Supporting Information

For

Chiral Bis-pyridinium Salts as Novel Stereoselective Catalysts for the Metal-free Diels-Alder Cycloaddition of α,β-Unsaturated Aldehydes.

Andrea Genoni, Maurizio Benaglia,* Alessandra Puglisi and Sergio Rossi

Dipartimento di Chimica Organica e Industriale, Universita’ degli Studi di Milano – via Golgi 19, I-20133 Milano, Italy
Fax: +39 0250314159.
E-mail: maurizio.benaglia@unimi.it

Table of Contents:

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Methods</td>
<td>S2</td>
</tr>
<tr>
<td>Synthesis of catalyst 1</td>
<td>S2</td>
</tr>
<tr>
<td>Diels-Alder reaction: typical procedure</td>
<td>S2</td>
</tr>
<tr>
<td>Characterization of products</td>
<td>S3</td>
</tr>
<tr>
<td>NMR data</td>
<td>S5</td>
</tr>
<tr>
<td>HPLC data</td>
<td>S7</td>
</tr>
<tr>
<td>References</td>
<td>S8</td>
</tr>
</tbody>
</table>
**General Methods:**

All reactions were carried out in oven-dried glassware with magnetic stirring under nitrogen atmosphere, unless otherwise stated. Dry solvents were purchased and stored under nitrogen over molecular sieves (bottles with crown cap). Flash chromatography was carried out on silica gel (230-400 mesh). Reactions were monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F_{254} pre-coated glass plates (0.25 mm thickness) and visualized using UV light or phosphomolibdic acid. Proton NMR spectra were recorded on spectrometers operating at 200 and 300 MHz respectively. Proton chemical shifts are reported in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard (CDCl₃ δ = 7.26 ppm). ¹³C-NMR spectra were recorded on 300 MHz spectrometers operating at 75 MHz, with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard (CDCl₃, δ = 77.0 ppm). Optical rotations were obtained on a polarimeter at 589 nm using a 5 mL cell with a length of 1 dm. HPLC for e.e. determination was performed under the conditions reported below.

**Synthesis of catalyst 1:**

To a solution of chiral diamine (10 mmol) in dry toluene (20 mL) aromatic aldehyde (20.2 mmol) was added. The mixture was stirred in presence of molecular sieves for 40-72 h at 110°C. The reaction mixture was cooled to room temperature, filtered and the solvent was evaporated under vacuum to give the corresponding imines in yields >90%. Eventually the bis-imine may be crystallized from ethanol.

Catalyst 1 ¹H-NMR: 8.53 (m, 2H), 8.43 (s, 2H), 8.07 (d, 2H, J=8.7 Hz), 7.99 (d, 2H, J=8.2 Hz), 7.63 (t, 2H), 7.47-7.50 (m, 4H), 7.44 (t, 2H), 7.29-7.32 (m, 4H), 7.17 (d, 2H, J=8.7 Hz); ¹³C NMR: δ 162.5, 155.4, 150.6, 148.8, 137.6, 132.9, 130.3, 129.1, 127.8, 127.6, 127.1, 126.3, 126.2, 121.6, 119.9, 118.2.

**Diels-Alder reaction: typical procedure**

The catalysts were prepared by treating the diamine in DCM dry with the proper amount of acid and removing the solvent after 15 minutes stirring at 25°C; the salt was used without any further purification. To a stirring solution of the catalyst (0.03 mmol.) in 0.3 mL of CHCl₃ under inert atmosphere aldehyde (0.3 mmol.) was added; after 5 minutes cyclopentadiene (1.5 mmol.) was added and the reaction mixture was allowed to stir for 72 hours at 25°C. The reaction mixture was evaporated under reduced pressure and analyzed by NMR. The yield and diastereoisomeric ratio were then confirmed on the isolated product purified by flash chromatography on a short silica gel column with ethylacetate/hexaner mixtures as eluant. The e.e. were determined by HPLC on the alcohol obtained by NaBH₄ reduction of the cycloadducts (Chiralpak OJ-H column, hexane: isopropanol 7:3; flow rate 0.8 ml/min; λ 225 nm: tᵣ 12.6 min (endo-major), tᵣ 29.1 in (endo- minor) tᵣ 38.7 min (exo-major), tᵣ 51.8 min (exo-minor)).
Characterization of products

Synthesis of bis-imines catalysts:

Products 1, 2, 3, 4, 6, 7, 8, 9, 13 are known compounds. These known products and the following ones were prepared according to the procedure described for 1.

Yellow prisms; $[\alpha]_D^{25}-105 (C\ 4.0 \times 10^{-3} \ M, \ CHCl_3)$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta\ 8.54$ (brs, 2H), 8.48 (brs, 2H), 8.29 (s, 2H), 7.92 (d, J=8.7 Hz, 2H), 7.85 (d, J=8.1 Hz, 2H), 7.62 (d, J=7.8 Hz, 2H), 7.25-7.48 (m, 4H), 7.22 (dd, J=5.4, 12.4 Hz, 2H), 6.96-7.17 (m, 4H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta\ 157.2,\ 154.7,\ 151.6,\ 150.3,\ 147.8,\ 134.6,\ 133.5,\ 131.9,\ 129.4,\ 128.1,\ 127.0,\ 126.7,\ 126.6,\ 125.2,\ 123.5,\ 118.5.$

Synthesis of (1S, 2S, 3S, 4R)-3-phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde and (1R, 2S, 3S, 4S)-3-phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde:

This product is known$^{10}$ and was purified by flash column chromatography on silica gel with a 98:2 hexane/ethyl acetate mixture as eluant affording a mixture of endo and exo Diels-Alder adducts.

Data for endo:

$R_f = 0.42$ (hex/EtOAc 9:1 stained blue with phosphomolibdic acid)

$^1$H-NMR (300 MHz, CDCl$_3$): $\delta\ 9.61$ (d, J=2.2 Hz, 1H, CHO), 7.14-7.34 (m, 5H, Ph), 6.43 (dd, J=3.3, 5.6 Hz, 1H, CH=CH), 6.18 (dd, J=2.8, 5.7 Hz, 1H, CH=CH), 3.34 (brs, 1H, CHCH=CHCH),
3.14 (brs, 1H, CHCH=CHCH), 3.10 (d, J=4.8, 1H, CHPh), 2.99 (dd, J=2.7, 5.4, 1H, CHCHO), 1.82 (d, J=8.7, 1H, CHH), 1.61-1.64 (m, 1H, CHH).

Data for exo:

R_f = 0.42 (hex/EtOAc 9:1 stained blue with phosphomolibdic acid)

¹H-NMR (300 MHz, CDCl₃): δ 9.93 (d, J=2.0 Hz, 1H, CHO), 7.14-7.34 (m, 5H, Ph), 6.34 (dd, J=3.4, 5.5 Hz, 1H, CH=CH), 6.08 (dd, J=3.0, 5.5 Hz, 1H, CH=CH), 3.73 (t, J=3.8, 1H, CHCH=CHCH), 3.23 (m, 2H, CHCH=CHCH, CHPh), 2.60 (dd, J=1.5, 3.4, 1H, CHCHO), 1.61-1.64 (m, 2H, CHH, CHH).

Synthesis of ((1S, 2S, 3S, 4R) 3-phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol and ((1R, 2S, 3S, 4S)-3-phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol:

This product is known¹¹ and was injected into the HPLC without further purification.

Data of a mixture endo:exo:

¹H-NMR (300 MHz, CDCl₃): δ 7.18-7.31 (m, 10H), 6.34-6.41 (m, 2H), 6.15-6.20 (m, 1H), 5.93-5.98 (m, 1H), 3.86-3.94 (m, 1H), 3.59-3.70 (m, 3H), 3.39 (t, J=12.8 Hz, 1H), 3.04 (burs, 2H), 2.83-2.88 (m, 3H), 2.30-2.42 (m, 2H), 2.15-2.18 (m, 2H), 1.76-1.82 (d, J=8.9, 1H), 1.65-1.68 (d, J=8.7, 1H).

The enantiomeric excess was determined by chiral HPLC with Daicel Chiralcel OJ-H column [eluant: 7:3 hex/IPA; 0.8 mL/min flow rate, detection: 225 nm; t_R 12.6 min (endo-major), t_R 29.1 in (endo-minor) t_R 38.7 min (exo-major), t_R 51.8 min (exo-minor)
NMR spectra:
HPLC spectra:
References:

1) Telfer, Shane G.; Sato, Tomohiro; Harada, Takunori; Kuroda, Reiko; Lefebvre, Julie; Leznoff, Daniel B. Inorganic Chemistry 2004, 43(20), 6168-6176; Colombo, Federica; Benaglia, Maurizio; Orlandi, Simonetta; Usuelli, Fabio; Celentano, Giuseppe Journal of Organic Chemistry 2006, 71(5), 2064-2070

2) Deschamp, Julia; Olier, Clarisse; Schulz, Emmanuelle; Guillot, Regis; Hannedouche, Jerome; Collin, Jacqueline Advanced Synthesis & Catalysis 2010, 352(13), 2171-2176; Huang, Hanmin; Okuno, Tomoko; Tsuda, Kazuomi; Yoshimura, Masahiro; Kitamura, Masato Journal of the American Chemical Society 2006, 128(27), 8716-8717

3) Guizzetti, Stefania; Benaglia, Maurizio; Cozzi, Franco; Rossi, Sergio; Celentano, Giuseppe Chirality 2008, 21(1), 233-238 Lin, Jian Hua; Che, Chi Ming; Lai, Ting Fong; Poon, Chung Kwong; Cui, Yu Xin Journal of Chemical Communications 1991, 7, 468-470

4) Guizzetti, Stefania; Benaglia, Maurizio; Celentano, Giuseppe European Journal of Organic Chemistry 2009, 22, 3683-3687

5) Constant, Samuel; Tortoioli, Simone; Mueller, Jessica; Linder, David; Buron, Frederic; Lacour, Jerome Angewandte Chemie, 2007, 46(47), 8979-8982

6) Murphy, Andrew; Pace, Allyson; Stack, T. Daniel P. Organic Letters 2004, 6(18), 3119-3122

7) Trost, Barry M.; Andersen, Neil G. Journal of the American Chemical Society 2002, 124(48), 14320-14321

8) Ter Halle, Rob; Breheret, Alexandra; Schulz, Emmanuelle; Pinel, Catherine; Lemaire, Marc Tetrahedron: Asymmetry 1997, 8(13), 2101-2108

9) Suga, Hiroyuki; Ishimoto, Daisuke; Higuchi, Satoshi; Ohtsuka, Motoo; Arikawa, Tadashi; Tsuchida, Teruko; Kakehi, Akikazu; Baba, Toshihide Organic Letters 2007, 9(21), 4359-4362

10) Ahrendt, Kateri A.; Borths, Christopher J.; MacMillan, David W. C. Journal of the American Chemical Society 2000, 122(17), 4243-4244