Chapter 2
NHC-Catalyzed Annulations of Nitroalkenes

2.1 Introduction

As described in the previous chapter, the NHCs are powerful catalysts for the reaction of C–X (X = O, S, N) bonds, however the reactions of C–C unsaturated bonds catalyzed by NHC are far less developed. In 2006, Fu and coworkers [1] disclosed an NHC-catalyzed umpolung of Michael acceptors. Nucleophilic addition of the triazolium-derived carbene to the Michael acceptor gives the adduct A. The sequential proton shift forms a β-anion intermediate B. Therefore, the umpolung of Michael acceptors was realized by reversing the polarity of the β-carbon of the Michael acceptor from an acceptor to a donor (Fig. 2.1).

In 2011, Matsuoka and coworkers [2] expanded this method to the dimerization of methacrylates. Later on, a better substrate scope was realized by Glorius and coworkers [3] (Fig. 2.2).

Besides that, the NHC was also a suitable catalyst for Morita–Baylis–Hillman (MBH) reaction. In 2007, Ye and coworkers [4] found that the reaction of cyclic enones with a variety of N-tosylarylimines went well under the catalyst of stable NHC 1b, giving the aza-MBH adduct in good to excellent yields (Fig. 2.3).

In 2011, Scheidt and coworkers [5] reported an NHC-catalyzed [3+2] annulation of nitrones and vinyl sulfone. The [3+2] annulation products were afforded in good yields with high diastereoselectivities in the presence of sodium tert-butoxide and 20 mol% of triazolium cat. 5f (Fig. 2.4).

1,3-Dipolar annulation reactions of nitrile oxides and alkynes are efficient approaches to obtain isoxazoles. In 2011, Vasam and coworkers [6] demonstrated the [3+2] annulation of nitrile oxides and alkynes catalyzed by NHC. In the presence of NHC cat.1d, a variety of nitrile oxides reacted well with the alkynes to provide the desired isoxazoles in good yields (Fig. 2.5).

Nitroalkenes, due to their high reactivity, have become one of the most powerful reagents to construct functionalized cyclic compounds [7–17]. We envision that the
NHC could attack nitroalkenes and finish the [4+2] annulation with oxodienes (Fig. 2.6).

2.2 Optimization of Conditions

Initially, we evaluated the model reaction of nitroalkene 2.1a with oxodiene 2.2a in the presence of various azolium salts. It was found that the use of imidazolium precatalyst cat.1a and triazolium precatalyst cat.5e gave no reaction (Table 2.1, entries 1 and 2). Gratifyingly, thioazolium cat.8b–8c showed reactivity for the reaction. And further solvent screening revealed that the reactions in toluene gave best yields of the desired product (entries 3–6, 9, and 10). It is necessary to note...
that DABCO or PPh₃ offered no or little catalytic activity under current reaction conditions (entries 7 and 8). In the absence of catalyst, no reaction was observed (entry 11).
2.3 Substrate Scope

Under the optimized reaction conditions, we conducted the reactions of nitroalkene 2.1 with oxodiene 2.2. As shown in Table 2.2, in the presence of precatalyst cat.8b (20 mol%). Both electron-rich (4-Me, 4-MeO) and electron-poor (4-Cl, 4-Br) para-substituted nitroalkenes were tolerated, giving the cycloadducts 2.3b–2.3f in good yield with good diastereoselectivity. meta-Substituted aromatic nitroalkenes also worked well (2.3g and 2.3h). Moreover, introducing a heterocyclic thienyl group on the nitroalkene gave the corresponding dihydropyran 2.3i in 76% yield with a
Table 2.1 Optimization of the reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>2.3a:2.4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cat.1a</td>
<td>DCM</td>
<td>Trace</td>
<td>/</td>
</tr>
<tr>
<td>2</td>
<td>Cat.5e</td>
<td>DCM</td>
<td>Trace</td>
<td>/</td>
</tr>
<tr>
<td>3</td>
<td>Cat.8a</td>
<td>DCM</td>
<td>Trace</td>
<td>/</td>
</tr>
<tr>
<td>4</td>
<td>Cat.8b</td>
<td>DCM</td>
<td>33</td>
<td>4:1</td>
</tr>
<tr>
<td>5</td>
<td>Cat.8c</td>
<td>DCM</td>
<td>84</td>
<td>1:2</td>
</tr>
<tr>
<td>6</td>
<td>Cat.8b</td>
<td>THF</td>
<td>55</td>
<td>5:1</td>
</tr>
<tr>
<td>7</td>
<td>DABCO</td>
<td>THF</td>
<td>Trace</td>
<td>/</td>
</tr>
<tr>
<td>8</td>
<td>PPh3</td>
<td>THF</td>
<td>13</td>
<td>2:1</td>
</tr>
<tr>
<td>9</td>
<td>Cat.8b</td>
<td>Toluene</td>
<td>88</td>
<td>18:1</td>
</tr>
<tr>
<td>10</td>
<td>Cat.8c</td>
<td>Toluene</td>
<td>90</td>
<td>1:3</td>
</tr>
<tr>
<td>11</td>
<td>None</td>
<td>Toluene</td>
<td>NR</td>
<td>/</td>
</tr>
</tbody>
</table>

*a*Isolated yield of the mixture of stereoisomers

*b*Determined by $^1$H NMR (300 MHz) of the raw product

*c*Beside 2.3a and 2.4a, another stereoisomer was also observed in the reaction mixture but not isolable

*d*No base of NaOAc was added when DABCO or PPh3 was used

diestereomeric ratio (d.r.) of 7:1. It is worth noting that good results were also obtained when $\beta$-alkyl nitroalkenes (R = cyclohexyl, $n$-butyl, $n$-propyl; cycloaducts 2.3j, 2.3k and 2.3l) were employed. The $\alpha$-cyano-$\beta$-aryl-$\alpha,\beta$-unsaturated ketones were also varied. Different aryl groups (Ar = Ph, 4-ClC$_6$H$_4$, 4-BrC$_6$H$_4$)
Table 2.2 NHC-precursor cat.8b catalyzed [4+2] cycloadditions of nitroalkenes with oxodienes

<table>
<thead>
<tr>
<th>R’</th>
<th>Ar</th>
<th>X</th>
<th>Isolated yield, followed by dr (trans/cis) of the reaction mixture</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>Ph</td>
<td>Cl</td>
<td>2.3b (X = H), 70%, dr = 7:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3c (X = Me), 74%, dr = 9:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3d (X = MeO), 72%, dr = 8:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3e (X = Cl), 68%, dr = 6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Br</td>
<td>2.3f (X = Br), 64%, dr = 5:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3g (X = Cl), 70%, dr = 6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3h (X = MeO), 71%, dr = 6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3i, 76%, dr = 7:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3j (R = cyclohexyl), 50%, dr = 3:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3k (R = n-Bu), 72%, dr = 5:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3l (R = n-Pr), 64%, dr = 6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3m (X = H), 52%, dr = 7:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3n (X = Me), 64%, dr = 5:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3o (X = MeO), 55%, dr = 7:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3p (X = Cl), 64%, dr = 4:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3q (X = Br), 73%, dr = 6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3r, 76%, dr = 6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3s, (X = H), 81%, dr = 3:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3t, (X = Br), 65%, dr = 5:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cl</td>
<td>2.3u, 60%, dr = 4:1</td>
</tr>
</tbody>
</table>

Reproduced from Ref. [18] by permission of John Wiley & Sons Ltd.

aUnless otherwise noted, isolated yield of pure 2,3-trans isomer (2.3) is shown
bDetermined by ¹H NMR spectroscopy (300 MHz)
cAs well as the 2,3-trans (2.3) and 2,3-cis isomers (2.4), another stereoisomer was observed by ¹H NMR analysis of the reaction mixture, although it was not isolable
dIsolated yield of a mixture of 2.3j and 2.4j (d.r. = 14:1)
eIsolated yield of a mixture of 2.3k and 2.4k (d.r. = 7:1)
fIsolated yield of the mixture of stereoisomers
were tolerable under current reaction conditions, giving the desired dihydropyrans 2.3m–2.3u in good yield with moderate-to-good diastereoselectivity.

The structure of dihydropyran 2.3e was confirmed by the X-ray analysis of its crystal (Fig. 2.7).

The synthesis of cis-cycloadduct 2.4 as the major product using NHC-precursor cat.8c was also investigated (Table 2.3). Both electron-donating and electron-withdrawing substituents at the para or meta positions of the β-phenyl group were well tolerated (2.4m–2.4q, 2.4r, and 2.4v). Moreover, the variation on the oxodienes was also investigated. Both para and meta-substituents on the aryl group of the oxodienes were well tolerated (2.4s–2.4t and 2.4a). Much better diastereoselectivity was achieved when ortho chlorophenyl-substituted nitroalkenes were employed (2.4w).

The structure of dihydropyran 2.4s was unambiguously established by the X-ray analysis of its crystal (Fig. 2.8).

2.4 Reduction of the Nitro Group of Dihydropyran

Some possible chemical transformations could be provided by the resulted highly functionalized dihydropyrans. For example, the nitro group in dihydropyran 2.3 could be easily reduced by Zn/HCl, giving the corresponding 3-amino dihydropyran 2.5 in good yield (Table 2.4).
2.5 Studies on the Enantioselectivity of the Annulation Process

We envisioned that a thiourea may be suitable catalyst to activate nitroalkenes. Therefore, a catalytic enantioselective variant of the annulation process was further studied with a series thioureas as co-catalysts. However, most of the thioureas have
no catalytic effects and only gave trace of products. Thiourea 2.7d could provide good yield but without enantioselectivity (Table 2.5).

Although further optimization was extensively studied by a series of chiral NHCs, no more improvement could be achieved so far. Only chiral triazolium NHC cat.2d could catalyze the reaction, providing the desired dihydropyran 2.3b in 24% yield with 29% ee (Table 2.6).

In order to improve the enantioselectivity, a series of additives and bases were also examined, but no further improvement was achieved (Table 2.7).

### 2.6 Mechanistic Studies

A plausible mechanism for the reaction is suggested in Fig. 2.9. Addition of the NHC catalyst to the nitroalkenes delivers the carbon anion intermediate I, this species could feasibly react with the electron-deficient oxodiene via Michael addition, providing adduct II. Intramolecular alkoxide attack at the carbonyl group leads to the desired dihydropyran and regenerates the NHC catalyst.

The deuterium experiment was then carried out to investigate the mechanism. It was found that in the presence of NHC-precursor cat.8b (20 mol%), 1.0 equivalent of base, and D$_2$O, 19 and 14% deuteration of the α- and β-position of nitroalkene was observed. We proposed that the α-deuterium nitroalkenes were afforded via deuteration of adduct I followed by elimination. The acidity of the β-proton was enhanced by the addition of NHC to the β-position of nitroalkenes, and thus led to the β-deuterium nitroalkenes (Fig. 2.10).
2.7 Summary

In this chapter, \(N\)-heterocyclic carbene-catalyzed \([4+2]\) annulation of nitroalkenes and oxodienes was developed, affording the corresponding dihydropyran s in good yield with good diastereoselectivity [18]. The reaction is possibly initiated by the addition of an \(N\)-heterocyclic carbene to nitroalkenes, which was revealed by deuteriation experiments.
**Table 2.5** Screening of co-catalysts

![Chemical structures](image)

**2.1a**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Co-cat.</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>2.3b:2.4b&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ee&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>2.7a</td>
<td>Trace</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>2</td>
<td>Toluene</td>
<td>2.7b</td>
<td>Trace</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>3</td>
<td>Toluene</td>
<td>2.7c</td>
<td>Trace</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>2.7d</td>
<td>76</td>
<td>7/1</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>Toluene</td>
<td>2.6</td>
<td>Trace</td>
<td>/</td>
<td>/</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yield of pure 2,3-trans isomer 2.3a

<sup>b</sup>Determined by <sup>1</sup>H NMR spectroscopy (300 MHz)

<sup>c</sup>Determined by chiral-phase HPLC analysis
2.8 Experimental Part

2.8.1 Materials

The nitroalkenes were prepared according to literature methods [19], purified by chromatography and recrystallization from ethanol. α-cyano-α,β-unsaturated ketones were prepared according to literature methods [20], purified by chromatography.

2.8.2 [4+2] Annulation of Nitroalkenes with α-Cyano-α,β-Unsaturated Ketones Catalyzed by NHC-Precursor Cat.8b

An oven-dried 50 mL Schlenk tube was charged with nitroalkenes 2.1 (0.4 mmol, 2.0 eq.), α-cyano-α,β-unsaturated ketones 2.2 (0.2 mmol, 1.0 eq.), cat.8b (0.04 mmol, 12 mg, 0.2 eq.), and AcONa (0.2 mmol, 16 mg, 1.0 eq.).
To this mixture was added freshly distilled toluene (2 mL). The reaction mixture was stirred at room temperature until the full consumption of the \( \alpha \)-cyano-\( \alpha, \beta \)-unsaturated ketones (typically, 18 h). The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleumether/EtOAc as the eluent, typically 20:1-0:100) to furnish the corresponding cycloadduct.
**Fig. 2.9** Possible catalytic cycle. Reproduced from Ref. [18] by permission of John Wiley & Sons Ltd.

**Fig. 2.10** Deuteration experiment. Reproduced from Ref. [18] by permission of John Wiley & Sons Ltd.
(2R*,3S*,4R*)-4-(3-chlorophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 73 mg, 88%; yellow solid; mp 174–176 °C; Rf = 0.4 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, DMSO) δ 7.74 (d, J = 8.0 Hz, 3H), 7.65–7.61 (m, 2H), 7.56–7.44 (m, 9H), 5.85–5.83 (m, 2H), 4.78 (dd, J = 6.9, 3.6 Hz, 1H); 13C NMR (75 MHz, DMSO) δ 165.4, 138.4, 133.7, 133.4, 131.6, 131.5, 130.9, 130.2, 128.9, 128.7, 128.5, 128.4, 128.3, 128.2, 127.7, 117.7, 87.9, 86.6, 79.6, 45.8; IR (KBr) 2211, 1616, 1556, 1277, 1149, 778, 696; HRMS (ESI) calcd for C24H18ClN2O3 [M+H]+ 417.10005, found 417.09998.

(2R*,3S*,4R*)-4-(3,5-dichlorophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 63 mg, 70%; yellow solid; mp 211–213 °C; Rf = 0.4 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.83 (d, J = 7.1 Hz, 2H), 7.53–7.25 (m, 9H), 7.19 (d, J = 1.7 Hz, 2H), 5.45 (d, J = 9.7 Hz, 1H), 4.89 (t, J = 10.0 Hz, 1H), 4.58 (d, J = 10.2 Hz, 1H); 13C NMR (75 MHz, CDCl3) δ 166.5, 139.0, 136.4, 132.4, 132.3, 130.8, 130.8, 130.0, 129.4, 128.9, 128.6, 127.3, 126.6, 117.2, 90.3, 86.0, 80.4, 46.6; IR (KBr) 2360, 2210, 1622, 1556, 1297, 1161, 804, 694; HRMS (ESI) calcd for C24H17Cl2N2O3 [M+H]+ 451.06107, found 451.06161.

(2R*,3S*,4R*)-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-2-p-tolyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 68 mg, 74%; yellow solid; mp 238–240 °C; Rf = 0.4 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.82 (d, J = 7.1 Hz, 2H), 7.51–7.37 (m, 4H), 7.30–7.18 (m, 6H), 5.41 (d, J = 9.7 Hz, 1H), 4.89 (t, J = 9.9 Hz, 1H), 4.56 (d, J = 10.2 Hz, 1H), 2.35 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 166.6, 140.9, 139.1, 136.3, 132.3, 130.9, 130.0, 129.8, 129.4, 128.8, 128.6, 127.3, 126.6,
117.3, 90.2, 85.9, 80.3, 46.6, 21.4; IR (KBr) 2360, 2211, 1557, 1273, 1151, 805, 694; HRMS (ESI) calcd for C_{25}H_{19}Cl_{2}N_{2}O_{3} [M+H]^+ 465.07672, found 465.07685.

(2R*,3S*,4R*)-4-(3,5-dichlorophenyl)-2-(4-methoxyphenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 69 mg, 72%; yellow solid; mp 242–244 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 5:1); ^1H NMR (300 MHz, CDCl_3) δ 7.82 (d, J = 6.9 Hz, 2H), 7.52–7.25 (m, 6H), 7.19 (d, J = 1.8 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 5.39 (d, J = 9.7 Hz, 1H), 4.88 (t, J = 10.0 Hz, 1H), 4.56 (d, J = 10.2 Hz, 1H), 3.80 (s, 3H); ^13C NMR (75 MHz, CDCl_3) δ 166.7, 161.3, 139.1, 136.3, 132.2, 130.9, 129.9, 128.9, 128.8, 128.6, 126.5, 124.2, 117.3, 114.7, 90.2, 85.9, 80.2, 55.5, 46.7; IR (KBr) 2210, 1613, 1557, 1516, 1250, 1150, 833, 694; HRMS (ESI) calcd for C_{25}H_{19}Cl_{2}N_{2}O_{4} [M+H]^+ 481.07164, found 481.07241.

(2R*,3S*,4R*)-2-(4-chlorophenyl)-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 66 mg, 68%; yellow solid; mp 227–230 °C; R_f = 0.4 (petroleum ether/ethyl acetate = 5:1); ^1H NMR (300 MHz, CDCl_3) δ 7.83–7.80 (m, 2H), 7.54–7.25 (m, 8H), 7.18 (d, J = 1.7 Hz, 2H), 5.43 (d, J = 9.7 Hz, 1H), 4.85 (t, J = 10.0 Hz, 1H), 4.56 (d, J = 10.2 Hz, 1H); ^13C NMR (75 MHz, CDCl_3) δ 166.4, 138.7, 136.9, 136.4, 132.4, 130.9, 130.6, 130.0, 129.7, 128.7, 128.6, 126.5, 117.1, 90.1, 86.2, 79.7, 46.6; IR (KBr) 2212, 1616, 1557, 1272, 1151, 830, 694; HRMS (ESI) calcd for C_{24}H_{16}Cl_{3}N_{2}O_{3} [M+H]^+ 485.02210, found 485.02224.
(2R*,3S*,4R*)-2-(4-bromophenyl)-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 68 mg, 64%; yellow solid; mp 230–233 °C; Rf = 0.33 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) \(\delta\) 7.81 (d, \(J = 7.5\) Hz, 2H), 7.57–7.39 (m, 6H), 7.28–7.25 (m, 2H), 7.18 (d, \(J = 1.6\) Hz, 2H), 5.42 (d, \(J = 9.7\) Hz, 1H), 4.84 (t, \(J = 10.0\) Hz, 1H), 4.55 (d, \(J = 10.2\) Hz, 1H); 13C NMR (75 MHz, CDCl3) \(\delta\) 166.3, 138.7, 136.4, 132.6, 132.4, 131.4, 130.6, 130.0, 128.9, 128.6, 126.5, 125.1, 117.1, 90.0, 86.2, 79.7, 46.5; IR (KBr) 2359, 2212, 1617, 1557, 1264, 1151, 805, 695; HRMS (ESI) calcd for C\(_{24}\)H\(_{16}\)BrCl\(_2\)N\(_2\)O\(_3\) [M+H]\(^+\) 528.97159, found 528.97161.

(2R*,3S*,4R*)-2-(3-chlorophenyl)-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 67 mg, 70%; yellow solid; mp 191–193 °C; Rf = 0.25 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) \(\delta\) 7.82 (d, \(J = 7.2\) Hz, 2H), 7.55–7.35 (m, 7H), 7.26 (d, \(J = 5.7\) Hz, 1H), 7.19 (d, \(J = 1.5\) Hz, 2H), 5.43 (d, \(J = 9.7\) Hz, 1H), 4.86 (t, \(J = 10.0\) Hz, 1H), 4.56 (d, \(J = 10.2\) Hz, 1H); 13C NMR (75 MHz, CDCl3) \(\delta\) 166.3, 138.7, 136.5, 135.4, 134.4, 132.4, 131.0, 130.6, 130.0, 128.9, 128.6, 127.4, 126.5, 125.6, 117.0, 90.0, 86.3, 79.5, 46.5; IR (KBr) 2212, 1610, 1557, 1301, 1151, 805, 694; HRMS (ESI) calcd for C\(_{24}\)H\(_{16}\)Cl\(_3\)N\(_2\)O\(_3\) [M+H]\(^+\) 485.02210, found 485.02232.
(2R*,3S*,4R*)-4-(3,5-dichlorophenyl)-2-(3-methoxyphenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 68 mg, 71%; yellow solid; mp 224–226 °C; Rf = 0.5 (petroleum ether/ethyl acetate = 5:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.83 (d, \(J = 7.2\) Hz, 2H), 7.53–7.43 (m, 3H), 7.38–7.25 (m, 2H), 7.19 (d, \(J = 1.5\) Hz, 2H), 6.97–6.91 (m, 3H), 5.42 (d, \(J = 9.6\) Hz, 1H), 4.88 (t, \(J = 9.9\) Hz, 1H), 4.56 (d, \(J = 10.2\) Hz, 1H), 3.80 (s, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 166.5, 160.2, 139.0, 136.4, 133.8, 132.3, 130.8, 130.5, 129.9, 128.9, 128.6, 126.6, 119.5, 117.2, 116.0, 113.1, 90.2, 86.0, 80.2, 55.5, 46.6; IR (KBr) 2211, 1611, 1557, 1274, 1149, 862, 774, 695; HRMS (ESI) calcd for C\(_{25}\)H\(_{19}\)Cl\(_2\)N\(_2\)O\(_4\) [M+H]\(^+\) 481.07164, found 481.07206.

(2R*,3S*,4R*)-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-2-(thiophen-2-yl)-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 69 mg, 76%; yellow solid; mp 218–220 °C; Rf = 0.33 (petroleum ether/ethyl acetate = 5:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.84 (d, \(J = 7.5\) Hz, 2H), 7.54–7.39 (m, 5H), 7.19–7.15 (m, 3H), 7.04–7.01 (m, 1H), 5.79 (d, \(J = 9.6\) Hz, 1H), 4.92 (t, \(J = 9.9\) Hz, 1H), 4.54 (d, \(J = 10.1\) Hz, 1H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 166.1, 138.8, 136.4, 134.2, 132.4, 130.6, 130.0, 128.9, 128.8, 128.6, 128.5, 127.5, 126.6, 117.1, 90.4, 86.2, 76.3, 46.7; IR (KBr) 2359, 2214, 2211, 1557, 1274, 1149, 807, 697; HRMS (ESI) calcd for C\(_{22}\)H\(_{15}\)Cl\(_2\)N\(_2\)O\(_3\)S [M+H]\(^+\) 457.01749, found 457.01795.
(2R*,3S*,4R*)-2-cyclohexyl-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 46 mg, 50%; 2.3j/2.4j = 14/1, yellow solid; Rf = 0.5 (2.3j), Rf = 0.51 (4j) (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ (2.3j) 7.79 (dd, J = 8.1, 1.5 Hz, 2H), 7.55—7.47 (m, 3H), 7.40 (t, J = 1.8 Hz, 1H), 7.15 (d, J = 1.8 Hz, 2H), 4.81 (t, J = 10.0 Hz, 1H), 4.42 (d, J = 10.2 Hz, 1H), 4.35 (d, J = 10.0 Hz, 1H), 1.82—1.62 (m, 7H), 1.33—1.18 (m, 4H); 13C NMR (75 MHz, CDCl3) δ (2.3j) 166.4, 139.4, 136.4, 132.2, 131.2, 129.9, 128.9, 128.4, 126.6, 117.4, 86.2, 85.5, 81.7, 46.5, 38.3, 29.8, 26.3, 26.0, 25.8, 25.1; IR (KBr) 2210, 1619, 1556, 1282, 1162, 805, 694; HRMS (ESI) calcd for C24H23Cl2N2O3 [M+H]+ 457.10802, found 457.10883.

(2R*,3S*,4R*)-2-butyl-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 62 mg, 72%; 2.3k/2.4k = 7/1; yellow solid; Rf = 0.5 (2.3k and 2.4k) (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ (2.3k) 7.79 (d, J = 6.9 Hz, 2H), 7.54—7.46 (m, 3H), 7.39 (s, 1H), 7.15 (d, J = 1.6 Hz, 2H), 4.65 (t, J = 9.9 Hz, 1H), 4.50—4.38 (m, 2H), 1.78—1.68 (m, 3H), 1.43—1.37 (m, 3H), 0.94 (t, J = 7.1 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ (2.3k) 166.1, 139.3, 136.3, 132.2, 131.1, 129.8, 128.9, 128.4, 126.6, 117.3, 88.8, 85.7, 77.9, 46.1, 30.6, 26.4, 22.3, 13.9; IR (KBr) 2354, 2210, 1616, 1556, 1281, 1162, 805, 693; HRMS (ESI) calcd for C22H21Cl2N2O3 [M+H]+ 431.09237, found 431.09312.
(2R*,3S*,4R*)-4-(3,5-dichlorophenyl)-3-nitro-6-phenyl-2-propyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 53 mg, 64%; 2.3l/2.4l = 5/1; yellow solid; Rf = 0.6 (2.3l and 2.4l) (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ (2.3l) 7.79 (d, J = 6.9 Hz, 2H), 7.55–7.46 (m, 3H), 7.39 (s, 1H), 7.15 (d, J = 1.6 Hz, 2H), 4.64 (t, J = 9.9 Hz, 1H), 4.68–4.39 (m, 2H), 1.78–1.67 (m, 2H), 1.62–1.53 (m, 2H), 1.00 (t, J = 6.9 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ (2.3l) 166.1, 139.3, 136.4, 132.2, 131.1, 129.8, 128.9, 128.4, 126.6, 117.3, 88.8, 85.7, 77.7, 46.1, 32.9, 17.9, 13.7; IR (KBr) 2213, 1616, 1556, 1306, 1189, 735, 697; HRMS (ESI) calcd for C21H19Cl2N2O3 [M+H]+ 417.07672, found 417.07700.

O
Ph
O2N
Ph
CN
Cl
2.3m

(2R*,3S*,4R*)-4-(4-chlorophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 44 mg, 52%; yellow solid; mp 223–225 °C; Rf = 0.33 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.84–7.81 (m, 2H), 7.52–7.39 (m, 10H), 7.27–7.25 (m, 2H), 5.46 (d, J = 9.8 Hz, 1H), 4.88 (t, J = 10.1 Hz, 1H), 4.62 (d, J = 10.3 Hz, 1H); 13C NMR (75 MHz, CDCl3) δ 166.1, 135.5, 134.0, 132.7, 132.1, 131.1, 130.7, 130.1, 129.3, 128.8, 128.6, 127.4, 117.5, 90.8, 87.0, 80.5, 46.8; IR (KBr) 2359, 2210, 1616, 1557, 1275, 1150, 835, 694; HRMS (ESI) calcd for C24H18ClN2O3 [M+H]+ 417.10005, found 417.09991.

O
Ph
O2N
CN
Cl
2.3n

(2R*,3S*,4R*)-4-(4-chlorophenyl)-3-nitro-6-phenyl-2-p-toly l-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 55 mg, 64%; yellow solid; mp 197–199 °C; Rf = 0.33 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.82 (d, J = 7.1 Hz, 2H),
7.50–7.37 (m, 5H), 7.29–7.19 (m, 6H), 5.41 (d, J = 9.8 Hz, 1H), 4.88 (t, J = 10.1 Hz, 1H), 4.59 (d, J = 10.4 Hz, 1H), 2.35 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 166.2, 140.8, 135.4, 134.1, 132.1, 131.1, 130.0, 130.0, 129.7, 129.3, 128.8, 128.6, 127.3, 117.5, 90.7, 86.9, 80.4, 46.8, 21.4; IR (KBr) 2359, 2211, 1615, 1557, 1274, 1149, 818, 695; HRMS (ESI) calcd for C25H20ClN2O3 [M+H]+ 431.11570, found 431.11616.

(2R*,3S*,4R*)-4-(4-chlorophenyl)-2-(4-methoxyphenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 52 mg, 58%; yellow solid; mp 194–196 °C; Rf = 0.33 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.81 (dd, J = 8.2, 1.2 Hz, 2H), 7.50–7.23 (m, 9H), 6.91 (d, J = 8.7 Hz, 2H), 5.40 (d, J = 9.8 Hz, 1H), 4.87 (t, J = 10.1 Hz, 1H), 4.58 (d, J = 10.4 Hz, 1H), 3.79 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 166.3, 161.3, 135.4, 134.1, 132.1, 131.1, 130.0, 129.3, 128.9, 128.8, 128.6, 124.5, 117.6, 114.7, 90.7, 86.8, 80.3, 55.5, 46.9; IR (KBr) 2210, 1614, 1556, 1252, 1178, 1148, 737, 698; HRMS (ESI) calcd for C25H20ClN2O4 [M+H]+ 447.11061, found 447.11091.

(2R*,3S*,4R*)-2,4-bis(4-chlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 58 mg, 64%; yellow solid; mp 189–191 °C; Rf = 0.33 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.82–7.80 (m, 2H), 7.53–7.32 (m, 9H), 7.26–7.23 (m, 2H), 5.44 (d, J = 9.8 Hz, 1H), 4.84 (t, J = 10.1 Hz, 1H), 4.59 (d, J = 10.4 Hz, 1H); 13C NMR (75 MHz, CDCl3) δ 165.9, 136.8, 135.5,
133.8, 132.2, 131.2, 130.9, 130.1, 129.6, 129.3, 128.9, 128.7, 128.5, 117.3, 90.6, 87.2, 79.7, 46.7; IR (KBr) 2360, 2211, 1616, 1557, 1272, 1149, 827, 696; HRMS (ESI) calcd for C$_{24}$H$_{17}$Cl$_2$N$_2$O$_3$ [M+H]$^+$ 451.06107, found 451.06121.

(2R*,3S*,4R*)-2-(4-bromophenyl)-4-(4-chlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 72 mg, 73%; yellow solid; mp 194–196 °C; R$_f$ = 0.4 (petroleum ether/ethyl acetate = 5:1); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.82–7.79 (m, 2H), 7.55–7.37 (m, 7H), 7.27–7.22 (m, 4H), 5.41 (d, $J$ = 9.8 Hz, 1H), 4.84 (t, $J$ = 10.1 Hz, 1H), 4.58 (d, $J$ = 10.4 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 165.9, 135.5, 133.7, 132.5, 132.2, 131.7, 130.8, 130.0, 129.3, 128.9, 128.8, 128.5, 125.0, 117.3, 90.5, 87.1, 79.7, 46.7; IR (KBr) 2360, 2211, 1617, 1557, 1271, 1149, 824, 695; HRMS (ESI) calcd for C$_{24}$H$_{17}$BrClN$_2$O$_3$ [M+H]$^+$ 495.01056, found 495.01025.

(2R*,3S*,4R*)-4-(4-chlorophenyl)-2-(3-methoxyphenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 69 mg, 76%; yellow solid; mp 192–194 °C; R$_f$ = 0.33 (petroleum ether/ethyl acetate = 5:1); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.83 (d, $J$ = 7.6 Hz, 2H), 7.52–7.24 (m, 8H), 6.97–6.92 (m, 3H), 5.42 (d, $J$ = 9.8 Hz, 1H), 4.87 (t, $J$ = 10.1 Hz, 1H), 4.60 (d, $J$ = 10.3 Hz, 1H), 3.79 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 166.1, 160.2, 135.5, 134.1, 134.0, 132.1, 131.1, 130.5, 130.1, 129.3, 128.8, 128.6, 119.6, 117.5, 115.8, 113.2, 90.7, 87.0, 80.4, 55.5, 46.8; IR (KBr) 2359, 2210, 1614,
1557, 1273, 1151, 778, 697; HRMS (ESI) calcd for C$_{25}$H$_{20}$ClN$_2$O$_4$ [M+H]$^+$ 447.11061, found 447.11115.

(2R*,3S*,4R*)-3-nitro-2,4,6-triphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 62 mg, 81%; 2.3s/2.4s = 3/1; yellow solid. A small amount of 2.3s was obtained by careful recrystallization. Analytical data for 2.3s: mp 238–240 °C; R$_f$ = 0.4 (petroleum ether/ethyl acetate = 5:1); $^1$H NMR (300 MHz, DMSO) δ 7.73 (d, J = 6.8 Hz, 2H), 7.63–7.39 (m, 13H), 5.83 (d, J = 9.7 Hz, 1H), 5.71 (t, J = 10.0 Hz, 1H), 4.70 (d, J = 10.2 Hz, 1H); $^{13}$C NMR (75 MHz, DMSO) δ 165.2, 136.0, 133.4, 131.7, 131.5, 130.2, 129.1, 128.8, 128.6, 128.5, 128.4, 128.3, 117.8, 88.5, 87.3, 79.8, 46.5; IR (KBr) 2211, 1617, 1556, 1273, 1148, 773, 697. HRMS (ESI) calcd for C$_{24}$H$_{19}$N$_2$O$_3$ [M+H]$^+$ 383.13902, found 383.13993.

(2R*,3S*,4R*)-4-(4-bromophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 60 mg, 65%; yellow solid; mp 220–222 °C; R$_f$ = 0.33 (petroleum ether/ethyl acetate = 5:1); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.84–7.81 (m, 2H), 7.57–7.39 (m, 10H), 7.19 (dd, J = 8.8, 2.2 Hz, 2H), 5.45 (d, J = 9.8 Hz, 1H), 4.88 (t, J = 10.1 Hz, 1H), 4.60 (d, J = 10.3 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 166.2, 134.6, 133.0, 132.7, 132.1, 131.7, 130.7, 129.6, 129.3, 128.8, 128.6, 127.4, 123.6, 117.5, 90.7, 86.9, 80.5, 46.9; IR (KBr) 2210, 1617, 1556, 1273, 1148, 830, 696; HRMS (ESI) calcd for C$_{24}$H$_{18}$BrN$_2$O$_3$ [M+H]$^+$ 461.04953, found 461.05042.
(2R*,3S*,4R*)-3-nitro-4,6-diphenyl-2-propyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 42 mg, 60%; yellow solid; mp 173–175 °C; Rf = 0.5 (petroleum ether/ethyl acetate = 5:1); 1H NMR (300 MHz, CDCl3) δ 7.80 (dd, J = 8.0, 1.4 Hz, 2H), 7.51–7.37 (m, 6H), 7.26 (dd, J = 7.4, 1.5 Hz, 2H), 4.69 (t, J = 9.9 Hz, 1H), 4.53–4.42 (m, 2H), 1.81–1.52 (m, 4H), 0.99 (t, J = 7.0 Hz, 3H); 13CN M R (75 MHz, CDCl3) δ 165.3, 135.9, 131.8, 131.5, 129.7, 129.3, 128.8, 128.4, 127.9, 117.7, 89.6, 87.2, 77.7, 46.7, 33.0, 17.9, 13.7; IR (KBr) 2359, 2209, 1616, 1556, 1306, 1159, 761, 697; HRMS (ESI) calcd for C21H21N2O3 [M+H]+ 349.15467, found 349.15506.

2.8.3 [4+2] Annulation of Nitroalkenes with α-Cyano-α,β-Unsaturated Ketones Catalyzed by NHC-Precursor Cat.8c

An oven-dried 50 mL Schlenk tube was charged with nitroalkenes 2.1 (0.4 mmol, 2.0 eq.), α-cyano α,β-unsaturated ketones 2.2 (0.2 mmol, 1.0 eq.), cat.8c (16 mg, 0.04 mol, 0.2 eq.), and AcONa (0.2 mmol, 16 mg, 1.0 eq.). To this mixture was added freshly distilled toluene (2 mL). The reaction mixture was stirred at room temperature until the full consumption of the α-cyano α,β-unsaturated ketones (typically, 18 h). The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleumether/EtOAc as the eluent, typically 20:1-0:100) to furnish the corresponding cycloadduct as a mixture of trans- and cis isomers.

(2S*,3S*,4R*)-4-(3-chlorophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile
Total yield: 74 mg, 90%; \textbf{2.4a/2.3a} = 3/1; yellow solid. A small amount of \textbf{2.4a} was obtained by recrystallization. Analytical data for \textbf{2.4a}: \( R_f = 0.4 \) (petroleum ether/ethyl acetate = 5:1); \(^1\text{H} \) NMR (300 MHz, DMSO) \( \delta \) 7.91 (dd, \( J = 7.4, 2.1 \) Hz, 2H), 7.79 (s, 1H), 7.62–7.59 (m, 3H), 7.53–7.49 (m, 3H), 7.38 (d, \( J = 1.6 \) Hz, 5H), 5.75 (d, \( J = 2.0 \) Hz, 1H), 5.55 (d, \( J = 1.3 \) Hz, 1H), 4.85 (s, 1H); \(^{13}\text{C} \) NMR (75 MHz, DMSO) \( \delta \) 165.6, 140.5, 134.1, 133.7, 132.1, 131.4, 130.8, 129.2, 128.7, 128.6, 128.5, 128.2, 127.8, 125.6, 118.8, 85.8, 84.0, 73.6, 41.7. IR (KBr) 2210, 1622, 1556, 1156, 776, 696; HRMS (ESI) calcd for C\(_{24}\)H\(_{18}\)ClN\(_2\)O\(_3\) [M +H]\(^+\) 417.10005, found 417.10039.

\[ \text{(2S*,3S*,4R*)-4-(4-chlorophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile} \]

Total yield: 73 mg, 87%; \textbf{2.4 m/2.3 m} = 3/1; yellow solid. A small amount of \textbf{2.4 m} was obtained by careful chromatograph. Analytical data for \textbf{2.4 m}: mp 176–178 °C; \( R_f = 0.35 \) (petroleum ether/ethyl acetate = 5:1); \(^1\text{H} \) NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.95–7.93 (m, 2H), 7.53–7.46 (m, 5H), 7.39–7.37 (m, 5H), 7.25–7.23 (m, 2H), 5.35 (d, \( J = 2.3 \) Hz, 1H), 5.01 (t, \( J = 2.2 \) Hz, 1H), 4.38 (s, 1H); \(^{13}\text{C} \) NMR (75 MHz, CDCl\(_3\)) \( \delta \) 166.5, 136.4, 135.4, 133.3, 131.9, 131.8, 130.2, 129.9, 129.7, 129.2, 128.8, 128.5, 125.7, 118.5, 87.2, 83.4, 74.0, 43.6; IR (KBr) 2210, 1624, 1555, 1298, 1159, 828, 697; HRMS (ESI) calcd for C\(_{24}\)H\(_{18}\)ClN\(_2\)O\(_3\) [M +H]\(^+\) 417.10005, found 417.09975.

\[ \text{(2S*,3S*,4R*)-4-(4-chlorophenyl)-3-nitro-6-phenyl-2-(p-tolyl)-3,4-dihydro-2H-pyran-5-carbonitrile} \]

Total yield: 78 mg, 91%; \textbf{2.4n/2.3n} = 3/1; yellow solid. A small amount of \textbf{2.4n} was obtained by careful chromatograph. Analytical data for \textbf{2.4n}: mp 159–161 °C;
$R_f = 0.35$ (petroleum ether/ethyl acetate = 5:1); $^1$H NMR (300 MHz, CDCl$_3$)  δ 7.93 (dd, $J = 7.9$, 1.5 Hz, 2H), 7.52–7.45 (m, 5H), 7.37 (d, $J = 8.5$ Hz, 2H), 7.14 (dd, $J = 19.6$, 8.2 Hz, 4H), 5.33 (d, $J = 2.3$ Hz, 1H), 4.98 (t, $J = 2.4$ Hz, 1H), 4.36 (d, $J = 1.5$ Hz, 1H), 2.34 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 166.5, 139.7, 136.4, 135.3, 131.9, 131.8, 130.3, 130.1, 129.9, 129.8, 128.8, 128.5, 125.6, 118.6, 87.3, 83.4, 74.1, 43.5, 21.3; IR (KBr) 2210, 1624, 1555, 1298, 1159, 830, 696; HRMS (ESI) calcd for C$_{25}$H$_{20}$ClN$_2$O$_3$ [M+H]$^+$ 431.11570, found 431.11618.

(2S*,3S*,4R*)-4-(4-chlorophenyl)-2-(4-methoxyphenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Total yield: 75 mg, 85%; $2.4o/2.3o = 2/1$; yellow solid. A small amount of $2.4o$ was obtained by careful chromatograph. Analytical data for $2.4o$: mp 179–181 °C; $R_f = 0.35$ (petroleum ether/ethyl acetate = 5:1); $^1$H NMR (300 MHz, CDCl$_3$)  δ 7.94–7.91 (m, 2H), 7.55–7.45 (m, 5H), 7.37 (d, $J = 8.5$ Hz, 2H), 7.15 (d, $J = 8.8$ Hz, 2H), 6.88 (d, $J = 8.7$ Hz, 2H), 5.31 (d, $J = 2.5$ Hz, 1H), 4.97 (t, $J = 2.3$ Hz, 1H), 4.36 (d, $J = 1.6$ Hz, 1H), 3.79 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 166.6, 160.6, 136.4, 135.3, 131.9, 131.8, 130.1, 129.9, 128.8, 128.5, 127.1, 125.2, 118.6, 114.6, 87.3, 83.4, 74.0, 55.5, 43.5; IR (KBr) 2210, 1615, 1555, 1524, 1555, 1254, 1159, 826, 772, 696; HRMS (ESI) calcd for C$_{25}$H$_{20}$ClN$_2$O$_4$ [M+H]$^+$ 447.11061, found 447.11062.

(2S*,3S*,4R*)-2,4-bis(4-chlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Total yield: 83 mg, 92%; $2.4p/2.3p = 2/1$; yellow solid. A small amount of $2.4p$ was obtained by careful chromatograph. Analytical data for $2.4p$: mp 174–176 °C;
Rf = 0.35 (petroleum ether/ethyl acetate = 5:1); ¹H NMR (300 MHz, CDCl₃) δ 7.93–7.91 (m, 2H), 7.57–7.46 (m, 5H), 7.39–7.34 (m, 4H), 7.18 (d, J = 8.5 Hz, 2H), 5.31 (d, J = 2.2 Hz, 1H), 4.97 (t, J = 2.1 Hz, 1H), 4.40 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 166.3, 136.2, 135.7, 135.5, 132.0, 131.9, 131.6, 130.3, 129.4, 128.9, 128.4, 127.1, 118.3, 87.0, 83.5, 73.4, 43.5; IR (KBr) 2210, 1624, 1555, 1298, 1159, 830, 696; HRMS (ESI) calcd for C₂₄H₁₇Cl₂N₂O₃ [M+H]⁺ 451.06107, found 451.06127.

(2S*,3S*,4R*)-2-(4-bromo phenyl)-4-(4-chlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Total yield: 82 mg, 83%; 2.4q/2.3q = 2/1; yellow solid. A small amount of 2.4q was obtained by careful chromatograph. Analytical data for 2.4q: mp 186–188 °C; Rf = 0.42 (petroleum ether/ethyl acetate = 5:1); ¹H NMR (300 MHz, CDCl₃) δ 7.93–7.90 (m, 2H), 7.56–7.46 (m, 7H), 7.37 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 5.29 (d, J = 1.8 Hz, 1H), 4.97 (d, J = 1.8 Hz, 1H), 4.40 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 166.3, 136.2, 135.5, 132.4, 132.4, 132.0, 131.6, 130.2, 129.8, 128.9, 128.4, 127.3, 123.9, 118.3, 86.9, 83.5, 73.4, 43.5; IR (KBr) 2210, 1620, 1555, 1297, 1158, 826, 695; HRMS (ESI) calcd for C₂₄H₁₇BrClN₂O₃ [M+H]⁺ 495.01056, found 495.01076.

(2S*,3S*,4R*)-4-(4-chlorophenyl)-2-(3-methoxyphenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

(2S*,3S*,4R*)-2-(4-bromo phenyl)-4-(4-chlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Experimental Part
Total yield: 80 mg, 90%; \(2.4r/2.3r = 4/1\); yellow solid. A small amount of \(2.4r\) was obtained by careful chromatograph. Analytical data for \(2.4r\): mp 154–156 °C; \(R_p = 0.35\) (petroleum ether/ethyl acetate = 5:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.94 (dd, \(J = 8.0, 1.6\) Hz, 2H), 7.55–7.45 (m, 5H), 7.36 (d, \(J = 8.5\) Hz, 2H), 7.28–7.25 (m, 1H), 6.91–6.88 (m, 1H), 6.80–6.78 (m, 2H), 5.30 (d, \(J = 2.2\) Hz, 1H), 5.00 (t, \(J = 2.1\) Hz, 1H), 4.37 (d, \(J = 0.9\) Hz, 1H), 3.76 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 166.4, 160.1, 136.4, 135.4, 134.8, 131.9, 130.3, 130.2, 129.9, 128.8, 128.5, 118.5, 117.8, 114.6, 111.8, 87.2, 83.4, 73.8, 55.5, 43.5; IR (KBr) 2210, 1613, 1555, 1293, 1151, 772, 694; HRMS (ESI) calcd for \(C_{25}H_{20}ClN_2O_4\) [M+H]\(^+\) 447.11061, found 447.11061.

![2.4s](image)

\((2S^*,3S^*,4R^*)-3\text{-nitro-2,4,6-triphenyl-3,4-dihydro-2H-pyran-5-carbonitrile}\)

Total yield: 68 mg, 89%; \(2.4s/2.3s = 5/1\); yellow solid. A small amount of \(2.4s\) was obtained by careful recrystallization. Analytical data for \(2.4s\): \(R_p = 0.5\) (petroleum ether/ethyl acetate = 5:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.96 (dd, \(J = 7.8, 1.6\) Hz, 2H), 7.53–7.35 (m, 11H), 7.25 (s, 2H), 5.38 (d, \(J = 2.1\) Hz, 1H), 5.10 (t, \(J = 2.1\) Hz, 1H), 4.42 (s, 1H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 166.3, 138.0, 133.6, 132.0, 131.7, 129.9, 129.6, 129.4, 129.2, 129.1, 128.8, 128.5, 125.7, 118.8, 87.5, 83.7, 73.8, 44.3; IR (KBr) 2210, 1623, 1556, 1290, 1152, 769, 698. HRMS (ESI) calcd for \(C_{24}H_{19}N_2O_3\) [M+H]\(^+\) 383.13902, found 383.13918.

![2.4t](image)

\((2S^*,3S^*,4R^*)-4-(4\text{-bromophenyl})-3\text{-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile}\)

Total yield: 85 mg, 93%; \(2.4t/2.3t = 4/1\); yellow solid. A small amount of \(2.4t\) was obtained by careful chromatograph. Analytical data for \(2.4t\): mp 170–172 °C; \(R_p = 0.35\) (petroleum ether/ethyl acetate = 5:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.94 (d, \(J = 6.6\) Hz, 2H), 7.63–7.05 (m, 5H), 7.38–7.22 (m, 7H), 5.35 (d, \(J = 1.9\) Hz, 1H), 5.01 (d, \(J = 1.8\) Hz, 1H), 4.36 (s, 1H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\))
δ 166.5, 136.9, 133.3, 133.1, 131.9, 131.8, 130.2, 129.7, 129.1, 128.8, 128.5, 125.6, 123.5, 118.5, 87.1, 83.3, 74.0, 43.6; IR (KBr) 2210, 1624, 1555, 1298, 1159, 824, 696; HRMS (ESI) calcd for C_{24}H_{18}BrN_{2}O_{3} [M+H]^+ 461.04953, found 461.04928.

(2S*,3S*,4R*)-2-(3-chlorophenyl)-4-(4-chlorophenyl)-3-nitro-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Total yield: 79 mg, 88%; 2.4v/2.3v = 2/1; yellow solid. A small amount of 2.4v was obtained by careful chromatograph. Analytical data for 2.4v: mp 100–102 °C; R_f = 0.4 (petroleum ether/ethyl acetate = 5:1); ^1H NMR (300 MHz, CDCl_3) δ 7.93 (dd, J = 8.0, 1.4 Hz, 2H), 7.57–7.47 (m, 5H), 7.49–7.23 (m, 5H), 7.13 (d, J = 7.3 Hz, 1H), 5.29 (s, 1H), 4.99 (dd, J = 2.3, 1.6 Hz, 1H), 4.42 (s, 1H); ^13C NMR (75 MHz, CDCl_3) δ 166.3, 136.1, 135.5, 135.4, 135.2, 132.0, 131.6, 130.5, 130.3, 129.8, 128.9, 128.5, 125.9, 123.8, 118.3, 86.9, 83.6, 73.1, 43.6; IR (KBr) 2210, 1556, 1298, 1151, 831, 694; HRMS (ESI) calcd for C_{24}H_{17}Cl_{2}N_{2}O_{3} [M+H]^+ 451.06107, found 451.06113.

(2S*,3S*,4R*)-4-(2-chlorophenyl)-3-nitro-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 37 mg, 44%; white solid; mp 158–160 °C; R_f = 0.33 (petroleum ether/ethyl acetate = 5:1); ^1H NMR (300 MHz, CDCl_3) δ 7.97–7.94 (m, 2H), 7.57–7.47 (m, 5H), 7.43–7.35 (m, 5H), 7.24–7.21 (m, 2H), 5.26 (d, J = 1.8 Hz, 1H), 5.04 (dd, J = 2.4, 1.1 Hz, 1H), 4.84 (s, 1H); ^13C NMR (75 MHz, CDCl_3) δ 167.2, 134.8, 134.2, 133.4, 131.9, 131.8, 131.0, 130.6, 130.3, 129.6, 129.1, 128.8, 128.5, 128.1, 125.7, 118.6, 85.5, 83.0, 74.1, 41.8; IR (KBr) 2359, 2210, 1622, 1555, 1295, 1156, 856, 695; HRMS (ESI) calcd for C_{24}H_{18}Cl_{2}N_{2}O_{3} [M+H]^+ 417.10005, found 417.10029.
2.8.4 Reduction of the Nitro Group of 2.3

Typical procedure: To a stirred solution of 2.3c (128 mg, 0.28 mmol) in EtOH (4 mL) was added zinc powder (330 mg, 18.0 eq.) and 1.5 mL of 6 M HCl (aq.). The resulting reaction mixture was stirred at room temperature for 1.0 h. followed by the filtration through Celite with washing by ether. The solvent was removed in vacuo. NaOH (15%) was added to the above mixture until pH 10. The aqueous layer was extracted with ether, the combined organic layer was washed with brine, dried (MgSO₄), and concentrated to give the products 2.5c.

(2R*,3S*,4R*)-3-amino-4-(3,5-dichlorophenyl)-2,6-diphenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 79%; yellow solid; mp 181–183 °C; Rₚ = 0.5 (petroleum ether/ethyl acetate = 1:1); ¹H NMR (300 MHz, CDCl₃) δ 7.82 (dd, J = 8.1, 1.5 Hz, 2H), 7.47–7.35 (m, 9H), 7.28 (d, J = 1.8 Hz, 2H), 4.86 (d, J = 9.5 Hz, 1H), 3.60 (d, J = 9.5 Hz, 1H), 3.23 (t, J = 9.5 Hz, 1H), 0.93 (br, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 166.8, 143.0, 135.9, 132.1, 131.6, 129.7, 129.2, 128.8, 128.6, 128.5, 127.8, 127.1, 118.9, 86.7, 84.6, 56.3, 49.9; IR (KBr) 2359, 2207, 1613, 1587, 1270, 1156, 801, 698; HRMS (ESI) calcd for C₂₄H₁₉Cl₂N₂O [M+H]+ 421.08690, found 421.08717.
(2R*,3S*,4R*)-3-amino-4-(3,5-dichlorophenyl)-6-phenyl-2-(p-tolyl)-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 86%; yellow solid; mp 100–102 °C; R_f = 0.33 (petroleum ether/ethyl acetate = 1:1); 1H NMR (300 MHz, CDCl3) δ 7.82–7.79 (m, 2H), 7.45–7.20 (m, 10H), 4.82 (d, J = 9.5 Hz, 1H), 3.57 (d, J = 9.5 Hz, 1H), 3.22 (t, J = 9.5 Hz, 1H), 2.37 (s, 3H), 0.98 (br, 2H); 13C NMR (75 MHz, CDCl3) δ 166.7, 143.1, 139.6, 135.8, 132.9, 132.1, 131.4, 129.7, 128.6, 128.5, 128.5, 127.7, 127.1, 118.9, 86.5, 84.6, 56.1, 50.0, 21.3; IR (KBr) 2360, 2207, 1613, 1567, 1269, 1156, 803, 696; HRMS (ESI) calcd for C25H21Cl2N2O [M+H]+ 435.10255, found 435.10376.

(2R*,3S*,4R*)-3-amino-4-(4-chlorophenyl)-6-phenyl-2-(p-tolyl)-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 90%; yellow solid; mp 169–171 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 1:1); 1H NMR (300 MHz, CDCl3) δ 7.81 (dd, J = 7.9, 1.3 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 4.85 (d, J = 9.5 Hz, 1H), 3.62 (d, J = 9.5 Hz, 1H), 3.23 (t, J = 9.5 Hz, 1H), 2.37 (s, 3H), 0.96 (br, 2H); 13C NMR (75 MHz, CDCl3) δ 166.4, 139.6, 137.9, 134.2, 133.3, 132.4, 131.3, 129.9, 129.8, 129.6, 128.8, 128.5, 127.7, 119.2, 87.4, 84.6, 56.3, 49.8, 21.4; IR (KBr) 2359, 2206, 1613, 1516, 1274, 1154, 816, 697; HRMS (ESI) calcd for C25H22ClN2O [M+H]+ 401.14152, found 401.14203.

(2R*,3S*,4R*)-3-amino-4-(4-chlorophenyl)-2-(4-methoxyphenyl)-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

Yield: 90%; yellow solid; mp 169–171 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 1:1); 1H NMR (300 MHz, CDCl3) δ 7.81 (dd, J = 7.9, 1.3 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 4.85 (d, J = 9.5 Hz, 1H), 3.62 (d, J = 9.5 Hz, 1H), 3.23 (t, J = 9.5 Hz, 1H), 2.37 (s, 3H), 0.96 (br, 2H); 13C NMR (75 MHz, CDCl3) δ 166.4, 139.6, 137.9, 134.2, 133.3, 132.4, 131.3, 129.9, 129.8, 129.6, 128.8, 128.5, 127.7, 119.2, 87.4, 84.6, 56.3, 49.8, 21.4; IR (KBr) 2359, 2206, 1613, 1516, 1274, 1154, 816, 697; HRMS (ESI) calcd for C25H22ClN2O [M+H]+ 401.14152, found 401.14203.
Yield: 70%; yellow solid; mp 180–182 °C; Rf = 0.5 (petroleum ether/ethyl acetate = 1:1); 1H NMR (300 MHz, CDCl3) δ 7.73 (dd, J = 8.0, 1.5 Hz, 2H), 7.38–7.25 (m, 9H), 6.88 (d, J = 8.7 Hz, 2H), 4.77 (d, J = 9.5 Hz, 1H), 3.75 (s, 3H), 3.55 (d, J = 9.5 Hz, 1H), 3.16 (t, J = 9.5 Hz, 1H), 1.18 (br, 2H); 13C NMR (75 MHz, CDCl3) δ 166.4, 160.6, 138.0, 134.2, 132.5, 131.3, 129.9, 129.6, 129.1, 128.5, 128.2, 119.2, 114.5, 87.4, 84.4, 56.3, 55.5, 49.8; IR (KBr) 23580, 2206, 1613, 1515, 1277, 1153, 829, 698; HRMS (ESI) calcd for C25H22ClN2O2 [M+H]+ 417.13643, found 417.13700.

2.8.5 Reaction Catalyzed by Chiral NHC-Precursor Cat.2d

![Reaction scheme]

The reaction was carried out as the same procedure in Table 2.1: Yield: 24%; HPLC analysis: 29% ee. [Daicei CHIRALPAK AD-H column; 20 °C; 0.8 mL/min; solvent system: isopropanol/hexanes = 8:92; retention times: 13.5 min (minor), 14.9 min (major)].

References

New Strategies for N-Heterocyclic Carbenes Catalyzed Annulations
Chen, X.
2017, XIV, 123 p. 66 illus., 13 illus. in color., Hardcover
ISBN: 978-981-10-2898-4