. The resulting dark green solution was continued to stir at −45 °C for 45 min and quenched with 10% aqueous NH_4Cl solution (20 mL). After the extraction with EtOAc (2×25 mL), The combined organic extract was washed with saturated NaCl aqueous solution (15 mL) and then concentrated. Chromatographic purification on silica gel (hexane–EtOAc 0.5:9.5) afforded **11** as a colorless oil (101 mg, 70%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.22 (d, J=1.4 Hz, 1H), 6.22 (dd, J=3.1, 1.9 Hz, 1H), 5.91 (d, J=3.1 Hz, 1H), 3.55–3.53 (m, 1H), 2.90–2.87 (m, 1H), 2.47–2.41 (m, 2H), 2.35–2.28 (m, 2H), 2.14 (dd, J=17.5,

4.3, 1H), 2.05 (dd, J=7.5, 4.3, 1H), 1.65 (s, 3H), 1.62 (s, 3H), 1.0 (t, J=7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 212.4 (CO), 153.3 (C), 140.7 (CH), 124.1 (C), 123.3 (C), 110.1 (CH), 105.3 (CH), 49.3 (CH), 35.2 (CH_2), 35.0 (CH), 33.9 (CH_2), 30.2 (CH_2), 19.0 (CH_3), 18.9 (CH_3), 7.8 (CH_3); IR (neat): 2976, 2916, 1710, 1672, 1450, 1337, 1009 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{20}O_2$: 232.1463; found: 232.1461.

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Supplementary data

Crystallographic diagrams of compounds **8d**, **8h**, **9a**, **9b**, **9g**, **9i**, and NMR spectra (^{1}H, ^{13}C NMR and DEPT) of new compounds are available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.11.105.

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