Synthesis of (−)-mesembrine using the quaternary carbon-construction allylic substitution

Takuri Ozaki and Yuichi Kobayashi*

Department of Bioengineering, Tokyo Institute of Technology
Box B-52, Nagatsuta-cho 4259, Midori-ku, Yokohama 226-8501, Japan
ykobayas@bio.titech.ac.jp

Experimental and Spectral Data
References
HPLC analysis
$^1$H NMR and $^{13}$C NMR Spectra
**General Methods.** The $^1$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) spectra were measured in CDCl$_3$ using SiMe$_4$ (δ = 0 ppm), residual CHCl$_3$ (δ = 7.26 ppm), and the center line of CDCl$_3$ triplet (δ = 77.1 ppm) as internal standards, respectively.

7-[(tert-Butyldimethylsilyloxy)oxy]hept-4-yn-3-one (24)

![Chemical Structure](image)

To an ice-cold solution of 3-butyln-1-ol (23) (1.40 g, 20.0 mmol) in DMF (40 mL) were added imidazole (1.64 g, 24.0 mmol) and TBSCl (3.38 g, 22.4 mmol). The mixture was stirred at rt overnight, and diluted with saturated NH$_4$Cl and EtOAc with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over MgSO$_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford silyl ether (3.57 g, 97%) as a colorless oil: $R_f$ = 0.78 (hexane/EtOAc, 3:1). $^1$H NMR (300 MHz, CDCl$_3$) δ 0.08 (s, 6 H), 0.90 (s, 9 H), 1.96 (t, $J = 2.7$ Hz, 1 H), 2.41 (dt, $J = 7.2$, 2.7 Hz, 2 H), 3.75 (t, $J = 7.2$ Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ –5.2 (CH$_3$, +), 18.4 (C, –), 22.9 (CH$_2$, –), 25.9 (CH$_3$, +), 61.8 (CH$_2$, –), 69.4 (CH (propagyl), –), 81.6 (C, –). The $^1$H and $^{13}$C NMR spectra were consistent with those reported.$^81$

To a solution of silyl ether (875 mg, 4.75 mmol) in THF (40 mL) was added $n$-BuLi (1.55 M in hexane, 4.30 mL, 6.67 mmol) dropwise at –78 ºC. After 1 h at –78 ºC, $N$-methoxy-$N$-methylpropionamide (848 mg, 7.24 mmol) in THF (3 mL) was added to it dropwise. The mixture was stirred at –78 ºC to –30 ºC overnight, and diluted with saturated NH$_4$Cl and EtOAc with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over MgSO$_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford ynone 24 (1.07 g, 94%) as a colorless oil: $R_f$ = 0.72 (hexane/EtOAc, 3:1). $^1$H NMR (300 MHz, CDCl$_3$) δ 0.08 (s, 6 H), 0.90 (s, 9 H), 1.14 (t, $J = 7.4$ Hz, 3 H), 2.56 (q, $J = 7.4$ Hz, 2 H), 2.58 (t, $J = 6.9$ Hz, 2 H), 3.78 (t, $J = 6.9$ Hz, 2 H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ –5.3 (CH$_3$, +), 8.1 (CH$_3$, +), 18.3 (C,
\( - \), 23.4 \((\text{CH}_2, -)\), 25.9 \((\text{CH}_3, +)\), 38.8 \((\text{CH}_2, -)\), 60.9 \((\text{CH}_2, -)\), 81.4 \((\text{C}, -)\), 91.1 \((\text{C}, -)\), 188.7 \((\text{CO}, -)\). The \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectra were consistent with those reported.\(^{S2}\)

**References**


$^1$H NMR, CDCl$_3$, 300 MHz

APT, CDCl$_3$, 75 MHz
$^{1}H$ NMR, CDCl$_3$, 300 MHz

APT, CDCl$_3$, 75 MHz
$^{1}$H NMR, CDCl$_3$, 300 MHz

((S)-14)

APT, CDCl$_3$, 75 MHz

((S)-14)
$^1\text{H NMR, CDCl}_3, \text{300 MHz}$

$^1\text{H NMR, CDCl}_3, \text{300 MHz}$

$\text{APT, CDCl}_3, \text{75 MHz}$
\[^1\text{H NMR, CDCl}_3, 300 \text{ MHz}\]

\[^1\text{H NMR, CDCl}_3, 300 \text{ MHz}\]

\[^1\text{H NMR, CDCl}_3, 75 \text{ MHz}\]
$^{1}$H NMR, CDCl$_3$, 300 MHz

APT, CDCl$_3$, 75 MHz
$^1$H NMR, CDCl$_3$, 300 MHz

APT, CDCl$_3$, 75 MHz

S13