Efficient Enantioselective Synthesis of Dihydropyrans Using a Chiral $N,N'$-dioxide as Organocatalyst

Juhua Feng, Xuan Fu, Zhenling Chen, Lili Lin, Xiaohua Liu, and Xiaoming Feng*
Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, P. R. China

xmfeng@scu.edu.cn

Supporting Information

1. General..........................................................................................................................S2
2. General procedure for the preparation of the racemic products...........................................S2
3. General experimental procedure for the catalytic asymmetric Michael/hemiacetalization reaction..S2
4. Experimental procedure for the synthesis of the β, γ-unsaturated-α-ketoester.........................S2
5. Extra condition optimizations for the asymmetric Michael/hemiacetalization reaction............S3
6. Characterization of the catalysts......................................................................................S5
7. Characterization of the alkyl 2-oxo-4-arylbut-3-enoate.....................................................S7
8. Characterization of the products.......................................................................................S8
9. Copy of $^1$H NMR and $^{13}$C NMR spectra for the catalysts................................................S33
10. Copy of $^1$H NMR and $^{13}$C NMR spectra for the substrates............................................S42
11. Copy of $^1$H NMR and $^{13}$C NMR spectra for the products...............................................S46
12. Mechanism Evidence and Corresponding NMR spectra..................................................S73
13. Reference......................................................................................................................S79
1. General

$^1$H NMR spectra were recorded on commercial instruments (400 MHz). The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz) and integration. $^{13}$C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel ADH/IB/IC/OD-H in comparison with the authentic racemates. Optical rotations were reported as follows: $[\alpha]_D^2 = (c: g/100 mL, in solvent)$. ESI-HRMS was recorded on a commercial apparatus (ESI Source, TOF). Unless otherwise indicated, all compounds and reagents were purchased from commercial suppliers and used without further purification. Toluene, Et$_2$O and THF were dried and distilled from sodium benzenophenone under nitrogen just before use. 4 Å MS was powdered <50 µm, which was activated at 300 °C for 2 h and stored under nitrogen. The $N,N'$-dioxides were prepared according to the methods reported in the literature.$^1$

2. General procedure for the preparation of the racemic products

$$
\begin{align*}
\text{R}^1\text{C}=\text{O}+\text{CN} & \quad \text{DMAP (10 mol %)} \quad \text{Et}_2\text{O} \\
\text{R}^2\text{CN} & \quad \text{R}^3\text{CN} \quad \text{race-3}
\end{align*}
$$

The reaction was conducted with $\beta,\gamma$-unsaturated $\alpha$-ketoester 1 (0.11 mmol), $\alpha$-substituted cyano ketone 2 (0.10 mmol) and DMAP (4-dimethylaminopyridin, 0.01 mmol) in 3.0 mL of Et$_2$O (diethyl ether). The mixture was stirred at room temperature for 12 hours, then the crude product was purified directly by column chromatography on silica gel (petroleum ether / acetone = 6:1) to afford the corresponding products.

3. General experimental procedures for the catalytic asymmetric Michael/hemiacetalization reaction

$$
\begin{align*}
\text{R}^1\text{C}=\text{O}+\text{CN} & \quad \text{C3 (10 mol %)} \\
\text{R}^2\text{CN} & \quad \text{R}^3\text{CN} \quad \text{3}
\end{align*}
$$

$\beta,\gamma$-unsaturated $\alpha$-ketoester 1 (0.12 mmol), $\alpha$-substituted cyano ketone 2 (0.10 mmol), $p$-$\text{BuC}_6\text{H}_4\text{COOH}$ (0.05 mmol), and 4 Å MS (20 mg) were dissolved in 3.0 mL of MTBE at -30°C. The mixture was stirred in a test tube under N$_2$ atmosphere. Then the crude product was purified directly by column chromatography on silica gel (petroleum ether / acetone = 7:1, petroleum ether / acetone = 5:1) to afford the corresponding products.

4. Experimental procedure for the synthesis of the $\beta,\gamma$-unsaturated $\alpha$-ketoester

A modification of procedure reported by Alexakis et al. was followed.$^2$

(1): Aldol condensation$^3$:

$$
\begin{align*}
\text{R}^1\text{CHO} + \text{R}^2\text{CHO} & \quad \text{a) KH, MeOH, 10-40°C, 36 h} \\
\text{R}^1\text{CHO} & \quad \text{b) AcCl, R'CH, 0°C to r.t, 6 h}
\end{align*}
$$

To a benzaldehyde derivatives (0.20 mol) solution in methanol (15 mL) was added pyruvic acid (0.20 mol), and the mixture was cooled to 10 °C under the atmosphere of nitrogen. To this was added a solution of KOH (0.30 mol) in methanol (60 mL) dropwise at 15-20 °C, after the addition of two thirds of the alkali, the rest of the alkali was added in one part before precipitation of potassium pyruvate could occur. Then the ice-bath was removed, and the temperature of the reaction mixture increased from 20 °C to 35-40 °C. The reaction mixture was stirred at this temperature for 3 h and then maintained at 10 °C for 10 h. The solid precipitated out was filtered on a Buchner funnel under suction and washed with chilled methanol (75 mL) followed by diethyl ether (75 mL) to afford potassium 4-phenyl-2-oxo-but-3-enoate as a yellow solid. Acetyl chloride (50 mL) was added dropwise to the corresponding dry alcohol (350 mL) cooled in an ice bath to produce dry hydrochloric acid. Potassium benzylidene pyruvate (10.7 g, 50 mmol) was added at 0 °C. The
reaction was warmed to room temperature and stirred for 2 h and then refluxed for 6 h. The solvent was removed by evaporation. Water (75 mL) was added to the crude product which was then extracted with CH₂Cl₂ (80 mL × 2). The combined organic phase was washed with a saturated solution of NaHCO₃ (50 mL × 2) and then with water (50 mL). After, the organic layer was separated and dried over MgSO₄, the solvent was evaporated, the crude product was recrystallized in ethanol (-5 °C) to give the corresponding β,γ-unsaturated-α-ketoester or purified by flash chromatography.

(2): Mukaiyama aldol addition:

a) Preparation of alkyl or aryl acetal derivatives⁴:

A solution of aldehyde (100 mmol), p-toluenesulfonic acid monohydrate (5 mmol) and trimethyl orthoformate (1.0 mol) in dry methanol (200 mL) was heated to reflux for 24 h. A part of the solvent was evaporated in vacuo, Et₂O (250 mL) was added to the residue (ca. 50 mL), and the mixture was washed with a saturated solution of NaHCO₃ (250 mL). After drying (MgSO₄), the organic layer was concentrated in vacuo and the residue was purified by flash chromatography.

b) Preparation of methyl 2-((trimethylsilyl)oxy)acrylate⁵:

To a solution of methyl pyruvate (1.42 mol) in dry benzene were added DMAP (2.5 mmol) and trimethylsilyl chloride (2.48 mol). Triethylamine (2.84 mol) was then added dropwise to the mixture, which was kept under gentle reflux by controlling the dropping rate. After the addition was complete, the mixture was refluxed for an additional 2 h. After cooling of the mixture, a white precipitate of triethylamine hydrochloride was filtered off via a glass filter under a stream of argon. The solvent was removed under reduced pressure, and the residue was distilled to afford methyl 2-((trimethylsilyl)oxy)acrylate as a colorless oil.

c) Preparation of alkyl 2-oxo-4-arylbut-3-enoate:

Mukaiyama aldol addition⁶:

To a mixture of acetald (10 mmol) and methyl 2-((trimethylsilyl)oxy)acrylate (12 mmol) in dry dichloromethane (50 mL) under argon at -78 °C was added dropwise boron trifluoride diethyl ether (11 mmol). The reaction mixture was warmed to 0 °C for over 1 h and stirred at the same temperature for 2 h. Saturated NaHCO₃ was added, and the mixture was extracted with CH₂Cl₂. The organic layer was dried over MgSO₄ and concentrated under reduce pressure to afford crude γ-alkoxy-α-oxo esters, which were dissolved in benzene (100 mL). Then, silica gel was added and the mixture was heated at reflux with vigorous stirring for 24 h. After being cooled to room temperature, the mixture was filtered and the residual solid was washed with ether several times. The filtrate was combined, concentrated and dried with Na₂SO₄ to give the crude β,γ-unsaturated-α-ketoester. The purification was done by flash column chromatography with the appropriate mixture of hexane/ethyl acetate to obtain a yellow oil or solid.

5. Extra condition optimizations for the asymmetric Michael/hemiacetalization reaction

Table 1: Exploring the efficiency of catalyst and solvent on the asymmetric Michael/hemiacetalization reaction⁴
entry & catalyst & solvent & yield (%) & ee (%) \\
--- & --- & --- & --- & --- \\
1 & C3 & THF & 78 & 55 \\
2 & C12 & THF & 90 & 3 \\
3 & C13 & THF & 52 & 52 \\
4 & C3 & CH2Cl2 & 67 & 8 \\
5 & C3 & PhMe & 89 & 40 \\
6 & C3 & Ethyl acetate & 62 & 50 \\

* Unless otherwise noted, all reactions were conducted with 1a (0.12 mmol), 2a (0.10 mmol), and catalyst (10 mol %) in solvent (1.0 mL) under N2 at 0 °C for 24 h. † Isolated yields. ‡ Determined by chiral HPLC analysis.

**Table 2:** Exploring the efficiency of additive and temperature on the asymmetric Michael/hemiacetalization reaction

entry & additive & temperature (°C) & time & yield (%) & ee (%) \\
--- & --- & --- & --- & --- & --- \\
1 & DMAP & 0 & 48h & 93 & 61 \\
2 & Et3N & 0 & 48h & 90 & 60 \\
3 & o-Nitrobenzoic acid & 0 & 48h & 84 & 53 \\
4 & o-Phthalic acid & 0 & 48h & 77 & 33 \\
5 & p-Toluenesulfonic acid & 0 & 48h & 77 & 60 \\
6 & p-BuC6H4COOH & 0 & 48h & 86 & 71 \\
7 & p-Chlorobenzoic acid & 0 & 48h & 81 & 72 \\
8 & Benzoic acid & 0 & 48h & 88 & 71 \\
9 & no & -30 & 72h & 78 & 82 \\
10 & 4-tert-Butylphenol & -30 & 72h & 83 & 83 \\
11 & p-BuC6H4COOH & -30 & 72h & 83 & 78 \\
12 & p′-BuC6H4COOH & -30 & 72h & 87 & 82 \\
13 & p′-BuC6H4COOH & -30 & 72h & 92 & 86 \\
14 & p′-BuC6H4COOH & -30 & 72h & 86 & 85 \\

* Unless otherwise noted, all reactions were conducted with 1a (0.12 mmol), 2a (0.10 mmol), additive (10 mol %), 4 Å MS (20 mg) and C3 (10 mol %) in MTBE (3.0 mL) under N2. † Isolated yields. ‡ Determined by HPLC analysis. § 20 mol % of p-BuC6H4COOH were used. ‡ 50 mol % of p-BuC6H4COOH were used. § 70 mol % of p-BuC6H4COOH were used.
6. Characterization of the catalysts

chiral $N,N'$-dioxide C3:

Prepared according to the methods reported in the literature.\textsuperscript{1} \textsuperscript{1}H NMR (400 MHz, CDCl$_3$): δ = 12.22 – 11.85 (m, 2H), 7.23 – 7.06 (m, 10H), 5.42 – 5.30 (m, 2H), 3.76 (s, 1H), 3.63 – 3.53 (m, 2H), 3.40 – 3.31 (m, 2H), 3.24 – 3.12 (m, 2H), 2.98 – 2.86 (m, 2H), 2.56 – 2.31 (m, 6H), 2.27 – 2.17 (m, 2H), 1.96 – 1.81 (m, 4H), 1.74 – 1.59 (m, 4H), 1.55 – 1.45 (m, 2H), 1.43 – 1.32 (m, 2H), 1.28 – 1.23 (m, 1H), 1.08 – 0.90 (m, 6H). \textsuperscript{13}C NMR (100 MHz, CDCl$_3$): δ = 168.4, 139.1, 128.2, 127.5, 127.3, 75.6, 72.3, 65.2, 57.5, 28.1, 27.5, 27.4, 25.3, 25.1, 24.9, 20.2. ES-HRMS Calcd for C$_{36}$H$_{51}$N$_{6}$O$_{3}$ [M + H]$^+$ m/z 603.3910, Found: m/z 603.3909.

chiral $N,N'$-dioxide C4:

Prepared according to the methods reported in the literature.\textsuperscript{1} \textsuperscript{1}H NMR (400 MHz, CDCl$_3$): δ = 11.81 (brs, 2H), 7.48 – 7.43 (m, 4H), 7.37 – 7.31 (m, 5H), 7.24 – 7.21 (m, 1H), 5.50 – 5.32 (m, 2H), 3.67 – 3.51 (m, 2H), 3.35 – 3.12 (m, 5H), 2.79 – 2.58 (m, 3H), 2.48 – 2.37 (m, 4H), 2.14 – 2.11 (m, 2H), 1.98 – 1.86 (m, 2H), 1.82 – 1.79 (m, 2H), 1.76 – 1.67 (m, 2H), 1.64 – 1.61 (m, 2H), 1.55 – 1.53 (m, 2H), 1.43 – 1.35 (m, 2H), 1.17 – 1.07 (m, 2H), 1.04 – 0.96 (m, 4H), 0.93 – 0.88 (m, 2H). \textsuperscript{13}C NMR (100 MHz, CDCl$_3$): δ = 169.0, 128.6, 127.3, 126.5, 75.2, 72.3, 65.3, 58.0, 28.4, 27.4, 26.7, 25.1, 24.9, 24.7, 19.9. ES-HRMS Calcd for C$_{36}$H$_{50}$N$_{6}$O$_{4}$Na [M + Na]$^+$ m/z 625.3730, Found: m/z 625.3737.

chiral $N,N'$-dioxide C5:

Prepared according to the methods reported in the literature.\textsuperscript{1} \textsuperscript{1}H NMR (400 MHz, CDCl$_3$): δ = 11.89 (brs, 2H), 7.28 – 7.12 (m, 10H), 5.39 – 5.37 (m, 2H), 4.10 – 3.80 (m, 2H), 3.71 – 3.67 (m, 2H), 3.20 – 3.07 (m, 3H), 2.87 – 2.82 (m, 2H), 2.68 – 2.55 (m, 3H), 2.40 – 2.34 (m, 2H), 2.17 – 2.01 (m, 5H), 1.91 – 1.88 (m, 2H), 1.65 – 1.50 (m, 14H), 1.32 – 1.27 (m, 2H), 1.17 – 1.15 (m, 2H), 1.03 – 0.87 (m, 5H). \textsuperscript{13}C NMR (100 MHz, CDCl$_3$): δ = 167.9, 139.2, 128.1, 127.8, 127.1, 80.5, 76.2, 65.8, 57.5, 41.9, 35.3, 32.1, 27.8, 27.7, 27.5, 25.5, 25.3, 25.0, 15.3. ES-HRMS Calcd for C$_{42}$H$_{59}$N$_{6}$O$_{4}$ [M + H]$^+$ m/z 683.4536, Found: m/z 683.4539.

chiral $N,N'$-dioxide C6:

Prepared according to the methods reported in the literature.\textsuperscript{1} \textsuperscript{1}H NMR (400 MHz, CDCl$_3$): δ =
11.78 (d, $J = 6.0$ Hz, 2H), 7.33 – 7.15 (m, 10H), 5.45 – 5.43 (m, 2H), 3.56 – 3.46 (m, 7H), 3.30 – 3.27 (m, 2H), 2.54 – 2.32 (m, 5H), 2.04 – 1.94 (m, 4H), 1.83 – 1.76 (m, 4H), 1.69 – 1.58 (m, 4H), 1.53 – 1.41 (m, 4H), 1.37 – 1.26 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.3$, 138.9, 128.1, 127.6, 127.2, 77.8, 75.2, 68.1, 57.7, 28.9, 27.3, 26.9, 24.2, 24.0, 20.6. ES-HRMS Calcd for C$_{13}$H$_{36}$N$_2$O$_4$Na [M + Na$^+$] m/z 597.3411, Found: m/z 597.3409.

**chiral N,N'-dioxide C7:**

Prepared according to the methods reported in the literature.$^1$ $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 11.97$ (brs, 2H), 7.32 – 7.15 (m, 10H), 5.44 (d, $J = 6.7$ Hz, 2H), 3.74 (s, 2H), 3.45 – 3.23 (m, 8H), 2.44 – 2.39 (m, 5H), 2.32 – 2.27 (m, 2H), 1.96 – 1.91 (m, 4H), 1.70 – 1.25 (m, 19H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.9$, 139.3, 128.1, 127.5, 127.2, 71.9, 63.3, 57.6, 53.4, 29.1, 28.3, 27.9, 27.8, 27.0, 25.5, 24.6, 20.2. ES-HRMS Calcd for C$_{13}$H$_{36}$N$_2$O$_4$ [M + H]$^+$ m/z 631.4218, Found: m/z 631.4214.

**chiral N,N'-dioxide C8:**

Prepared according to the methods reported in the literature.$^1$ $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 12.00$ (brs, 2H), 7.32 – 7.14 (m, 10H), 5.45 – 5.43 (m, 2H), 3.74 – 3.55 (m, 3H), 3.36 – 3.24 (m, 6H), 2.41 – 2.26 (m, 7H), 1.88 – 1.79 (m, 4H), 1.65 – 1.31 (m, 22H), 1.05 – 0.96 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.8$, 139.2, 128.2, 127.5, 127.2, 75.4, 72.0, 65.8, 63.0, 57.6, 28.6, 28.0, 26.1, 25.8, 25.7, 24.9, 20.2, 15.3. ES-HRMS Calcd for C$_{49}$H$_{99}$N$_2$O$_4$ [M + H]$^+$ m/z 659.4536, Found: m/z 659.4532.

**chiral N,N'-dioxide C9:**

Prepared according to the methods reported in the literature.$^1$ $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.24$ (d, $J = 5.2$ Hz, 2H), 7.19 – 7.11 (m, 10H), 5.30 – 5.28 (m, 2H), 3.24 – 3.22 (m, 2H), 3.09 – 3.05 (m, 2H), 2.51 – 2.44 (m, 2H), 2.17 – 2.11 (m, 2H), 2.05 – 1.94 (m, 2H), 1.82 – 1.79 (m, 2H), 1.74 – 1.62 (m, 8H), 1.50 – 1.48 (m, 6H), 1.11 – 0.75 (m, 10H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 175.9$, 139.2, 128.3, 127.4, 63.9, 61.3, 57.0, 49.9, 32.2, 30.9, 29.7, 25.9, 25.5, 25.3, 24.7. ES-HRMS Calcd for C$_{16}$H$_{36}$O$_2$ [M + H]$^+$ m/z 571.4012, Found: m/z 571.4008.

**chiral N,N'-dioxide C10:**

S6
Prepared according to the methods reported in the literature.\(^1\) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 11.92\) (s, 1H), 8.41 (s, 1H), 7.22 – 7.11 (m, 10H), 5.32 – 5.30 (m, 2H), 3.80 – 3.70 (m, 1H), 3.49 – 3.45 (m, 1H), 3.26 – 3.18 (m, 2H), 3.14 – 3.11 (m, 1H), 2.94 – 2.88 (m, 1H), 2.55 – 2.49 (m, 1H), 2.43 – 2.38 (m, 3H), 2.30 – 2.23 (m, 1H), 2.16 – 2.13 (m, 1H), 2.00 – 1.79 (m, 3H), 1.74 – 1.63 (m, 7H), 1.56 – 1.49 (m, 3H), 1.38 – 1.32 (m, 1H), 1.19 – 1.08 (m, 4H), 1.04 – 0.86 (m, 6H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 175.6, 168.8, 139.4, 138.5, 128.2, 128.0, 127.7, 127.5, 127.4, 127.2, 75.3, 72.4, 64.9, 63.8, 61.2, 57.6, 53.5, 49.8, 32.3, 30.9, 29.5, 27.9, 27.4, 27.3, 26.0, 25.6, 25.3, 25.2, 25.1, 24.9, 24.6, 20.1. ES-HRMS Calcd for \(\text{C}_{36}\text{H}_{31}\text{N}_4\text{O}_5\) [M + H]\(^+\) m/z 587.3961, Found: m/z 587.3958.

\[\text{C10}\]

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

chiral N,N'-dioxide C11:

Prepared according to the methods reported in the literature.\(^1\) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 11.51\) (s, 1H), 7.65 – 6.67 (m, 5H), 5.08 (s, 1H), 4.20 – 2.80 (m, 4H), 2.75 – 2.23 (m, 4H), 2.23 – 2.05 (m, 1H), 2.05 – 1.77 (m, 3H), 1.77 – 1.55 (m, 3H), 1.54 – 1.01 (m, 6H). \(^1\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 168.0, 143.7, 128.5, 126.9, 125.9, 76.2, 72.7, 66.2, 48.4, 28.40, 27.6, 27.5, 25.4, 25.3, 25.0, 22.8, 20.0. ES-HRMS Calcd for \(\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_2\) [M + H]\(^+\) m/z 317.2229, Found: m/z 317.2232.

7. Characterization of the alkyl 2-oxo-4-arylbut-3-enolate

(E)-methyl 1-(2,6-dichlorophenyl)-2-oxobut-3-enolate 1m

\[\text{1m}\]

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.92\) (d, \(J = 16.4\) Hz, 1H), 7.47 (d, \(J = 16.8\) Hz, 1H), 7.31 (d, \(J = 8.0\)Hz, 2H), 7.19 – 7.14 (m, 1H), 3.88 (s, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 182.4, 162.1, 141.6, 135.6, 131.4, 130.7, 129.0, 128.5, 53.2.\) ES-HRMS Calcd for \(\text{C}_{11}\text{H}_{6}\text{Cl}_2\text{O}_2\text{Na} \) [M + Na]\(^+\) m/z 280.9748, Found: m/z 280.9753.

(E)-methyl 1-(2,6-difluorophenyl)-2-oxobut-3-enolate 1n

\[\text{1n}\]

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.94\) (d, \(J = 16.4\) Hz, 1H), 7.63 (d, \(J = 16.8\) Hz, 1H), 7.41 – 7.34 (m, 1H), 6.97 (t, \(J = 8.8\) Hz, 2H), 3.94 (s, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 182.8, 163.5, 163.4, 162.2, 160.9, 160.8, 134.3, 132.7, 132.6, 132.5, 125.9, 125.8, 125.7, 112.2, 112.1, 112.0, 111.9, 53.1. ES-HRMS Calcd for \(\text{C}_{11}\text{H}_{6}\text{F}_2\text{O}_2\text{Na} \) [M + Na]\(^+\) m/z 249.0339, Found: m/z 249.0338.

(E)-methyl 1-(2,6-dimethylphenyl)-2-oxobut-3-enolate 1o

S7
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.08 (dd, $J$ = 16.8 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.09 – 7.07 (m, 2H), 7.01 (dd, $J$ = 16.4 Hz, 1H), 3.93 (s, 3H), 2.39 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 122.6, 52.8, 41.2, 31.3, 25.8, 25.6. ES-HRMS Calcd for C$_{13}$H$_{14}$O$_3$Na [M + Na]$^+$ m/z 219.0841, Found: m/z 219.0842.

( $E$)-methyl 4-cyclohexyl-2-oxobut-3-enoate 1s

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.08 (dd, $J$ = 16.0, 6.8 Hz, 1H), 6.56 (d, $J$ = 16.0 Hz, 1H), 3.84 (s, 3H), 2.20 – 2.16 (m, 1H), 1.77 – 1.71 (m, 4H), 1.66 – 1.63 (m, 1H), 1.32 – 1.10 (m, 5H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 183.4, 162.8, 159.8, 122.6, 52.8, 41.2, 31.3, 25.8, 25.6. ES-HRMS Calcd for C$_{13}$H$_{14}$O$_3$Na [M + Na]$^+$ m/z 219.0997, Found: m/z 219.0995.

8. Characterization of the products

methyl 5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3aa:

Prepared according to general procedure. Wax solid. 92% yield, 86% ee. $[\alpha]_D^{20}$ = -8.8 (c = 0.29, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_r$(major) = 12.88 min, $t_r$(minor) = 18.49 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.81 – 7.75 (m, 2H), 7.48 – 7.31 (m, 8H), 4.85 (brs, 1H), 4.01 – 3.96 (m, 1H), 3.88 (s, 3H), 2.41 – 2.26 (m, 2H). ES-HRMS Calcd for C$_{20}$H$_{17}$NO$_3$Na [M + Na]$^+$ m/z 358.1055, Found: m/z 358.1060.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.313</td>
</tr>
<tr>
<td>2</td>
<td>19.030</td>
</tr>
<tr>
<td>3</td>
<td>30.177</td>
</tr>
<tr>
<td>4</td>
<td>20.620</td>
</tr>
<tr>
<td>5</td>
<td>14.505</td>
</tr>
<tr>
<td>6</td>
<td>2.670</td>
</tr>
<tr>
<td>7</td>
<td>3.018</td>
</tr>
<tr>
<td>8</td>
<td>0.000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.313</td>
</tr>
<tr>
<td>2</td>
<td>19.030</td>
</tr>
<tr>
<td>3</td>
<td>30.177</td>
</tr>
<tr>
<td>4</td>
<td>20.620</td>
</tr>
<tr>
<td>5</td>
<td>14.505</td>
</tr>
<tr>
<td>6</td>
<td>2.670</td>
</tr>
<tr>
<td>7</td>
<td>3.018</td>
</tr>
<tr>
<td>8</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Ethyl 5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ba:

![3ba](image)

Prepared according to general procedure. Wax solid, 84% yield, 84% ee. \([\alpha]_D^{20} = -7.2\) (c = 0.29, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t_m\) (major) = 9.72 min, \(t_m\) (minor) = 15.16 min. ¹H NMR (400 MHz, CDCl₃): δ = 8.05 – 7.75 (m, 2H), 7.59 – 7.27 (m, 8H), 4.88 (brs, 1H), 4.41 – 4.27 (m, 2H), 4.07 – 3.97 (m, 1H), 2.75 – 2.25 (m, 2H), 1.40 – 1.31 (m, 3H). C₂₁H₁₉NO₄Na [M + Na]⁺ m/z 372.1212, Found: m/z 372.1215.

<table>
<thead>
<tr>
<th></th>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.895</td>
<td>50.23</td>
</tr>
<tr>
<td>2</td>
<td>15.346</td>
<td>49.77</td>
</tr>
</tbody>
</table>

Isopropyl-5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ca:

![3ca](image)

Prepared according to general procedure. Wax solid, 80% yield, 85% ee. \([\alpha]_D^{20} = -5.9\) (c = 0.29, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t_m\) (major)
= 7.49 min, \( t_{\text{r(minor)}} = 11.80 \) min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.80 – 7.76 \) (m, 2H), 7.48 – 7.32 (m, 8H), 5.22 – 5.07 (m, 1H), 4.90 – 3.97 (m, 1H), 2.73 – 2.24 (m, 2H), 1.37 – 1.29 (m, 6H). \( \text{C}_{22}\text{H}_{21}\text{NO}_4\text{Na} [\text{M + Na}]^{+} \) m/z 386.1368, Found: m/z 386.1373.

Allyl-5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3da:

\[
\text{3da:}
\]

Prepared according to general procedure. Wax solid. 90% yield, 83% ee. \([\alpha]_{D}^{20} = -9.3 \) (c = 0.34, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \( t_{\text{r(major)}} = 10.24 \) min, \( t_{\text{r(minor)}} = 15.97 \) min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.81 – 7.75 \) (m, 2H), 7.48 – 7.32 (m, 8H), 5.96 – 5.86 (m, 1H), 5.43 – 5.29 (m, 2H), 4.88 (brs, 1H), 4.80 – 4.70 (m, 2H), 4.00 (dd, \( J = 12.4, 6.8 \) Hz, 1H), 2.41 – 2.26 (m, 2H). \( \text{C}_{22}\text{H}_{20}\text{NO}_4\text{Na} [\text{M + Na}]^{+} \) m/z 384.1212, Found: m/z 384.1208.
### t-Butyl 5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ea:

![Chemical structure of t-Butyl 5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ea](image)

Prepared according to general procedure. Wax solid. 76% yield, 92% ee. $[\alpha]_{20}^D = -6.7$ (c = 0.19, EtOH). The ee was determined by HPLC analysis using a chiralcel IB column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_{\text{r(major)}} = 11.73$ min, $t_{\text{r(minor)}} = 17.08$ min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.78 – 7.76$ (m, 2H), 7.47 – 7.31 (m, 8H), 4.92 (brs, 1H), 4.01 – 3.95 (m, 1H), 2.32 – 2.24 (m, 2H), 1.51 (s, 9H). C$_{23}$H$_{23}$NO$_4$Na [M + Na]$^+$ m/z 400.1525, Found: m/z 400.1526.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.901</td>
<td>49.75</td>
</tr>
<tr>
<td>16.901</td>
<td>50.25</td>
</tr>
</tbody>
</table>

### Methyl 5-cyano-2-hydroxy-4-(2-nitrophenyl)-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3fa:

![Chemical structure of Methyl 5-cyano-2-hydroxy-4-(2-nitrophenyl)-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3fa](image)

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.728</td>
<td>95.86</td>
</tr>
<tr>
<td>17.077</td>
<td>4.14</td>
</tr>
</tbody>
</table>
Prepared according to **general procedure**. Wax solid, 98% yield, 91% ee. $[\alpha]_{D}^{20} = -66.6 (c = 0.44, \text{EtOH})$. The ee was determined by HPLC analysis using a chiralcel ADH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_{r}$(minor) = 30.27 min, $t_{r}$(major) = 39.05 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.02 – 7.93 (m, 1H), 7.81 – 7.64 (m, 4H), 7.50 – 7.41 (m, 4H), 5.06 (brs, 1H), 4.64 (dd, $J$ = 12.0, 5.6 Hz, 1H), 3.88 (s, 3H), 2.72 – 2.68 (m, 1H), 2.37 – 2.32 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 168.6, 163.8, 149.9, 135.1, 133.7, 132.3, 131.3, 131.1, 128.7, 128.5, 128.3, 125.0, 118.3, 95.2, 88.5, 54.0, 42.0, 29.2. ES-HRMS Calcd for C$_{20}$H$_{16}$N$_{2}$O$_{6}$Na $[M + Na]^{+}$ m/z 403.0906, Found: m/z 403.0906.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30.141</td>
</tr>
<tr>
<td>2</td>
<td>37.900</td>
</tr>
</tbody>
</table>

Methyl-4-(2-bromophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ga:

Prepared according to **general procedure**. Wax solid, 99% yield, 93% ee. $[\alpha]_{D}^{20} = 40.9 (c = 0.82, \text{EtOH})$. The ee was determined by HPLC analysis using a chiralcel IC column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_{r}$(major) = 11.68 min, $t_{r}$(minor) = 16.60 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.82 – 7.76 (m, 2H), 7.62 – 7.31 (m, 6H), 7.20 – 7.13
Methyl 4-(2-fluorophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ha:

\[
\text{(m, 1H), 4.90 (brs, 1H), 4.59 – 4.45 (m, 1H), 3.87 (s, 3H), 2.46 – 2.00 (m, 2H). ES-HRMS Calcd for C}_{20}\text{H}_{16}\text{BrNO}_{2}\text{Na [M + Na]}^+ m/z 436.0160, Found: m/z 436.0161.}
\]

![Methyl 4-(2-fluorophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ha](image)

**Retention Time % Area**

<table>
<thead>
<tr>
<th></th>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.785</td>
<td>51.48</td>
</tr>
<tr>
<td>2</td>
<td>16.574</td>
<td>48.52</td>
</tr>
</tbody>
</table>

Methyl 4-(2-fluorophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ha:

![Methyl 4-(2-fluorophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ha](image)

Prepared according to **general procedure**. Wax solid. 98% yield, 90% ee. \([\alpha]_D^{20} = -8.6 \text{ (c= 0.58, EtOH)} \). The ee was determined by HPLC analysis using a chiralcel IC column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \( t_r\) (major) = 11.40 min, \( t_r\) (minor) = 21.11 min. \(^1\text{H NMR (400 MHz, CDCl}_3\):} \( \delta = 7.95 – 7.74 \text{ (m, 2H), 7.55 – 7.29 \text{ (m, 5H)}, 7.21 – 7.05 \text{ (m, 2H)}, 4.90 \text{ (brs, 1H), 4.36 – 4.28 \text{ (m, 1H), 3.87 (s, 3H), 2.43 (t, } J = 13.0 \text{ Hz, 1H), 2.38 – 2.29 \text{ (m, 1H).} \)} ^{13}\text{C NMR (100 MHz, CDCl}_3\):} \( \delta = 169.0, 162.6, 162.3, 159.9, 132.6, 131.0, 129.6, 129.5, 129.2, 128.4, 128.3, 126.9, 126.8, 124.8, 124.7, 118.4, 116.2, 116.0, 95.0, 88.8, 53.9, 33.8, 31.2. \) ES-HRMS Calcd for C\(_{20}\)H\(_{16}\)FNO\(_2\)Na [M + Na]\(^+\) m/z 376.0961, Found: m/z 376.0960.
Methyl-4-(2-chlorophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ia:

\[
\begin{align*}
\text{NC} & \quad \text{OH} \\
\text{Cl} & \quad \text{COOMe}
\end{align*}
\]

3ia

Prepared according to general procedure. Wax solid, 99% yield, 93% ee. \([\alpha]\)\text{D}^{20} = 31.0 (c = 0.73, EtOH). The ee was determined by HPLC analysis using a chiralcel IC column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t_{\text{major}} = 11.28\) min, \(t_{\text{minor}} = 17.20\) min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.85 – 7.79\) (m, 2H), 7.50 – 7.24 (m, 7H), 4.93 (brs, 1H), 4.61 – 4.49 (m, 1H), 3.89 (s, 3H), 2.43 – 2.19 (m, 2H). \(^{13}\)C NMR (100MHz, CDCl\(_3\)): \(\delta = 168.9, 164.1, 137.2, 134.0, 132.6, 131.1, 130.0, 129.0, 128.4, 128.3, 127.7, 127.1, 118.4, 95.1, 88.8, 53.9, 35.5, 33.3. ES-HRMS Calcd for C\(_{20}\)H\(_{16}\)ClNO\(_4\)Na [M + Na]\(^+\) m/z 392.0666, Found: m/z 392.0666.
Methyl-4-(2-methoxyphenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ja:

![Chemical Structure](image)

Prepared according to general procedure. Wax solid, 97% yield, 98% ee. \([\alpha]_D^{20} = 12.9\) (c = 0.71, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), \(t_\text{r}(\text{major}) = 36.35\) min, \(t_\text{r}(\text{minor}) = 49.13\) min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.78 – 7.62\) (m, 2H), 7.42 – 7.30 (m, 3H), 7.29 – 7.14 (m, 2H), 6.98 – 6.80 (m, 2H), 4.84 (brs, 1H), 4.41 – 4.23 (m, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 2.41 – 2.15 (m, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 169.4, 162.2, 157.5, 132.9, 130.8, 128.9, 128.4, 128.3, 128.0, 121.1, 118.8, 111.1, 95.3, 90.1, 55.5, 53.8, 33.6, 29.2\). ES-HRMS Calcd for C\(_{21}\)H\(_{19}\)NO\(_5\)Na [M + Na]\(^+\) m/z 388.1155, Found: m/z 388.1154.

### Retention Time % Area

<table>
<thead>
<tr>
<th></th>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36.62</td>
<td>45.8443</td>
</tr>
<tr>
<td>2</td>
<td>50.30</td>
<td>54.1557</td>
</tr>
</tbody>
</table>

Methyl-4-(2-methylphenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ka:
Prepared according to general procedure. Wax solid, 98% yield, 94% ee. $\left[\alpha\right]_{D}^{20} = 12.3$ (c = 0.64, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), $t_r$(major) = 19.44 min, $t_r$(minor) = 34.97 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.84 – 7.75 (m, 2H), 7.46 – 7.20 (m, 7H), 4.86 (brs, 1H), 4.31 – 4.26 (m, 1H), 3.87 (s, 3H), 2.43 – 2.27 (m, 5H). $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ = 169.2, 162.5, 138.0, 136.1, 132.7, 130.9, 128.4, 128.2, 127.5, 126.9, 126.7, 118.6, 95.1, 90.1, 53.9, 35.0, 32.3, 19.3. ES-HRMS Caled for C$_{21}$H$_{19}$NO$_4$Na [M + Na]$^+$ m/z 372.1212, Found: m/z 372.1210.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18.914</td>
</tr>
<tr>
<td></td>
<td>49.75</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.436</td>
</tr>
<tr>
<td></td>
<td>96.93</td>
</tr>
</tbody>
</table>

4-(2,4-Dichlorophenyl)-2-hydroxy-2-(methylperoxymethyl)-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile $3la$:

Prepared according to general procedure. Wax solid, 94% yield, 90% ee. $\left[\alpha\right]_{D}^{20} = 23.8$ (c = 0.80, EtOH). The ee was
determined by HPLC analysis using a chiralcel IC column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \( t_r \) (major) = 7.90 min, \( t_r \) (minor) = 13.69 min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.74 – 7.64 \) (m, 2H), 7.41 – 7.18 (m, 6H), 4.80 (brs, 1H), 4.49 (m, 1H), 3.81 (s, 3H), 2.30 – 1.97 (m, 2H). ES-HRMS Calcd for C\(_{20}\)H\(_{15}\)Cl\(_2\)NO\(_4\)Na [M + Na]\(^+\) m/z 426.0276, Found: m/z 426.0279.

4-(2,6-Dichlorophenyl)-2-hydroxy-2-(methylperoxymethyl)-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile 3ma:

Prepared according to general procedure. White solid, 99% yield, 99% ee. \([a]_D^{20} = 3.3 \) (c = 0.31, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \( t_r \) (major) = 9.85 min, \( t_r \) (minor) = 14.21 min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.76 – 7.74 \) (m, 2H), 7.47 – 7.36 (m, 5H), 7.22 – 7.18 (m, 1H), 5.04 (dd, \( J = 12.4, 6.0 \) Hz, 1H), 4.99 (brs, 1H), 3.89 (s, 3H), 2.87 (t, \( J = 13.2 \) Hz, 1H), 2.16 (dd, \( J = 13.2, 6.4 \) Hz, 1H). \(^1^3\)C NMR (100MHz, CDCl\(_3\)): \( \delta = 169.0, 161.6, 136.6, 135.3, 133.9, 132.7, 130.9, 130.4, 129.5, 128.9, 128.4, 128.2, 118.1, 95.2, 88.5, 54.0, 33.5, 29.4. ES-HRMS Calcd for C\(_{20}H_{19}Cl_2NO_4Na [M + Na]^+\) m/z 426.0276, Found: m/z 426.0273.
4-(2,6-Difluorophenyl)-2-hydroxy-2-(methylperoxymethyl)-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile 3na:

```
\begin{化学式}
\text{\textbf{3na}}
\end{化学式}
```

Prepared according to general procedure. Wax solid, 99% yield, 98% ee. [\(\alpha\)]\textsubscript{D}\textsuperscript{20} = -40.8 (c = 0.34, EtOH). The ee was determined by HPLC analysis using a chiralcel ADH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t\)\textsubscript{(minor)} = 13.83 min, \(t\)\textsubscript{(major)} = 17.83 min.\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta = 7.65 (d, J = 7.6 \text{ Hz}, 2H), 7.39 - 7.32 (m, 3H), 7.23 - 7.17 (m, 1H), 6.88 (t, J = 9.0 \text{ Hz}, 2H), 4.87 (brs, 1H), 4.44 (dd, J = 12.8, 5.6 \text{ Hz}, 1H), 3.81 (s, 3H), 2.55 (t, J = 13.2 \text{ Hz}, 1H), 2.16 (dd, J = 13.2, 5.6 \text{ Hz}, 1H).\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta = 168.9, 161.9, 132.6, 130.9, 129.8, 129.7, 129.6, 128.4, 128.3, 118.1, 115.5, 115.3, 115.1, 112.1, 111.9, 95.0, 88.4, 54.0, 31.6, 26.5. \) ES-MS Calcd for C\textsubscript{20}H\textsubscript{15}F\textsubscript{2}NO\textsubscript{4}Na [M + Na]\textsuperscript{+} m/z 394.0867, Found: m/z 394.0861.
4-(2,6-Dimethylphenyl)-2-hydroxy-2-(methylperoxymethyl)-6-phenyl-3,4-dihydro-2H-pyran-5-carbonitrile

**30a:**

Prepared according to general procedure. Wax solid. 95% yield, 96% ee. [α]D<sup>20</sup> = -2.2 (c = 0.27, EtOH). The ee was determined by HPLC analysis using a chiralcel ADH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), t<sub>1</sub>(major) = 9.10 min, t<sub>2</sub>(minor) = 16.49 min. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.79 – 7.74 (m, 2H), 7.47 – 7.41 (m, 3H), 7.13 – 7.05 (m, 3H), 4.92 (brs, 1H), 4.57 – 4.53 (m, 1H), 3.89 (s, 3H), 2.62 – 2.10 (m, 8H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 169.4, 161.1, 137.3, 136.7, 135.1, 132.9, 131.0, 130.9, 129.0, 128.6, 128.1, 127.6, 118.5, 95.4, 90.7, 54.1, 32.0, 31.0, 21.1, 20.5. ES-HRMS Calcd for C<sub>22</sub>H<sub>21</sub>NO<sub>2</sub>Na [M + Na]<sup>+</sup> m/z 386.1368, Found: m/z 386.1370.
Methyl-4-(3-methylphenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3pa:

![Chemical Structure](image)

Prepared according to **general procedure**. Wax solid, 84% yield, 85% ee, \([\alpha]_D^{20} = -18.4\) (c = 0.29, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t_{(\text{major})} = 11.03\) min, \(t_{(\text{minor})} = 17.90\) min. \(^1\)H NMR (400 MHz, CDCl₃): \(\delta = 7.81 – 7.75\) (m, 2H), 7.50 – 7.40 (m, 3H), 7.31 – 7.27 (m, 1H), 7.16 – 7.09 (m, 3H), 4.82 (brs, 1H), 3.97 – 3.92 (m, 1H), 3.88 (s, 3H). \(^1^3\)C NMR (100 MHz, CDCl₃): \(\delta = 169.1, 162.2, 140.1, 138.7, 132.6, 130.9, 129.0, 128.7, 128.4, 128.3, 125.0, 118.6, 95.1, 90.1, 53.9, 36.9, 36.0, 21.5\). ES-HRMS Calcd for C₂₁H₁₉NO₄Na \([M + Na]^+\) m/z 372.1212, Found: m/z 372.1216.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.254</td>
</tr>
<tr>
<td>2</td>
<td>17.851</td>
</tr>
</tbody>
</table>

Methyl-4-(4-methylphenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3qa:

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.030</td>
</tr>
<tr>
<td>2</td>
<td>17.851</td>
</tr>
</tbody>
</table>
Prepared according to general procedure. Wax solid, 85% yield, 83% ee. $[\alpha]_{D}^{20} = -13.4$ (c = 0.30, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_{r}$(major) = 11.25 min, $t_{r}$(minor) = 17.34 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.80 – 7.72$ (m, 2H), 7.47 – 7.40 (m, 3H), 7.27 – 7.18 (m, 4H), 4.82 (bbrs, 1H), 4.00 – 3.92 (m, 1H), 3.88 (s, 3H), 2.39 – 2.26 (m, 5H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 169.2, 162.2, 137.5, 137.1, 132.6, 130.9, 129.8, 128.4, 128.3, 127.9, 118.6, 95.1, 90.2, 53.9, 36.5, 35.9, 21.1. ES-HRMS Calcd for C$_{21}$H$_{19}$NO$_4$Na $[M + Na]^+$ m/z 372.1212, Found: m/z 372.1210.

Methyl-4-(4-chlorophenyl)-5-cyano-2-hydroxy-6-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ra:
Prepared according to general procedure. Wax solid, 76% yield, 80% ee. $[\alpha]_{D}^{20} = -14.4$ (c = 0.58, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_r$(major) = 13.59 min, $t_r$(minor) = 22.96 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.76 – 7.65 (m, 2H), 7.45 – 7.22 (m, 7H), 4.82 (brs, 1H), 3.95 (dd, $J$ = 11.6, 7.2 Hz, 1H), 3.86 (s, 3H), 2.33 – 2.19 (m, 2H).

Methyl-5-cyano-2-hydroxy-4-cyclohexyl-6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate 3sa:

Prepared according to general procedure. Wax solid, 91% yield, 89% ee. $[\alpha]_{D}^{20} = 17.1$ (c = 0.30, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), $t_r$(major) = 12.85 min, $t_r$(minor) = 20.73 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.72 – 7.66 (m, 2H), 7.44 – 7.37 (m, 3H), 4.76 (brs, 1H), 3.89 (s, 3H), 2.77 – 2.72 (m, 1H), 2.11 – 1.93 (m, 3H), 1.83 – 1.63 (m, 5H), 1.44 – 1.34 (m, 2H), 1.25 – 1.03 (m, 3H), 1.39 – 1.03 (m, 3H), 2.78 (m, 1H), 2.11 (m, 1H), 1.83 (m, 3H), 1.44 (m, 2H), 1.25 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 169.6, 162.6, 132.9, 130.7, 128.3, 128.2, 95.4, 90.1, 53.9, 39.4, 34.0, 30.9, 27.3, 26.8, 26.7, 26.5, 26.4. ES-HRMS Calcd for C$_{20}$H$_{23}$NO$_4$Na [M + Na]$^+$ m/z 364.1525, Found: m/z 364.1532.
Methyl-5-cyano-6-(3-fluorophenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ab:

\[
\begin{array}{c}
\text{Prepared according to general procedure. Wax solid, 98% yield, 88% ee. } [\alpha]_D^{20} = -12.5 \text{ (c = 0.59, EtOH). The ee was determined by HPLC analysis using a chiralcel IC column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), } t_\text{(major)} = 10.98 \text{ min, } t_\text{(minor)} = 14.96 \text{ min. } ^1H \text{ NMR (400 MHz, CDCl}_3): \delta = 7.66 - 7.60 \text{ (m, 1H), 7.44 - 7.31 \text{ (m, 7H), 7.18 - 7.13 \text{ (m, 1H), 5.00 (brs, 1H), 3.99 (dd, } J = 12.0, 6.8 \text{ Hz, 1H), 3.89 (s, 3H), 2.41 - 2.25 \text{ (m, 2H). } ^13C \text{ NMR (100MHz, CDCl}_3): } \delta = 169.0, 163.6, 161.2, 160.8, 139.8, 134.6, 134.5, 130.1, 130.0, 129.1, 128.0, 124.2, 124.1, 118.0, 117.9, 115.4, 115.2, 95.2, 90.8, 54.0, 37.0, 35.9. \text{ ES-HRMS Calcd for } C_{20}H_{13}FNO_4 \text{Na [M + Na]}^+ \text{ m/z } 376.0961, \text{ Found: m/z 376.0963.}
\end{array}
\]
Methyl-5-cyano-6-(3-chlorophenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-Carboxylate 3ac:

![Chemical Structure of 3ac](image)

Prepared according to general procedure. Wax solid, 95% yield, 86% ee. [α]$_D^{20}$ = -12.5 (c = 0.63, EtOH). The ee was determined by HPLC analysis using a chiralcel IE column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), t$_r$(minor) =15.15 min, t$_r$(major) = 20.32 min. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.75 – 7.67 (m, 2H), 7.45 – 7.31 (m, 7H), 5.02 (brs, 1H), 3.98 (dd, $J$ = 12.0, 6.8 Hz, 1H), 3.89 (s, 3H), 2.41 – 2.27 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 168.9, 160.8, 139.8, 134.5, 134.3, 131.0, 129.7, 129.1, 128.2, 128.0, 126.6, 118.0, 95.3, 91.0, 54.0, 36.9, 35.9. ES-HRMS Calcd for C$_{20}$H$_{16}$ClNO$_4$Na [M + Na]$^+$ m/z 392.0666, Found: m/z 392.0662.
Methyl-5-cyano-6-(3-bromophenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-Carboxylate 3ad:

Prepared according to general procedure. Wax solid. 93% yield, 90% ee. \([\alpha]^{20}_{D} = -9.5\) (c = 0.70, EtOH). The ee was determined by HPLC analysis using a chiralcel IC column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), t_(major) = 28.07 min, t_(minor) = 39.87 min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.81 – 7.73\) (m, 2H), 7.60 – 7.56 (m, 1H), 7.42 – 7.25 (m, 6H), 5.00 (brs, 1H), 3.97 (dd, \(J = 12.0, 6.4\)Hz, 1H), 3.88 (s, 3H), 2.40 – 2.27 (m, 2 H).

ES-HRMS Calcd for C\(_{20}\)H\(_{16}\)BrNO\(_4\)Na [M + Na]\(^+\) \(m/z\) 436.0160, Found: \(m/z\) 436.0162.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>27.959</td>
</tr>
<tr>
<td>2</td>
<td>37.987</td>
</tr>
</tbody>
</table>

Methyl-5-cyano-6-(3-methoxyphenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-Carboxylate 3ae:

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28.069</td>
</tr>
<tr>
<td>2</td>
<td>39.869</td>
</tr>
</tbody>
</table>

S25
Prepared according to **general procedure**. White solid, 88% yield, 85% ee. \([\alpha]_D^{20} = -5.9\) (c = 0.32, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t_{r}(\text{major}) = 18.65\) min, \(t_{r}(\text{minor}) = 30.21\) min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.51 – 7.28\) (m, 8H), 7.00 – 6.98 (m, 1H), 4.93 (brs, 1H), 3.98 (dd, \(J = 12.0, 6.4\) Hz, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 2.40 – 2.28 (m, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 169.1, 162.1, 159.4, 140.1, 133.8, 129.5, 129.1, 128.0, 127.9, 120.8, 118.5, 116.9, 113.6, 95.1, 90.1, 55.5, 53.9, 37.0, 35.9.

ES-HRMS Calcd for C\(_{21}\)H\(_{19}\)NO\(_5\)Na [M + Na]\(^+\) m/z 388.1161, Found: m/z 388.1158.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.116</td>
</tr>
<tr>
<td>2</td>
<td>30.688</td>
</tr>
</tbody>
</table>

Methyl-5-cyano-6-(3-methylphenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3af:

Prepared according to **general procedure**. White solid, 92% yield, 86% ee. \([\alpha]_D^{20} = -9.9\) (c = 0.84, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), \(t_{r}(\text{major}) = 26.55\) min, \(t_{r}(\text{minor}) = 42.43\) min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.60 – 7.52\) (m, 2H), 7.42 – 7.26 (m, 7H), 4.86 (brs, 1H), 3.97 (dd, \(J = 12.4, 6.8\) Hz, 1H), 3.87 (s, 3H), 2.41 – 2.27 (m, 5H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 169.1, 162.6, 140.2, 138.2, 132.5, 131.8, 129.1, 128.8, 128.3, 128.0, 127.8, 125.5, 118.6, 95.0, 89.8, 53.9, 36.9, 36.0, 21.4.

ES-HRMS Calcd for C\(_{21}\)H\(_{19}\)NO\(_4\)Na [M + Na]\(^+\) m/z 372.1212, Found: m/z 372.1212.
Methyl-5-cyano-6-(4-methylphenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-Carboxylate 3ag:

Prepared according to general procedure. Wax solid, 87% yield, 84% ee. \([\alpha]_{D}^{20} = 2.6\) (c = 0.30, EtOH). The ee was determined by HPLC analysis using a chiralcel IB column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), \(t_r\) (major) = 12.11 min, \(t_r\) (minor) = 20.13 min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.80 – 7.63\) (m, 2H), 7.41 – 7.21 (m, 7H), 4.83 (brs, 1H), 4.01 – 3.94 (m, 1H), 3.87 (s, 3H), 2.46 – 2.27 (m, 5H). \(^{13}\)C NMR (100MHz, CDCl\(_3\)): \(\delta = 169.2, 162.5, 141.4, 140.3, 129.7, 129.0, 128.9, 128.2, 128.0, 127.8, 118.7, 95.0, 89.3, 53.9, 36.9, 36.0, 21.5\). ES-HRMS Calcd for C\(_{21}\)H\(_{19}\)NO\(_4\)Na [M + Na] \(^{+}\) m/z 372.1215, Found: m/z 372.1212. 

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50.67</td>
</tr>
<tr>
<td>2</td>
<td>49.33</td>
</tr>
</tbody>
</table>

Methyl-5-cyano-6-(4-methylphenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-Carboxylate 3ag:
Methyl-5-cyano-6-(4-fluorophenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ah:

Prepared according to general procedure. White solid, 96% yield, 84% ee. \([\alpha]_{D}^{20} = -8.7 \text{ (c = 0.96, EtOH)}\). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), \(t_\text{(major)} = 27.75 \text{ min, } t_\text{(minor)} = 39.16 \text{ min}\). \(\text{H NMR (400 MHz, CDCl}_3\text{}): } \delta = 7.90 – 7.69 \text{ (m, 2H), 7.44 – 7.30 \text{ (m, 5H), 7.14 – 7.06 \text{ (m, 2H), 4.32 (brs, 1H), 4.01 – 3.95 \text{ (m, 1H), 3.87 (s, 3H), 2.53 – 2.10 \text{ (m, 2H)}).}

Methyl-5-cyano-6-(4-chlorophenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3ai:

Prepared according to general procedure. White solid, 96% yield, 84% ee. \([\alpha]_{D}^{20} = -8.7 \text{ (c = 0.96, EtOH)}\). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), \(t_\text{(major)} = 27.75 \text{ min, } t_\text{(minor)} = 39.16 \text{ min}\). \(\text{H NMR (400 MHz, CDCl}_3\text{}): } \delta = 7.90 – 7.69 \text{ (m, 2H), 7.44 – 7.30 \text{ (m, 5H), 7.14 – 7.06 \text{ (m, 2H), 4.32 (brs, 1H), 4.01 – 3.95 \text{ (m, 1H), 3.87 (s, 3H), 2.53 – 2.10 \text{ (m, 2H)}).}
Prepared according to **general procedure**. Wax solid, 95% yield, 82% ee. \([\alpha]_D^{20} = -1.9\) (c = 0.38, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), t_(major) = 28.06 min, t_(minor) = 42.23 min. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.76 – 7.68\) (m, 2H), 7.42 – 7.30 (m, 7H), 4.93 (brs, 1H), 3.97 (dd, \(J = 12.0, 6.4\)Hz, 1H), 3.87 (s, 3H), 2.40 – 2.26 (m, 2H). \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 169.0, 161.2, 139.9, 137.1, 131.0, 129.6, 129.1, 128.7, 128.0, 127.9, 118.3, 95.2, 90.4, 54.0, 36.9, 35.9\). ES-HRMS Calcd for C\(_{20}\)H\(_{16}\)ClNO\(_4\)Na \([M + Na]^+\) m/z 392.0666, Found: m/z 392.0668.

### Methyl-5-cyano-6-(4-bromophenyl)-2-hydroxy-4-phenyl-3,4-dihydro-2H-pyran-2-carboxylate 3aj:

Prepared according to **general procedure**. Wax solid, 95% yield, 83% ee. \([\alpha]_D^{20} = 1.6\) (c = 0.79, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), t_(major) = 28.058 min, t_(minor) = 42.227 min.
\( t = 29.50 \text{ min}, t_{\text{minor}} = 45.83 \text{ min.} \)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.66 - 7.62 \text{ (m, 2H)}, 7.56 - 7.54 \text{ (m, 2H)}, 7.44 - 7.31 \text{ (m, 5H)}, 4.85 \text{ (brs, 1H)}, 3.99 - 3.94 \text{ (m, 1H)}, 3.89 \text{ (s, 3H)}, 2.39 - 2.33 \text{ (m, 2H)}. \)

ES-HRMS Calcd for \( \text{C}_{20}\text{H}_{16}\text{BrNO}_4\text{Na} [M + Na]^+ \) \( m/z \) 436.0160, Found: \( m/z \) 436.0163.

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29.617</td>
</tr>
<tr>
<td>2</td>
<td>44.317</td>
</tr>
</tbody>
</table>

Methyl-5-cyano-6-(3-bromophenyl)-2-hydroxy-4-(2,6-Dichlorophenyl)-3,4-dihydro-2H-pyran-2-Carboxylate 3md:

\[
\begin{array}{c}
\text{Br} \\
\text{O} \\
\text{COOMe} \\
\text{NC} \\
\text{Cl} \\
\text{Cl} \\
\end{array}
\]

Prepared according to general procedure. Wax solid. 99% yield, 99% ee. \([\alpha]_{D}^{20} = 10.0 \text{ (c = 0.48, EtOH)} \). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm), \( t_m = 15.88 \text{ min}, t_c = 21.99 \text{ min.} \)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.82 - 7.63 \text{ (m, 2H)}, 7.55 - 7.46 \text{ (m, 1H)}, 7.38 - 7.26 \text{ (m, 2H)}, 7.25 - 7.11 \text{ (m, 2H)}, 5.10 \text{ (brs, 1H)}, 4.95 \text{ (dd, } J = 12.6, 6.2 \text{ Hz, 1H)}, 3.83 \text{ (s, 3H)}, 2.77 \text{ (t, } J = 13.0 \text{ Hz, 1H)}, 2.09 \text{ (dd, } J = 13.3, 6.1 \text{ Hz, 1H}). \)

\(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 168.9, 160.0, 136.6, 135.2, 134.6, 133.9, 133.6, 130.9, 130.4, 129.9, 129.6, 128.9, 127.0, 122.5, 117.6, 97.3, 95.3, 89.6, 54.1, 33.5, 29.4. \)

ES-HRMS Calcd for \( \text{C}_{20}\text{H}_{14}\text{BrClNO}_4\text{Na} [M + Na]^+ \) \( m/z \) 503.9381, Found: \( m/z \) 503.9388.
Methyl-5-cyano-6-(4-chlorophenyl)-2-hydroxy-4-(2,6-Dichlorophenyl)-3,4-dihydro-2H-pyran-2-Carboxylate 3mi:

![Chemical Structure](image)

Prepared according to **general procedure**. Wax solid, 99% yield, 99% ee. $[\alpha]_D^{20} = 8.7$ (c = 0.44, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 90/10, 1.0 mL/min, 254 nm), $t_r$(major) = 8.63 min, $t_r$(minor) = 11.72 min. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.69 – 7.55 (m, 2H), 7.37 – 7.22 (m, 4H), 7.20 – 7.10 (m, 1H), 5.06 (brs, 1H), 4.95 (dd, $J_1$ = 12.7, 6.2 Hz, 1H), 3.82 (s, 3H), 2.77 (t, $J_2$ = 13.0 Hz, 1H), 2.09 (dd, $J_3$ = 13.3, 6.2 Hz, 1H). $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ = 168.9, 160.5, 137.1, 136.6, 135.2, 133.7, 131.1, 130.4, 130.1, 129.6, 129.5, 128.9, 128.7, 125.5, 117.9, 95.3, 89.0, 54.1, 33.5, 29.4. ES-HRMS Caled for C$_{20}$H$_{14}$Cl$_3$NO$_4$Na [M + Na]$^+$ m/z 459.9881, Found: m/z 459.9879.
<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49.78</td>
</tr>
<tr>
<td>2</td>
<td>50.22</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>99.64</td>
</tr>
<tr>
<td>2</td>
<td>0.36</td>
</tr>
</tbody>
</table>
9. Copy of $^1$H NMR and $^{13}$C NMR spectra for the catalysts:
C5

-18.940
-12.240
12.0
12.5
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

128.53
128.77
122.67
122.64

-70.506
-65.943
-41.916
-22.333
-27.711
-20.500
-15.206

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

f1 (ppm)
10. Copy of $^1$H NMR and $^{13}$C NMR spectra for the substrates:

![NMR spectra](image)

**1m**

![Chemical structure](image)

**1m**
11. Copy of $^1$H NMR and $^{13}$C NMR spectra for the products:

**3aa**

**3ba**
3ea

3fa
3pa

**Chemical Structure**

The image shows a chemical structure labeled as 3pa.

**Spectroscopy Data**

A set of spectral data is also present, indicating various chemical shifts and peak intensities in both 1D and 2D NMR spectra.

**1D NMR Spectra**

- δ 7.8-7.7 ppm
- δ 6.9-6.8 ppm
- δ 3.0-3.1 ppm
- δ 1.6 ppm

**2D NMR Spectra**

- δ 190.1 ppm
- δ 118.5 ppm
- δ 38.8 ppm
- δ 24.5 ppm

**Other Data**

- δ 169.1, 190.7, 118.5, 121.4, 38.8 ppm

This data is typical of organic chemistry, showing the chemical shifts and multiplicities of the protons and carbon nuclei in the compound 3pa.
3md

Br

NC

Cl

O

COOME

OH

3mi

Cl

NC

Cl

Cl

O

COOME

OH
12. Mechanism Evidence and Corresponding NMR Spectra

the N-H proton

the N-H proton
the N-H proton

the N-H proton

the N-H proton
Scheme 1. Control experiments.

\[ \text{catalyst (10 mol %)} \]
\[ p-\text{BuC}_{6}H_{4}\text{COOH (50 mol %)} \]
\[ 4 \text{ Å MS (20 mg), MTBE (3.0 mL)} \]
\[ -30 \degree \text{C, 72 h} \]

1a + 2a \rightarrow 3aa

C9: 18% yield, 19% ee
C10: 92% yield, 65% ee
C11: 83% yield, 30% ee

solvent:

---

S75
In the literature:\(^7\):

\((2S,4R)-4\)-Bromobenzyl-5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate

\[
[\alpha]_D^{22.1} = -13.5 (c 1.95, EtOH); 94\% \text{ ee, determined by HPLC (Daicel® chiralcel OD-H column, hexane/}i\text{-PrOH = 80/20, flow rate 0.5 mL/min, }t_{\text{major}} = 19.4 \text{ min, } t_{\text{minor}} = 29.9 \text{ min, } \lambda = 254 \text{ nm}).
\]

\[\text{Our work:}\]

4-Bromobenzyl-5-cyano-2-hydroxy-4,6-diphenyl-3,4-dihydro-2H-pyran-2-carboxylate was determined as (2S, 4R).
Prepared according to **general procedure**. Solid, 37% yield, 77% ee. $[\alpha]_D^{17.1} = -7.2$ (c = 0.18, EtOH). The ee was determined by HPLC analysis using a chiralcel ODH column (hexane/2-propanol = 80/20, 0.5 mL/min, 254 nm), $t_{(\text{major})} = 19.74$ min, $t_{(\text{minor})} = 30.52$ min. $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 8.39 – 6.42$ (m, 14H), 5.48 – 4.96 (m, 2H), 4.91 – 4.39 (m, 1H), 4.07 – 3.78 (m, 1H), 2.66 – 2.16 (m, 2H).

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>% Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.28</td>
</tr>
<tr>
<td>2</td>
<td>29.06</td>
</tr>
<tr>
<td></td>
<td>Retention Time</td>
</tr>
<tr>
<td>---</td>
<td>---------------</td>
</tr>
<tr>
<td>1</td>
<td>19.74</td>
</tr>
<tr>
<td>2</td>
<td>30.52</td>
</tr>
</tbody>
</table>
Reference:


