Supporting Information

Lewis acid-catalyzed regio- and diastereoselective synthesis of spiroisoxazolines via one-pot sequential Knoevenagel condensation/1,3-dipolar cycloaddition reaction

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Materials and Methods.

Melting points were determined on a melting point apparatus and are uncorrected. IR spectra were taken with a Bomem FT-IR MB spectrometer. The NMR spectra were recorded on a BRUKER DRX-300AVANCE spectrometer. Mass spectra were recorded on an Agilent 5975C VL MSD with Tripe-Axis Detector operating at an ionization potential of 70 eV. Elemental analyses were performed using a Heraeus CHN–O–Rapid analyzer. All chemicals were purchased from Merck or Aldrich and were used without further purification.

The X-ray diffraction measurements were made with a STOE IPDS-II diffractometer with graphite-monochromated MoKa radiation. Cell constants and an orientation matrix for data collection were obtained by least-squares refinement of diffraction data from 6743 and 3408 unique reflections for 4g and 8b, respectively. Data were collected at a temperature of 298(2) K to a maximum 2q value of 51.988 and in a series of w scans in 18 oscillations and integrated using the Stoe X-AREA\textsuperscript{[1]} software package. The data were corrected for Lorentz and Polarizing effects. The structures were solved by direct methods and refined on F2 by full-matrix least-squares procedure. All hydrogen atoms were added at ideal positions and constrained to ride on their parent atoms, with Uiso(H)= 1.2Ueq. All refinements were performed by using the X-STEP32 crystallographic software package\textsuperscript{[2]} Complete crystallographic data for compound 4f and 6d has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC 1827670 and CCDC 1827669 for 4g and 8b, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
General procedure for the one-pot sequential synthesis of spiroisoxazolines
A mixture of aldehyde (1 mmol), C-H acid (oxindole, 1,3-indandione or 3H-pyrazol-3-one) (1 mmol), ZnCl$_2$ (10 mol%) and NaHCO$_3$ (1.5 mmol) in THF (4 mL) was stirred for 30 min at 45 °C. Then, dibromoformaldehyde (1 mmol) was added and stirred for 2.5 h. After completion of the reaction, the solvent was removed under vacuum and the crude mixture was washed with H$_2$O (10 mL). Then, the solid residue was crystallized from CH$_2$Cl$_2$/n-hexane (1:2) to afford the pure products.

**General procedure for the synthesis of spiroindene-isoazoles containing benzimidazole or benzothiazole** (14)

A mixture of arylidene compounds (1 mmol), dibromoformaldehyde (1 mmol), ZnCl$_2$ (10 mol%) and Na$_2$CO$_3$ (2 mmol) in THF (5 mL) was stirred at 45°C for 3 h. Then, 2-aminobenzimidazole (1 mmol) was added and stirred for 24 h. After completion, the solvent was removed under vacuum and the crude mixture was washed with hot H$_2$O (10 mL). Then, the solid residue was crystallized from CH$_2$Cl$_2$/n-hexane (1:2) to afford the pure products.

**General procedure for Suzuki reaction**

A mixture of phenylbromic acid (1.2 mmol), phenyl bromide (1.0 mmol), Pd(OAc)$_2$ (0.5 mol %), ligand (1 mol%) and K$_2$CO$_3$ (2 mmol) in H$_2$O-EtOH (3 mL, 1:1) was stirred at 60 °C for 20 min. After completion of the reaction, the catalyst was separated and the filtrate was extracted with ethyl acetate (2 × 5 ml). The organic solvents were removed under vacuum and the product 3 was purified by recrystallization.

**General procedure for synthesis of 2-arylbenzothiazoles** (20)
A 10-mL round-bottom flask was charged with benzothiazole (1 mmol), bromobenzenes (1 mmol), L3 (12 mol%), Ni(OAc)$_2$ (10 mol%), LiOt-Bu (2 mmol) and dry THF (5 mL). The mixture was stirred at reflux conditions for 24 h (TLC). Then, the mixture was cooled to ambient temperature and the solvent was evaporated under reduced pressure. Then, the mixture was diluted with EtOAc (10 mL), washed successively with water, and brine. The organic layer was dried over MgSO$_4$ and concentrated under reduced pressure. The residue was purified by thin-layer chromatography eluting with EtOAc/hexane (20:80, v/v) to afford

**References**


$^1$H NMR spectrum of compound 4a (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4a (DMSO, 75 MHz)
1H NMR spectrum of compound 4b (DMSO, 300 MHz)

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\text{\textsuperscript{13}C NMR spectrum of compound 4b (DMSO, 75 MHz)}
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$^1$H NMR spectrum of compound 4c (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4c (DMSO, 75 MHz)
$^1$H NMR spectrum of compound 4d (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4d (DMSO, 75 MHz)
$^1$H NMR spectrum of compound 4e (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4e (DMSO, 75 MHz)
$^1$H NMR spectrum of compound 4f (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4f (DMSO, 75 MHz)
$^1$H NMR spectrum of compound $4g$ (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound $4g$ (DMSO, 75 MHz)
$^{1}$H NMR spectrum of compound 4h (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4h (DMSO, 75 MHz)
$^1$H NMR spectrum of compound 4i (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4i (DMSO, 75 MHz)
$^{1}$H NMR spectrum of compound 4j (DMSO, 300 MHz)

$^{13}$C NMR spectrum of compound 4j (DMSO, 75 MHz)
$^1$H NMR spectrum of compound 7 (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 9a (CDCl$_3$, 75 MHz)

$^1$H NMR spectrum of compound 9b (CDCl$_3$, 300 MHz)
\(^{13}\)C NMR spectrum of compound 9b (CDCl\(_3\), 75 MHz)

\(^1\)H NMR spectrum of compound 9c (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 9e (DMSO, 75 MHz)

$^1$H NMR spectrum of compound 9d (CDCl$_3$, 300 MHz)
$^{13}$C NMR spectrum of compound 9d (DMSO, 75 MHz)

$^1$H NMR spectrum of compound 9e (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 9e (DMSO, 75 MHz)

$^1$H NMR spectrum of compound 11 (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 11 (DMSO, 75 MHz)

$^1$H NMR spectrum of compound 14a (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 14a (DMSO, 125 MHz)

$^1$H NMR spectrum of compound 14b (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 14b (DMSO, 75 MHz)

$^1$H NMR spectrum of compound 14c (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 14c (DMSO, 125 MHz)

$^1$H NMR spectrum of compound 14d (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 14d (DMSO, 75 MHz)

$^1$H NMR spectrum of compound 14e (DMSO, 300 MHz)
\(^{13}\)C NMR spectrum of compound 14e (DMSO, 75 MHz)

\(^{1}\)H NMR spectrum of compound 14f (DMSO, 300 MHz)
$^{13}$C NMR spectrum of compound 14f (DMSO, 125 MHz)

$^1$H NMR spectrum of compound 16a (CDCl$_3$, 300 MHz)
$^1$H NMR spectrum of compound 16b (CDCl$_3$, 300 MHz)

$^1$H NMR spectrum of compound 20a (CDCl$_3$, 300 MHz)
$^1$H NMR spectrum of compound 20b (CDCl$_3$, 300 MHz)

$^1$H NMR spectrum of compound 20c (DMSO, 300 MHz)
$^1$H NMR spectrum of compound 20d (CDCl$_3$, 300 MHz)

$^1$H NMR spectrum of compound 20e (DMSO, 300 MHz)
$^1$H NMR spectrum of compound 20f (DMSO, 300 MHz)

$^1$H NMR spectrum of compound 20g (DMSO, 300 MHz)