Supplementary Material

Stereoselective synthesis of megastigmatrien-3-one using catalytic olefin isomerization as key step

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1 General Information

The NMR spectra were recorded on Bruker AC-500 spectrometer (500 MHz for $^1$H NMR and 125 MHz for $^{13}$C NMR) with CDCl$_3$ as the solvent and TMS as internal reference. $^1$H NMR spectral data were reported as follows: chemical shift ($\delta$, ppm), multiplicity, integration, and coupling constant (Hz). $^{13}$C NMR spectral data were reported in terms of the chemical shift. The following abbreviations were used to indicate multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Low-resolution mass spectra were obtained on a Shimadzu LCMS-2010EV spectrometer in ESI mode and reported as m/z. High-resolution mass spectra (HRMS) were recorded on a Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS instrument. GC analysis was detected on an Agilent 8890B instrument. Melting points were obtained on a X-4 digital melting point apparatus without correction. Purification of products was accomplished by column chromatography packed with silica gel. Unless otherwise stated, all reagents were commercially purchased and used without further purification.

2 General Procedure

a) General Procedure for the synthesis of compound 2

\[
\begin{align*}
\text{3,5,5-trimethoxy-2-cyclohexen-1-one-4-carboxylic acid ethyl ester 1 (1.05 g, 5 mmol), Ethylene glycol (40 mmol, 3.09 mL), triethyl orthoformate (20 mmol, 3.32 mL), 4-methylbenzenesulfonic acid pyridine (0.5 mmol, 120.6 mg)} & \text{ in toluene (60 mL) , and the reaction vessel placed in an oil bath at 120 °C for 15 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford product 2.}
\end{align*}
\]

b) General Procedure for the synthesis of compound 3

\[
\begin{align*}
\text{7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylic acid ethyl ester 2 (4 mmol, 1.27 g) in dry THF (20 mL), and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with water and diluted with ethyl acetate. The layers were separated, and the aqueous layer was extracted with two additional portions of ethyl acetate. The combined organics were washed with brine before drying over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography on silica gel (eluent: PE:EA = 5: 1) to afford 3.}
\end{align*}
\]
c) **General Procedure for the synthesis of compound 4**

To a solution of oxalyl chloride (0.51 mL, 6 mmol) in 30 mL of CH₂Cl₂ at −78 °C was added DMSO (0.85 mL, 12 mmol) dropwise. After 5 min, a solution of 3a (4 mmol, 0.848 g) in 10 mL of CH₂Cl₂ was added, and stirring was continued at −78 °C for 15 min. Et₃N (37 mL, 264 mmol, 5 eq.) was then added, the cooling bath was removed, and stirring was continued. After 1 h, TLC analysis indicated complete consumption of the starting material and formation of the product. The reaction was quenched with saturated sodium bicarbonate and diluted with CH₂Cl₂. The layers were separated, and the aqueous layer was extracted with two additional portions of CH₂Cl₂. The combined organics were washed with brine before drying over anhydrous Na₂SO₄. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography on silica gel (eluent: PE:EA = 10: 1) to afford 4.

d) **General Procedure for the synthesis of compound 6**

In a Schlenk flask filled nitrogen the compound 4 (2 mmol, 0.42 g) in dry THF (10 mL) was carefully added Allyl magnesium bromide (4 mmol, 8 mL, 0.5 M in THF). The reaction mixture was stirring at 0 °C for 3 h. Then the residue was quenched with saturated NH₄Cl solution, extracted with ethyl acetate and dried on MgSO₄. After removal of the solvent under reduced pressure, the crude product put into a solution in 10 mL of THF followed by the addition of 36% sulfuric acid aqueous solution (4 mL) dropwise. The reaction mixture was stirring at at room temperature for 4 h. Then the residue was quenched with Saturated sodium bicarbonate aqueous solution, extracted with ethyl acetate and dried on MgSO₄. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography (eluent: PE:EA = 10: 1) to give 6.

e) **General Procedure for the synthesis of compound 7**

The cobalt catalyst (5 mol %), zinc powder (15 mol %) and zinc iodide (15 mol %) were combined under an atmosphere of nitrogen and suspended in CH₂Cl₂. Then compound 6 (0.95 g, 5 mmol) was added and the reaction mixture was stirred at room temperature until complete conversion of the starting material was observed. The reaction was quenched with saturated sodium bicarbonate and diluted with CH₂Cl₂. The layers were separated, and the aqueous layer was extracted with two additional portions of CH₂Cl₂. The combined organics were washed with brine before drying over
anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography on silica gel (eluent: PE:EA = 10: 1) to afford megastigmatrien-3-one 7.

Ratio of four isomers under r.t.

f) General Procedure for the synthesis of compound 8
To a cold solution (0 °C) of 7 (187.5 mg, 1 mmol) in dry dichloromethane (5 mL) was added m-chlirlperbenzoic acid (215.8 mg, 1.25 mmol) and the mixture was stirred at 0 °C for 2 h. The mixture was washed with a 1 % solution of NaOH and brine, dried over MgSO₄, and concentrated. The residue was added to a mixture of zinc power (326.7 mg) and acetic acid (1.5 mL) at room temperature. After the mixture was stirred for 2 h at room temperature, the precipitata was filtered off and washed with ether (10 mL). The filtrate was washed with a saturated solution of NaHCO₃ and brine, dried over MgSO₄, and then concentrated. Purification by silica-gel column chromatography (hexane-ether) afford 8 (65%).
3 $^1$H NMR and $^{13}$C NMR Spectra of All Compounds

Compound 1
Compound 2
Compound 3
Compound 4
Compound 5
Compound 6
Compound 7
Compound 8
4 HRMS of new compounds and significant compounds

HRMS of compound 1
HRMS of compound 2
HRMS of compound 3
HRMS of compound 4
HRMS of compound 5
HRMS of compound 6
HRMS of compound 7