Supporting Information

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Selectivity Guidelines and a Reductive Elimination-Based Model for Predicting the Stereochemical Course of Conjugate Addition Reactions of Organocuprates to \(\gamma\)-Alkoxy-\(\alpha,\beta\)-Enoates

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1. General Methods.

Unless otherwise noted all commercially obtained reagents were used without purification. THF was distilled from sodium-benzophenone ketyl prior to use. Dichloromethane and methanol were distilled from calcium hydride. Reactions were carried out under a nitrogen atmosphere in oven-dried glassware using standard syringe, cannula and septa techniques. Reactions were monitored by TLC (Silica Gel 60 F$_{254}$, 250 µm) and visualized with UV light and ceric ammonium molybdate solution. Flash chromatography was performed on silica gel (32-63 µm, 60 Å pore size).

Aryl bromides d$^1$ and f$^{2,3}$ were prepared as previously described.

2. Characterization data for cuprate addition product mixtures

Epimeric mixture 14a: 94%; $R_f$ 0.45 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.55 – 7.15 (m, 15H), 4.80 (d, $J$ = 11.6 Hz, 1H), 4.55 (d, $J$ = 11.6 Hz, 1H), 4.44 (s, 2H), 3.81 – 3.73 (m, 1H), 3.58 – 3.47 (m, 1H), 3.50 (s, 3H), 3.36 (dd, $J$ = 10.5, 5.2 Hz, 1H), 3.04 (dd, $J$ = 16.0, 5.8 Hz, 1H), 2.64 (dd, $J$=16.0, 9.1 Hz, 1H); HRMS $m/z$ (ESI) calcd for C$_{26}$H$_{28}$O$_4$Na (M+Na)$^+$ 427.1879, found 427.1891.

Epimeric mixture 14d: 76%; $R_f$ 0.55 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.63 – 7.15 (m, 10H), 6.68 – 5.59 (m, 3H), 5.92 (s, 2H), 4.75 (d, $J$ = 11.6 Hz, 1H), 4.50 (d, $J$ = 11.6 Hz, 1H), 4.42 (s, 2H), 3.78 – 3.30 (m, 4H), 3.50 (s, 3H), 2.96 (dd, $J$ = 16.0, 5.2 Hz, 1H), 2.53 (dd, $J$ = 16.0, 9.3 Hz, 1H); HRMS $m/z$ (ESI) calcd for C$_{27}$H$_{28}$O$_6$Na (M+Na)$^+$ 471.1778, found 471.1756.
Epimeric mixture 14f: 88%; $R_f$ 0.45 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.51 – 7.25 (m, 10H), 6.66 (d, $J = 8.5$ Hz, 1H), 6.39 (s, 1H), 5.99 (s, 1H), 5.92 (s, 1H), 4.75 (d, $J = 11.6$ Hz, 1H), 4.50 (d, $J = 11.6$ Hz, 1H), 4.43 (s, 2H), 3.94 (s, 3H), 3.81 (s, 3H), 3.68 – 3.32 (m, 4H), 3.51 (s, 3H), 2.93 (dd, $J = 16.0$, 5.5 Hz, 1H), 2.54 (dd, $J = 16.0$, 9.4 Hz, 1H); HRMS m/z (ESI) calcd for C$_{28}$H$_{30}$O$_7$Na (M+Na)$^+$ 501.1883, found 501.1906.

Epimeric mixture 15a: 89%; $R_f$ 0.54 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.50 – 7.19 (m, 10H), 4.65 (d, $J = 11.6$ Hz, 1H), 4.44 (d, $J = 11.6$ Hz, 1H), 3.69 – 3.62 (m, 1H), 3.48 (s, 3H), 3.35 – 3.23 (m, 1H), 3.06 (dd, $J = 16.0$, 6.0 Hz, 1H), 2.62 (dd, $J = 16.0$, 8.5 Hz, 1H), 1.07 (d, $J = 6.0$ Hz, 3H); HRMS m/z (ESI) calcd for C$_{19}$H$_{22}$O$_3$Na (M+Na)$^+$ 321.1461, found 321.1452.

Epimeric mixture 15d: 80%; $R_f$ 0.61 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.60 – 7.20 (m, 5H), 6.90 – 6.55 (m, 3H), 5.92 (s, 2H), 4.62 (d, $J = 11.6$ Hz, 1H), 4.44 (d, $J = 11.6$ Hz, 1H), 3.65 – 3.35 (m, 1H), 3.49 (s, 3H), 3.20 – 3.08 (m, 1H), 2.90 (dd, $J = 16.0$, 5.8 Hz, 1H), 2.51 (dd, $J = 16.0$, 8.8 Hz, 1H), 1.05 (d, $J = 6.0$ Hz, 3H); HRMS m/z (ESI) calcd for C$_{20}$H$_{22}$O$_5$Na (M+Na)$^+$ 365.1359, found 365.1364.
Epimeric mixture 15f: 82%; $R_f$ 0.46 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.62 – 7.21 (m, 5H), 6.66 (d, $J = 8.0$ Hz, 1H), 6.37 (s, 1H), 5.92 (s, 2H), 4.62 (d, $J = 11.6$ Hz, 1H), 4.39 (d, $J = 11.6$ Hz, 1H), 3.85 (s, 3H), 3.63 – 3.35 (m, 1H), 3.49 (s, 3H), 3.19 – 3.08 (m, 1H), 2.97 (dd, $J = 16.0$, 6.0 Hz, 1H), 2.52 (dd, $J = 16.0$, 8.5 Hz, 1H), 1.06 (d, $J = 6.0$ Hz, 3H); HRMS m/z (ESI) calcd for C$_{21}$H$_{24}$O$_6$Na (M+Na)$^+$ 395.1465, found 395.1462.

Epimeric mixture 16a: 87%; $R_f$ 0.35 (15% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.69 – 7.57 (m, 5H), 7.47 – 7.22 (m, 15H), 4.67 (d, $J = 11.6$ Hz, 1H), 4.39 (d, $J = 11.6$ Hz, 1H), 3.72 - 3.46 (m, 4H), 3.46 (s, 3H), 2.98 (dd, $J = 16.0$, 5.0 Hz, 1H), 2.62 (dd, $J = 16.0$, 8.8 Hz, 1H), 1.04 (s, 9H); selected $^1$H NMR (CDCl$_3$) data for the syn-isomer $\delta$ 7.69 – 7.57 (m, 5H), 7.47 – 7.22 (m, 15H), 4.57 (d, $J = 11.8$ Hz, 1H), 4.35 (d, $J = 11.8$ Hz, 1H), 3.72 - 3.46 (m, 4H), 3.55 (s, 3H), 2.86 (dd, $J = 16.0$, 7.2 Hz, 1H), 2.72 (dd, $J = 16.0$, 8.0 Hz, 1H), 1.05 (s, 9H).

Epimeric mixture 16d: 69%; $R_f$ 0.4 (15% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the anti-isomer $\delta$ 7.67 – 7.50 (m, 5H), 7.47 – 7.17 (m, 10H), 6.69 (d, $J = 8.0$ Hz, 3H), 5.92 (s, 2H), 4.67 (d, $J = 11.6$ Hz, 1H), 4.39 (d, $J = 11.6$ Hz, 1H), 3.72 - 3.39 (m, 4H), 3.46 (s, 3H), 2.93 (dd, $J = 16.0$, 5.0 Hz, 1H), 2.54 (dd, $J = 16.0$, 9.4 Hz, 1H), 1.04 (s, 9H); selected $^1$H NMR (CDCl$_3$) data for the syn-isomer $\delta$ 7.69 – 7.57 (m, 5H), 7.47 – 7.22 (m, 15H), 6.67 (d, $J = 8.0$ Hz,
3H), 5.90 (s, 2H), 4.57 (d, \( J = 11.8 \) Hz, 1H), 4.34 (d, \( J = 11.8 \) Hz, 1H), 3.72 - 3.46 (m, 4H), 3.56 (s, 3H), 2.77 (dd, \( J = 16.0, 6.9 \) Hz, 1H), 2.66 (dd, \( J = 16.0, 8.3 \) Hz, 1H), 1.05 (s, 9H).

Epimeric mixture 16f: 53%; \( R_f \) 0.6 (30% EtOAc/hexanes); selected \(^1\)H NMR (CDCl\(_3\)) data for the anti-isomer \( \delta 7.65 - 7.50 \) (m, 5H), 7.45 – 7.20 (m, 10H), 6.45 (m, 2H), 5.95 (s, 2H), 4.67 (d, \( J = 11.6 \) Hz, 1H), 4.39 (d, \( J = 11.6 \) Hz, 1H), 3.79 (s, 3H), 3.72 - 3.45 (m, 4H), 3.47 (s, 3H), 2.93 (dd, \( J = 16.0, 5.3 \) Hz, 1H), 2.52 (dd, \( J = 16.0, 9.5 \) Hz, 1H), 1.05 (s, 9H); selected \(^1\)H NMR (CDCl\(_3\)) data for the syn-isomer \( \delta 7.65 – 7.5 \) (m, 5H), 7.45 – 7.20 (m, 10H), 6.39 (s, 2H), 5.92 (s, 2H), 4.60 (d, \( J = 11.8 \) Hz, 1H), 4.36 (d, \( J = 11.8 \) Hz, 1H), 3.87 (s, 3H), 3.80 - 3.40 (m, 4H), 3.52 (s, 3H), 2.77 (dd, \( J = 16.0, 6.9 \) Hz, 1H), 2.66 (dd, \( J = 16.0, 8.3 \) Hz, 1H), 1.04 (s, 9H).

Epimeric mixture 17a: 72%; \( R_f \) 0.45 (30% EtOAc/hexanes); selected \(^1\)H NMR (CDCl\(_3\)) data for the anti-isomer \( \delta 7.55 - 7.15 \) (m, 15H), 4.80 (d, \( J = 11.6 \) Hz, 1H), 4.55 (d, \( J = 11.6 \) Hz, 1H), 4.44 (s, 2H), 3.81 – 3.73 (m, 1H), 3.58 – 3.47 (m, 1H), 3.50 (s, 3H), 3.36 (dd, \( J = 10.5, 5.2 \) Hz, 1H), 3.04 (dd, \( J = 16.0, 5.8 \) Hz, 1H), 2.64 (dd, \( J = 16.0, 9.1 \) Hz, 1H); selected \(^1\)H NMR (CDCl\(_3\)) data for the syn-isomer \( \delta 7.55 – 7.15 \) (m, 15H), 4.76 (d, \( J = 11.8 \) Hz, 1H), 4.57 (d, \( J = 11.8 \) Hz, 1H), 4.47 (s, 2H), 3.94 – 3.89 (m, 1H), 3.70 – 3.41 (m, 2H), 3.57 (s, 3H), 2.91 (dd, \( J = 16.0, 6.9 \) Hz, 1H), 2.79 (dd, \( J = 16.0, 8.3 \) Hz, 1H).
**Epimeric mixture 17d:** 68%; $R_f$ 0.55 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the *anti*-isomer $\delta$ 7.63 – 7.15 (m, 10H), 6.67 – 5.59 (m, 3H), 5.89 (s, 2H), 4.75 (d, $J = 11.6$ Hz, 1H), 4.50 (d, $J = 11.6$ Hz, 1H), 4.43 (s, 2H), 3.78 – 3.30 (m, 4H), 3.50 (s, 3H), 2.96 (dd, $J = 16.0$, 5.2 Hz, 1H), 2.53 (dd, $J = 16.0$, 9.3 Hz, 1H); selected $^1$H NMR (CDCl$_3$) data for the *syn*-isomer $\delta$ 7.63 – 7.15 (m, 10H), 6.67 – 5.59 (m, 3H), 5.91 (s, 2H), 4.72 (d, $J = 11.8$ Hz, 1H), 4.51 (d, $J = 11.8$ Hz, 1H), 4.44 (s, 2H), 3.87 – 3.79 (m, 1H), 3.78–3.30 (m, 3H), 3.56 (s, 3H), 2.78 (dd, $J = 16.0$, 6.6 Hz, 1H), 2.69 (dd, $J = 16.0$, 8.5 Hz, 1H).

![Epimeric mixture 17d](image1)

Epimeric mixture 17f: 63%; $R_f$ 0.45 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the *anti*-isomer $\delta$ 7.45 – 7.20 (m, 10H), 6.45 (d, $J = 8.5$ Hz, 1H), 6.39 (s, 1H), 5.99 (s, 1H), 5.92 (s, 1H), 4.75 (d, $J = 11.6$ Hz, 1H), 4.50 (d, $J = 11.6$ Hz, 1H), 4.43 (s, 2H), 2.94 (dd, $J = 16.0$, 5.5 Hz, 1H), 2.54 (dd, $J = 16.0$, 9.4 Hz, 1H); selected $^1$H NMR (CDCl$_3$) data for the *syn*-isomer $\delta$ 7.51 – 7.25 (m, 10H), 6.45 (d, $J = 8.5$ Hz, 1H), 6.39 (s, 1H), 5.99 (s, 1H), 5.92 (s, 1H), 4.43 (s, 2H), 3.94 (s, 3H), 3.81 (s, 3H), 3.68 – 3.32 (m, 4H), 3.51 (s, 3H), 2.93 (dd, $J = 16.0$, 6.9 Hz, 1H), 2.54 (dd, $J = 16.0$, 8.5 Hz, 1H).

![Epimeric mixture 17f](image2)

Epimeric mixture 18a: 65%; $R_f$ 0.54 (30% EtOAc/hexanes); selected $^1$H NMR (CDCl$_3$) data for the *anti*-isomer $\delta$ 7.50 – 7.19 (m, 10H), 4.65 (d, $J = 11.6$ Hz, 1H), 4.44 (d, $J = 11.6$ Hz, 1H), 3.69 – 3.62 (m, 1H), 3.48 (s, 3H), 3.35 – 3.23 (m, 1H), 3.06 (dd, $J = 16.0$, 6.0 Hz, 1H), 2.62 (dd, $J = 16.0$, 8.5 Hz, 1H), 1.07 (d, $J = 6.0$ Hz, 3H); selected $^1$H NMR (CDCl$_3$) data for the *syn*-isomer $\delta$ 7.50 – 7.19 (m, 10H), 4.60 (d, $J = 11.8$ Hz, 1H), 4.46 (d, $J = 11.8$ Hz, 1H), 3.82 – 3.74 (m, 1H), 3.57 (s, 3H), 3.45 – 3.39 (m, 1H), 2.93 (dd, $J = 16.0$, 6.6 Hz, 1H), 2.78 (dd, $J = 16.0$, 8.5 Hz, 1H), 1.06 (d, $J = 6.3$ Hz, 3H).

![Epimeric mixture 18a](image3)
Epimeric mixture 18d: 56%; \( R_f \) 0.61 (30% EtOAc/hexanes); selected \(^1\)H NMR (CDCl\(_3\)) data for the anti-isomer \( \delta 7.50 - 7.20 \) (m, 5H), \( 6.90 - 6.60 \) (m, 3H), 5.91 (s, 2H), 4.62 (d, \( J = 11.6 \) Hz, 1H), 4.41 (d, \( J = 11.6 \) Hz, 1H), 3.69 – 3.41 (m, 1H), 3.49 (s, 3H), 3.20 – 3.08 (m, 1H), 2.95 (dd, \( J = 16.0, 5.8 \) Hz, 1H), 2.52 (dd, \( J = 16.0, 8.8 \) Hz, 1H), 1.05 (d, \( J = 6.0 \) Hz, 3H); selected \(^1\)H NMR (CDCl\(_3\)) data for the syn-isomer \( \delta 7.50 - 7.20 \) (m, 5H), 6.90 – 6.60 (m, 3H), 5.91 (s, 2H), 4.60 (d, \( J = 11.8 \) Hz, 1H), 4.42 (d, \( J = 11.8 \) Hz, 1H), 3.84 (s, 3H), 3.80 – 3.67 (m, 1H), 3.59 (s, 3H), 3.32 – 3.21 (m, 1H), 2.84 (dd, \( J = 16.0, 6.3 \) Hz, 1H), 2.69 (dd, \( J = 16.0, 8.8 \) Hz, 1H), 1.05 (d, \( J = 6.3 \) Hz, 3H).

Epimeric mixture 18f: 54%; \( R_f \) 0.46 (30% EtOAc/hexanes); selected \(^1\)H NMR (CDCl\(_3\)) data for the anti-isomer \( \delta 7.45 - 7.21 \) (m, 5H), 6.45 (d, \( J = 8.0 \) Hz, 1H), 6.37 (s, 1H), 5.92 (s, 2H), 4.59 (d, \( J = 11.6 \) Hz, 1H), 4.41 (d, \( J = 11.6 \) Hz, 1H), 3.85 (s, 3H), 3.65 – 3.47 (m, 1H), 3.49 (s, 3H), 3.15 – 3.08 (m, 1H), 2.97 (dd, \( J = 16.0, 5.8 \) Hz, 1H), 2.52 (dd, \( J = 16.0, 8.5 \) Hz, 1H), 1.07 (d, \( J = 6.0 \) Hz, 3H); selected \(^1\)H NMR (CDCl\(_3\)) data for the syn-isomer \( \delta 7.45 - 7.21 \) (m, 5H), 6.45 (d, \( J = 8.0 \) Hz, 1H), 6.37 (s, 1H), 5.92 (s, 2H), 4.59 (d, \( J = 11.8 \) Hz, 1H), 4.40 (d, \( J = 11.8 \) Hz, 1H), 3.84 (s, 3H), 3.74 – 3.67 (m, 1H), 3.57 (s, 3H), 3.27 – 3.21 (m, 1H), 2.84 (dd, \( J = 16.0, 6.3 \) Hz, 1H), 2.67 (dd, \( J = 16.0, 8.5 \) Hz, 1H), 1.06 (d, \( J = 6.3 \) Hz, 3H).

3. References

\[ 1^H \]

\[ \text{RnCl} \] \[ \text{CEn} \] \[ \text{CO}_2\text{Me} \] + \[ \text{RnCl} \] \[ \text{CEn} \] \[ \text{CO}_2\text{Me} \]

9:1

14f

X: parts per Million: 1H