Electronic Supplementary Information

Approach to the functionalized cyclopentane core of marine prostanoids by applying a radical cyclization of \( \beta \)-disubstituted acrylates

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Contents

- Additional experimental procedures \hspace{1cm} S2
- Proposed radical cyclization transition structures \hspace{1cm} S3
- \( ^1 \text{H} \) and \( ^{13} \text{C} \) NMR spectra \hspace{1cm} S4

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t-Butyl(hex-5-ynloxy)dimethylsilane (SI-1)

To 5-hexyn-1-ol 11 (3.00 g, 30.5 mmol) in CH₂Cl₂ (60 mL) were added imidazole (2.18 g, 32.1 mmol) and TBS-Cl (4.60 g, 30.5 mmol) and the mixture was stirred at r.t. for 1 h. After diluting with H₂O (40 mL) the mixture was extracted with Et₂O (2 × 60 mL) and the combined organic layers were washed successively with H₂O (2 × 50 mL), dilute HCl (50 mL), dilute NaHCO₃ (50 mL) and brine (50 mL). The resultant organic layer was then dried (MgSO₄) and concentrated in vacuo to give the title compound SI-1 as a colourless oil (6.15 g, 95%) that was used without further purification. ¹H NMR (500 MHz, CDCl₃): δ = 0.05 (s, 6H, Si(Me)₂), 0.89 (s, 9H, Si'Bu), 1.54–1.65 (m, 4H, CH₂-2 and CH₂-3), 1.94 (t, J = 2.7 Hz, 1H, CH-6), 2.21 (td, J = 7.0, 2.7 Hz, 2H, CH₂-4), 3.63 (t, J = 6.1 Hz, 2H, CH₂-1); ¹³C NMR (125 MHz, CDCl₃): δ = 5.3, 18.2, 18.3, 25.0, 26.0, 31.8, 62.6, 68.2, 84.5.

The spectroscopic data (¹H and ¹³C NMR) were consistent with reported values.¹¹

Methyl-7-(t-utyldimethylsilyloxy)hept-2-ynoate (12)

Acetylene SI-1 (324 mg, 1.53 mmol) was dissolved in dry THF (6 mL) and the solution cooled to −65 °C. n-BuLi (732 µL, 1.83 mmol) was then added dropwise and the reaction allowed to stir for 40 min. Methyl chloroformate (154 µL, 1.99 mmol) was added dropwise and the reaction allowed to warm to r.t. over 2 h. The mixture was then diluted with H₂O (10 mL) and extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with brine (3 × 20 mL), dried (MgSO₄) and concentrated in vacuo. Flash column chromatography (EtOAc-PE, 1:9) yielded the title compound 12 (345 mg, 84%) as a colourless oil. Rᵣ = 0.36 (EtOAc-PE, 1:15); ¹H NMR (500 MHz, CDCl₃): δ = 0.04 (s, 6H, Si(Me)₂), 0.89 (s, 9H, Si'Bu), 1.60–1.69 (m, 4H, CH₂-5 and CH₂-6), 2.37 (t, J = 6.8 Hz, 2H, CH₂-4), 3.63 (t, J = 5.8 Hz, 2H, CH₂-7), 3.76 (s, 3H, CO₂Me).

The spectroscopic data (¹H NMR) were consistent with reported values.¹²

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Ketyl radical cyclization of β-disubstituted acrylate 23a

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\begin{align*}
\text{23a} & \quad \xrightarrow{\text{(TMS)3SiH, AIBN}} \quad \text{3,5-cis-26} \\
\text{23a} & \quad \xrightarrow{\text{3,5-trans-26}} \\
\end{align*}
\]

26 obtained in 94% yield as mixture of four diastereoisomers (35:25:20:20)
(Numbering used by analogy with corresponding 5-hexenyl radical)

Ketyl radical cyclization of β-disubstituted acrylate 29\textsuperscript{S3}

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\begin{align*}
\text{29} & \quad \xrightarrow{\text{Bu3SnH, AIBN}} \quad \text{30, chair-equatorial} \\
\text{29} & \quad \xrightarrow{\text{30, chair-equatorial}} \quad \text{2,5-trans-31} \\
\end{align*}
\]

2,5-trans-31 (58% yield; 2,5-cis not observed)
(Numbering used by analogy with corresponding 5-hexenyl radical)

$^{1}H$ NMR (500 MHz) spectrum of (E)-13b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of (E)-13b in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of (Z)-13b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of (Z)-13b in CDCl$_3$. 
\[ \text{PMBO} \quad \text{CO}_2\text{Me} \quad \text{OH} \]

\[ 14b \]

\(^1\text{H} \) NMR (500 MHz) spectrum of 14b in CDCl\(_3\).

\[ \text{PMBO} \quad \text{CO}_2\text{Me} \quad \text{OH} \]

\[ 14b \]

\(^{13}\text{C} \) NMR (125 MHz) spectrum of 14b in CDCl\(_3\).
$^1$H NMR (500 MHz) spectrum of 15b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 15b in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 18 in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 17b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 17b in CDCl$_3$. 
$^{1}$H NMR (500 MHz) spectrum of 16b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 16b in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 20 in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 20 in CDCl$_3$. 

S11
$^1$H NMR (500 MHz) spectrum of 21b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 21b in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 22b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 22b in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 23b in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 23b in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 21a in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 21a in CDCl$_3$. 

S15
$^1$H NMR (500 MHz) spectrum of 22a in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 22a in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 23a in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of 23a in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of SI-2 in CDCl$_3$.

$^{13}$C NMR (125 MHz) spectrum of SI-2 in CDCl$_3$. 
$^1$H NMR (500 MHz) spectrum of 26 in CDCl$_3$.

Partial $^1$H NMR (500 MHz) spectrum of 26 (4 diastereoisomers) showing OMe signals.